HEALTH & MEDICAL CASE STUDIES

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DR. TRANUM KAUR; ALICIA HIGGISON; ANGELA AWADA; ANIZA AUGNESH MRONG; AFNAN BINTE LIAQUAT; AND WEI LIU

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This “Health & Medical Case studies” is an online learning tool for professionals and students of any science discipline. This OER contains clinical cases ranging from renal diseases to hepatology to hematology to infertility to endocrinology to COVID-19.

With the help of PEARL grant funding, Dr. Tranum Kaur from the Department of Chemistry & Biochemistry, and Alicia Higgison from the Office of Open Learning, University of Windsor paired up with chemistry/biochemistry graduate students, Angela Awada, Aniza Augnesh Mrong, Afnan Binte Liaquat and Wei Liu; compiling real-world clinical scenarios from multiple sources. We hope this pressbook can be utilized by any science faculty for supplementing their teaching and learning.

This online learning tool provides clinical biochemistry case studies involving COVID-19, myocardial infractions, genetic bleeding disorders, and cancer, alongside various disease symptoms from a diverse group of patients.

Authors

Dr. Tranum Kaur

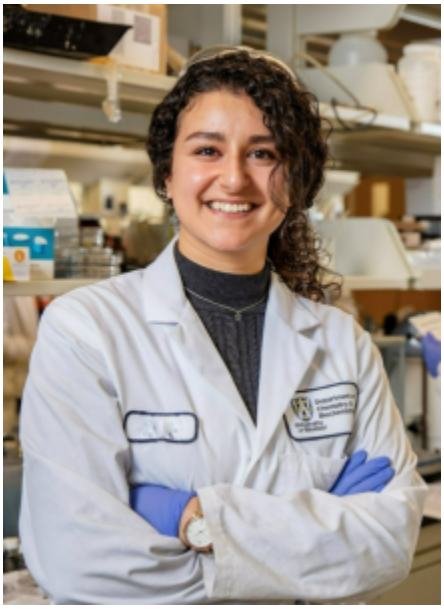
As a university faculty, **Dr. Tranum Kaur** has over 13 years of teaching experience in teaching undergraduate and graduate students. Dr. Kaur is currently associated with the Master of Medical Biotechnology program at the Department of Chemistry and Biochemistry, University of Windsor, ON, Canada. She has designed, developed, and delivered several new courses and promoted active pedagogical learning practices, facilitated discussion forums, case-based team presentations, and clicker-based evaluation quizzes. Tranum is passionate in advancing equity, inclusivity and diversity on campus and beyond. Dr. Kaur is

recipient of several prestigious awards including Dean of Science Recognition (2015), Roger Thibert Teaching Excellence (2017), and Excellence in Mentoring Award (2018).

Alicia Higgison

Alicia Higgison is an alumnus of the University of Windsor, with a B.A. Honours in Political Science, and was elected as a Trustee with the Greater Essex County District School Board in 2018. Alicia works in the University of Windsor's Office of Open Learning, championing innovations in open and online teaching and learning since 2013. With equal love for both writing & digital citizenship, Alicia has built on her blogging and social media background to administer UWindsor's Wordpress ePortfolio growth, providing workshops, training, and support. Bridging the gap between her political science roots and the opportunities at the edges of technology-enhanced teaching and learning, Alicia champions digital storytelling, reflective writing and taking charge of your online brand and footprint.

Angela Awada



Angela Awada is a PhD student working towards designing semiconductors for novel applications in the Rondeau-Gagne Research Group in the department of Chemistry and Biochemistry at the University of Windsor, ON, Canada. She has attained her Bachelor of Science in Biology and Biochemistry and Master of Science in Chemistry and Biochemistry working on fluorescent sensors for the detection of micronutrients. She is our team's research coordinator for the PEARLS Grant Project.

Aniza Augnesh Mrong

Aniza Augnesh Mrong is a is a recent graduate from Medical Biotechnology Master's student at the University of Windsor, ON, Canada. As a graduate student, she is enthusiastic about building a foundation of the theoretical concepts and practical knowledge on laboratory technique experiences used in medical

biotechnology industries. With her previous medical degree (MBBS) from the Sir Salimullah Medical College, Dhaka, Bangladesh and experience as a physician, she is always eager to apply and correlate the knowledge in related Biotechnology and Pharmaceutical industries. Her knowledge serves her imperative role as a research assistant for the PEARLS Grant Project.

Afnan Binte Liaquat

Afnan Binte Liaquat, is a graduate from the Master of Medical Biotechnology program at the University of Windsor, ON, Canada. She is highly motivated with a strong understanding of various laboratory techniques and protocol. Afnan has also attained a Bachelor of Medicine and Bachelor of Surgery (MBBS) from the University of Dhaka, Dhaka, Bangladesh. She has over two years of experience in facilitating student learning through demonstration, group work, projects, and assessment of student progress. Coming from a rich background in patient management, clinical cases, and teaching experience at the Delta Medical College, makes her a valuable research assistant in the selection of clinical cases, questionnaire prep and terminology organization for the PEARLS Grant Project.

Wei Liu

Wei Liu, a Medical Biotechnology Master's student at the University of Windsor, ON, Canada. He obtained his previous medical degree (Bachelor in Medicine) from North Sichuan Medical College, Sichuan, China and practiced for 10 years as a physician, radiologist and technician in Beijing. He also worked as a part of Picture Archiving and Communications System (PACS) system operation and maintenance engineer, also he was the coordinator between PACS service company and hospital department. He was excellent trained on problem solving, team work, as well as in medicine and diagnostic imaging area. As a graduate student now, he can easily combined his medical background to Biotechnology and Pharmaceutical industries. All of these characteristics and experiences made him serve his role as a research assistant focusing on research finding, copyright issues, html web design and IT problems in this PEARLS Grant Project.

Acknowledgement

- Special thanks to **Dave Johnston** from Leddy Library for his guidance to avoid copyright issues.
- Special thanks to **Nobuko Fujita** from Office of Open Learning for her instructions of Pressbook.
- Special thanks to **Hormoz Selahvarzi** who is a graduate student from the Class of 2021 MMB Program for his contribution to the cover design.

PART I

CARDIOLOGY CASE STUDIES

The cardiovascular system is the body's circulatory system. It comprises the heart and blood vessels (arteries, veins, and capillaries). This system maintains the internal homeostasis, supplies oxygen and nutrients to every tissue of the body in return for carrying back carbon dioxide to the lungs.

Cardiovascular diseases

1. Hypertension
2. Angina Pectoris
3. Myocardial Infarction
4. Heart Failure
5. Arrhythmias
6. Valve disease
7. Congenital heart diseases etc.

Common signs snd symptoms

1. Chest pain
2. Chest compression and discomfort
3. Fainting
4. Dizziness
5. Sweating
6. Fatigue
7. Shortness of breath
8. Edema
9. Irregular heartbeat etc.

Cardiovascular Investigations

1. Electrocardiogram or ECG/EKG
2. Echocardiogram
3. Holter monitoring
4. Exercise tolerance test or ETT

5. Cardiac catheterization
6. Cardiac MRI
7. Cardiac CT scan.

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1.

CASE 1-2013: A 72-YEAR-OLD FEMALE WITH TETRALOGY OF FALLOT AND INCREASING DYSPNEA

A 72-year-old woman with an uncorrected tetralogy of Fallot presenting with possible pulmonary endocarditis: a case report. Journal Of Medical Case Reports, 7(1). 2013. doi: 10.1186/1752-1947-7-150

Sousa, P., Santos, W., Marques, N., Cordeiro, P., Ferrinha, R., & Pereira, S. et al.

Case Summary [1]

A 72-year-old Caucasian female with complaints of dyspnea was admitted to the hospital with symptoms of fever and heart failure. The patient has a history of controlled ***hypertension*** *and healthy pregnancy. Prior to this hospital admission, she had started treatment of dental caries and tooth extraction with the use of prophylactic antibiotics. Physicians had conducted cardiac magnetic resonance imaging, a transthoracic echocardiogram, and laboratory investigations.*

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://ecampusontario.pressbooks.pub/clinicalcases/?p=53#audio-53-1

Clinical History [1]

Learning Objectives

- Investigating the clinical history of the patient and selecting appropriate examinations for the diagnosis of tetralogy of Fallot (TOF).
- Understanding the criteria for possible diagnosis and identifying those presented in the patient.
- Familiarizing and defining new medical terminology associated with the disorder.
- Extrapolating key lifestyle factors that have contributed to other diseases.

- Age: 72 years old
- Sex: Female
- Ethnicity: Caucasian

Medical History [1]

- Controlled hypertension
- Had **class II NYHA dyspnea**
- ~1 year prior to admission to hospital, started treatment of dental caries and tooth extraction was carried out under **antibiotic prophylaxis**.

Symptoms [1]

- Recurrent attack of persistent vespertine low-grade fever for 5 months.
- Weight loss and asthenia for same duration.
- Gradually dyspnea (class III NYHA – Comfortable at rest, limitations in physical activities and <ordinary activities cause palpitation, dyspnea and fatigue.)

Examinations (Clinical Assays/Tests/Imaging) [1]

Physical Examination [1]

- Slight peripheral cyanosis (blue extremities due to oxygen-poor blood)

- Finger clubbing
- Oxygen saturation of 91%
- Pulse rate 95 beats per minute
- Blood pressure of 149/70 mmHg

Cardiac Examinations [1]

- Single second heart sound.
- A systolic thrill and loud **systolic ejection murmur** (grade IV – associated with thrill and easily auditable) at the base of her heart.

Blood Investigations [1]

- Blood results showed leukocytosis (WBCs: 17, 700), elevation of C-reactive (inflammatory marker) protein with high sedimentation rate (indication of high inflammatory disease) and rheumatoid factor (RF – immune proteins that attack healthy tissues in body) and mild anemia (hemoglobin 11.7 g/L and hematocrit 0.35 L/L).
- No vascular or immunological phenomena (except RF) were detected.
- All blood cultures were negative inclusively for atypical organisms.
- Serology tests were negative.

Electrocardiogram [1]

- Showed normal sinus rhythm (normal and healthy impulses of the heart) with first degree atrioventricular block (slow conduction of atrioventricular node) and incomplete right bundle branch block (delay in pulse electrical pathway to conduct heart beat).

Cardiac Magnetic Resonance Imaging (MRI) [1]

- Revealed a large subaortic **VSD**, diameter of 26 mm and bidirectional flow (QP:QS = 0.9)
- An overriding of the aorta over the septum ≤50% (abnormal positions of aorta above VSD)
- A marked hypertrophy (thickness) of the right ventricle (RV) with **subpulmonary stenosis** (blockage due to dense muscle fibers) (max. gradient of 31 mmHg)
- Moderate pulmonary regurgitation (leaky pulmonary valve).
- A dilation of the pulmonary artery and its branches.
- A nondilated left ventricle with preserved systolic function.
- No patent ductus arteriosus (a condition where ductus arteriosus fails to close at birth) was present.

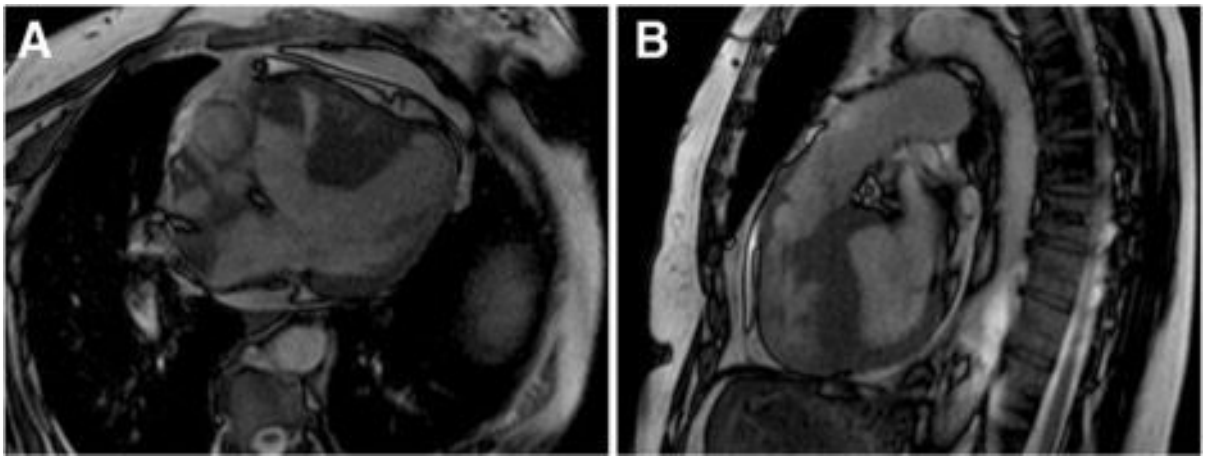

Figure 1: Cardiac magnetic resonance imaging revealing condition of tetralogy of Fallot. "A: Ventricular septal defect and overriding aorta over the septum. B: Right ventricular hypertrophy and subpulmonary stenosis." [1]

Transthoracic Echocardiography (TTE) [1]

- Showed the components of **TOF** and an echo dense, irregular and mobile mass, 10 mm long and 3mm wide, adherent and downstream to the pulmonary valve suggestive of vegetation (mass due to bacteria growth on a heart valve) without associated regurgitation (leaking of heart valve).
- Thus, she was hospitalized for suspected **infective endocarditis**.
- After 4 weeks of antibiotic therapy, no images suggestive of vegetation were detected on TTE (Figure 4).

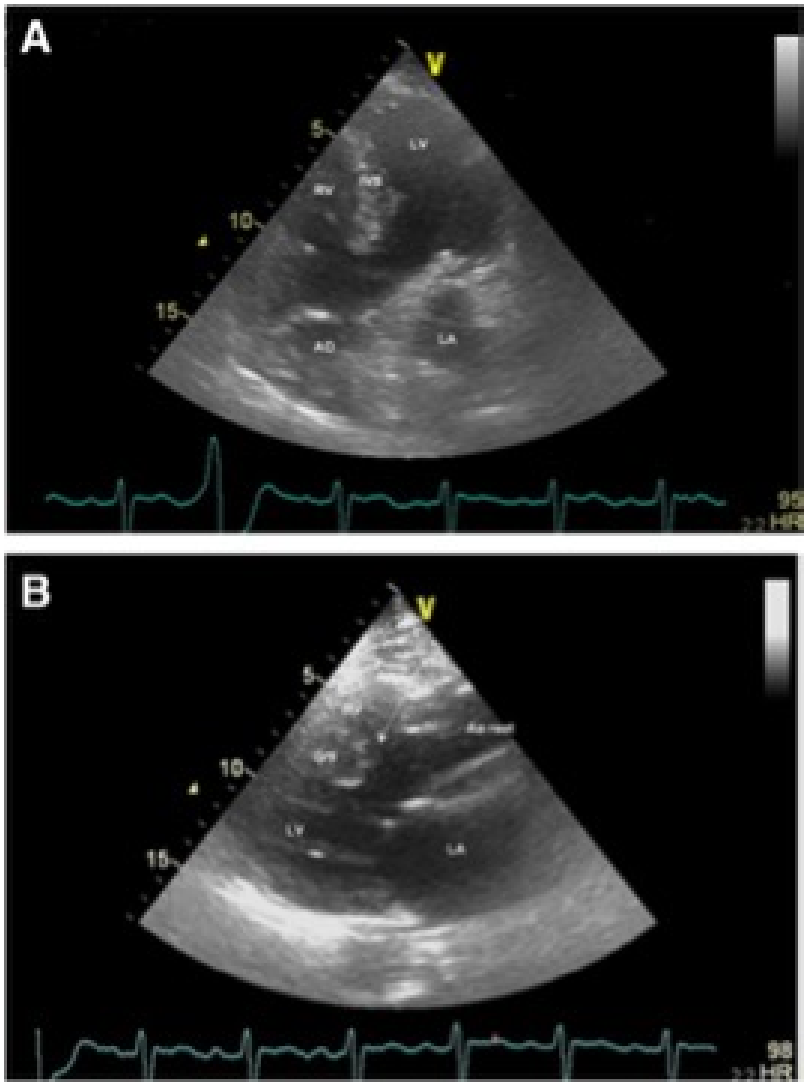

Figure 2: Tetralogy of Fallot diagnosis supported using transthoracic echocardiogram. "A: Five chamber view with the presence of the ventricular septal defect (VSD) and the overriding aorta over the septum. B: Parasternal long axis view revealing the VSD, the overriding of the aorta over the septum and also the right ventricle (RV) hypertrophy. AO, aorta; IVS, interventricular septum; LA, left atrium; LV, left ventricle." [1]

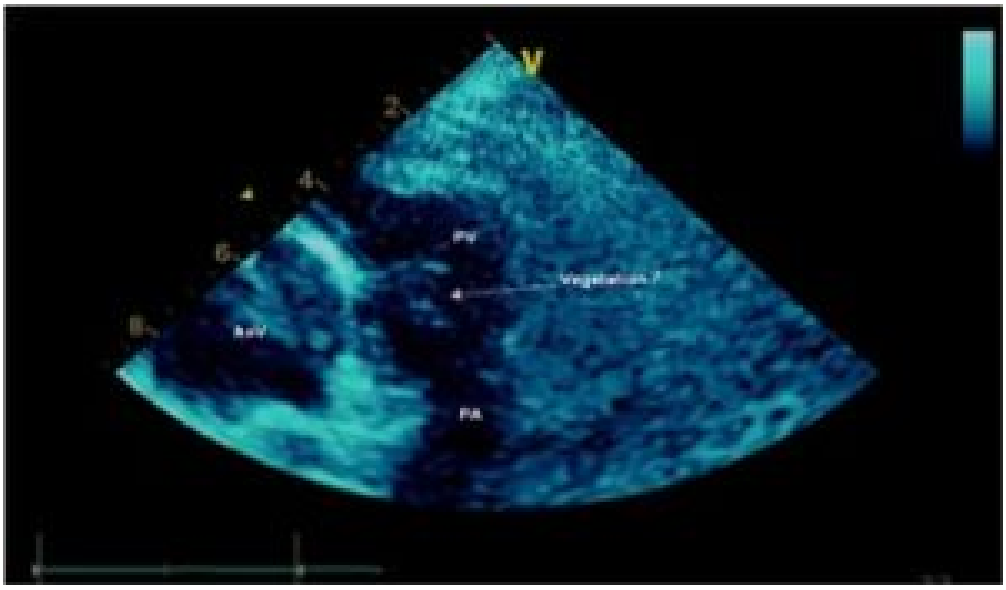

Figure 3: Suggestive vegetation in pulmonary valve due to erratic structure seen through transthoracic echocardiogram. "AoV, aortic valve; PA, pulmonary artery; PV, pulmonary valve."[1]

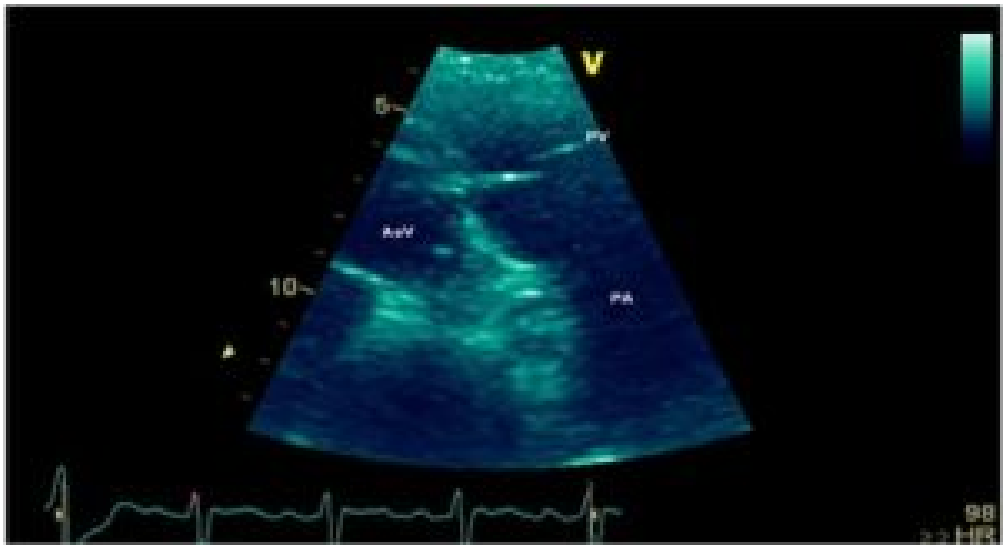

Figure 4: Pulmonary valve at discharge using transthoracic echocardiogram, 4 weeks after empiric antibiotherapy.[1]

Transesophageal Echocardiography (TEE) [1]

- Was not able to confirm or exclude the presence of pulmonary vegetation given the complex heart anatomy.

Computed Tomography Images [1]

- Revealed no signs of cerebral, thoracic, or abdominal embolization.

Question & Answers Leading to Diagnosis:

Question 1: The patient's clinical history includes a tooth extraction, recurrent fever and dyspnea, together what could be a possible diagnosis for this patient?

Question 2: Between the physical and imaging examinations, what results would support this patient's tetralogy of Fallot disease, does she meet all the criteria for this diagnosis?

Question 3: In the TTE, vegetations were apparent in the pulmonary valve, how would this support the previously suggested diagnosis?

** For answers please check the next chapter.

Medical terminology/Abbreviations:

- Antibiotic prophylaxis – antibiotic usage before surgery or procedure in order to prevent bacterial infection [6]
- Class II NYHA dyspnea – Mild symptoms of shortness of breath [1]
- Hypertension – A condition where blood vessels persistently have raised pressure [5]
- Hypoxia – A condition where the body or an area of the body is deprived of adequate oxygen in the tissues [8]
- Infective endocarditis – Inflammation of the heart that is caused by a fungal or bacterial infection of the heart valves or the inner lining of the heart [4]

- Pulmonary stenosis/outflow – Associated with structurally abnormal or immunocompromised states of the heart [3]
- Subpulmonary stenosis – A condition when there is blockage below the pulmonary valve due to too much muscle (muscular bundles) [9]
- Systolic ejection murmur – It is turbulent blood flow by the obstruction across semilunar valves, arteries, and outflow tracts [7]
- TOF – Tetralogy of Fallot, a form of cyanotic congenital heart disease [1]
- Transesophageal echocardiography – specific type of echocardiogram to look more closely at the heart to examine potential blood clots [10]
- Ventricular septal defect (VSD) – a hole in the wall (septum) that separates the lower chambers (ventricles) of the heart, this is a birth defect of the heart [2]

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Further Reading

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2.

CASE 1-2013: ANSWERS TO THE QUESTIONS

Answer to Question 1: The patient's recent tooth extraction proposes a potential bacterial infection as dental procedures have been reported to expose bacteria into the bloodstream through bleeding gums. [11] This can and has been shown to affect other parts of the body. The recurrent fever and dyspnea are symptoms of commensal bacteria in infective endocarditis. This infection affects endothelial surfaces of the heart but most notably for this patient, the valves. [11]

Answer to Question 2: The physical criteria that often support the diagnosis of tetralogy of Fallot include blue lips, mouths, fingertips and toenails due to a lack of oxygen, dyspnea, heart murmur, and the enlargement of fingers and toes (clubbing).15 Upon physical examination the patient experienced all of these symptoms, listed below. [1]

Physical examinations [1]

- Finger clubbing
- Cyanosis
- Single second heart sound
- Systolic thrill
- Loud systolic ejection murmur.

Four heart defects that make up the characteristics of tetralogy of Fallot (TOF) also include right ventricular hypertrophy – an enlargement of the right ventricle, the displacement of the aorta – causing blood flow from both right and left ventricle (overriding), ventricular septal defect (VSD) – a hole in the septum causing oxygen-poor blood from the right ventricle to mix with the oxygen-rich blood from the left

ventricle, and finally, the disturbed outflow of blood from the right ventricle to the lung, known as pulmonary stenosis. [15] In this case study, the patient shows all of the four criteria for TOF.

Imaging: Cardiac MRI [1]

- Subaortic VSD (figure 1)
- Overriding of aorta over septum ≤50% (figure 1)
- Marked hypertrophy of right ventricle (figure 1)
- Subpulmonary stenosis (figure 1)

Answer to Question 3: Vegetation in the pulmonary valve would suggest this patient has a rare disease of pulmonary infective endocarditis.12 A rare infection that has been shown to be due to central venous catheters, alcoholism and dental extractions. [12]

The imaging of the transthoracic echocardiography (TTE) showed the components of tetralogy of Fallot (TOF) – a heart birth defect affecting the normal blood flow in the heart. [1]

- A mobile mass (figure 2A) was adherent and downstream to the pulmonary valve, this was suggestive of vegetation (mass due to bacterial growth on a heart valve) without associated regurgitation (leaking of heart valve). This would support the previously suggested diagnosis of infective endocarditis due to lab investigations reporting high C-reactive protein – an inflammatory marker due to the inflamed pulmonary valve. [13] Negative blood cultures suggest it's unlikely the patient has a blood infection. [14]

Diagnosis [1]

- Uncorrected tetralogy of Fallot with suspected pulmonary endocarditis.

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3.

CASE 2-2021: A 54-YEAR-OLD MALE WITH CHEST PAIN

Clinical judgement in chest pain: a case report. Journal Of Medical Case Reports, 15(1). doi: 10.1186/s13256-021-02666-z

Goel, M., Dhillon, S., Kumar, S., & Tegeltija, V.

Case Summary [1]

A 54-year-old Caucasian male is admitted to the emergency department with chest pain. The patient has a history of tobacco smoking and gastroesophageal reflux (GERD). There was no family history of cardiac events. An asymptomatic ***electrocardiogram (ECG) stress test*** *was conducted. Cardiac catheterization and coronary computed tomography angiography (CCTA) would assist in diagnosing this patient.*

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Learning Objectives

- Investigating the clinical history of the patient and selecting appropriate examinations to diagnose this cardiological disease.
- Interpreting the patient's examinations to propose the appropriate diagnosis.
- Familiarizing and defining new medical terminology associated with cardiac disease.
- Extrapolating key lifestyle factors that have contributed to the cardiac disease and treatment measure that needs to be put in place.

Clinical History [1]

- Age: 54 years old
- Sex: Male
- Ethnicity: Caucasian

Medical History [1]

- History of tobacco smoking.
- No significant family history of cardiac events.
- BMI 29.

Symptoms [1]

- Three weeks of intermediate chest pain, radiating to his left arm and jaw.

Examinations (Clinical Assays/Tests/Imaging) [1]

Physical Examination [1]

- Blood pressure of 139/85 mmHg.
- Heart rate of 81 beats per minute.
- The intermediate pretest probability of**CAD (coronary artery disease)** is based on age and sex.

Electrocardiogram (EKG) [1]

- No ischemic changes, no left ventricular hypertrophy or left bundle branch block.

Laboratory Investigations [1]

- **Serial troponin enzyme** < 0.010 ng/mL (normal range: <0.04).[6]
- Lipid panel showed:
  - Total cholesterol: 235 mg/dL (normal range: < 200 mg/dL).[5]
  - **Triglycerides**: 408 (normal range: <149 mg/dL), HDL: 26 (normal range: < 40 mg/dL) and LDL could not be calculated (normal range: <100 mg/dL).[5]

Electrocardiogram (EKG) Stress Test [1]

- Patient achieved 95% of maximum predicted heart rate.
- 10 **METs (metabolic equivalents)** of exercise with normalization of **T wave** (ventricular repolarization) inversions were seen in **leads V2 (right ventricle), V3(septum) and V4 (septum)**at rest.[8]
  - Led to maximum asymptomatic stress test results.
    - Intermediate probability of ischemia.
- Showed normal left ventricular function with no wall motion or significant valvular abnormalities.

Echocardiogram[1]

- Normal left ventricular function and no significant valvular or wall motion abnormalities.

Coronary Computed Tomography Angiography (CCTA) [1]

- Showed approximate 70% **stenosis** (narrowing) of origin of the **left anterior descending artery (LAD)** and **noncalcified plaque** with an approximate length of 4 mm (figure 1, yellow lines).
  - Approximate 40-50% stenosis of proximal **ramus intermedius** (variant coronary artery) branch secondary to mixed calcified and **noncalcified plaque** and scattered noncalcified and calcified plaque along obtuse and **circumflex marginal branches** (branches from the main artery) with **luminal diameter stenosis** (diameter of permissible blood flow) of approximately 30-40%.[12]

Figure 1: Imaging from the coronary computed tomography angiography showing 70% stenosis of "the origin of the left anterior descending artery to secondary to non-calcified plaque extending over a length of approximately 4 mm" (yellow lines).[1]

Fractional Flow Reserve-Computed Tomography (FFR-CT) [1]

- Results showed a high likelihood of flow-limiting stenosis, less than 0.5 secondary to significant stenosis at LAD origin, with a low likelihood of flow-limiting stenosis in **ramus intermedius** (variant main coronary artery), right coronary arteries, and **left circumflex** (branch off left coronary artery).

Cardiac Catheterization [1]

- Showed 95% stenotic lesion of LAD with **partial perfusion (TIMI grade 2 flow)** –penetration without perfusion (incomplete filing of distal coronary bed).[7]
  - This would give rise to **diagonal 1** (a branch from the left anterior descending artery), with an ostial and proximal (narrowing of the ostium) 70% stenosis.
  - "**Ramus intermedius** (variant coronary artery) with proximal 70% segmental stenosis"
  - "Circumflex, nondominant vessel – a mild disease in proximal-distal segments – giving rise to

obtuse marginal 1 (on or close to the left obtuse margin of the heart) with proximal 70% stenosis."[16]

Question & Answers Leading to Diagnosis:

Question 1: Based on the patient's complaint of recurrent chest pains, EKG and serial troponin test, what could be the possible diagnosis?

Question 2: What investigations could be suggested to confirm this patient's diagnosis?

Question 3: In order to characterize further risk stratification for this patient, what other investigations could be done? How would you classify this patient on the TIMI scale?

** For answers please check the next chapter.

Medical terminology/Abbreviations:

- Bypass graft surgery – Procedure to treat coronary artery disease due to a buildup of fat in the walls of the arteries.[2]
- Cardiothoracic surgery – Field of medicine involving surgical treatment of organs within the thoracic cavity.[3]
- Circumflex marginal branches (obtuse marginal branches) – Arteries that curve to the left of the heart that branch from the circumflex arteries to supply the left ventricle.[4]
- Coronary artery bypass grafting (CABG) – Procedure to treat coronary heart disease from the narrowing of arteries.[14]
- Coronary artery disease (CAD) – Narrowing of coronary arteries due to plaque build-up.[14]
- Coronary computed tomography angiography (CCTA) – Imaging test used to determine plaque build-up in coronary arteries.[15]

- Diagonal 1 – Branches of the left anterior descending coronary artery that supply the left ventricle.[16]
- Electrocardiogram (ECG) stress test – Method used to record heart's blood pressure, electrical activity, and rate under physical exercise conditions.[17]
- Flow-limiting stenosis (and values) – "Lesion with a diameter narrowing exceeding 50%".[18]
- Fractional flow reserve computed tomography (FFR-CT) – Ratio of maximum flow between a stenotic artery to a maximum blood flow of a normal artery of the same type.[19]
- Gastroesophageal reflux disease (GERD) – The backflow of stomach acid between the stomach and the mouth through the esophagus.[20]
- HDL (high-density lipoprotein) – "Good" cholesterol is responsible for carrying absorbed cholesterol to the liver in order to remove it from the body.[21]
- LDL (low-density lipoprotein) – "Bad" cholesterol as an accumulation of this cholesterol leads to plaque build-up in arteries.[22]
- Leads V2, V3, and V4 – Electrodes that are used to monitor the heart during an electrocardiogram, V2 represents the right ventricle, V3 and V4 represent the septum.[23]
- Left anterior descending artery (LAD) – Artery which runs anterior to the interventricular septum and is the largest coronary artery.[24]
- Left circumflex – Branch off the left coronary artery.[25]
- Luminal diameter stenosis – Diameter of permissible blood flow.[12]
- METs – Metabolic equivalents, oxygen consumed while at rest.[26]
- Noncalcified plaque – Refers to plaque buildup that may be reversible in the arteries and risk of myocardial infractions.[27]
- Obtuse marginal 1 – Located on or close to left obtuse margin of the heart.[16]
- Partial perfusion (TIMI grade 2 flow) – Slow or delayed complete filling of distal coronary bed.[13]
- Ramus intermedius – Variant coronary artery.[16]
- Right coronary artery – One of the two main coronary blood vessels supplying blood to the right atrium, right ventricle, and sinoatrial and atrioventricular nodes – responsible for the heart's natural rhythm.[28]
- Serial troponin enzyme – Enzymes used to measure the potential evidence of a myocardial infraction.[29]
- Stenosis – In this case study, it represents the narrowing of blood flow and passage diameter.[1]
- TIMI grade flow – Method used for assessing coronary artery flow in acute coronary syndromes, below is the grading scale.[13]
- T wave – Ventricular repolarization during an electrocardiogram stress test.[1]
- Triglycerides – Fat type found within the blood.[30]

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Further Reading

4.

CASE 2-2021: ANSWERS TO THE QUESTIONS

Answer to Question 1: The patient's symptoms of radiating chest pain to the left arm, T wave inversion in the EKG, and normal troponin levels could propose a diagnosis of acute ischemia.[9] It's important to note this patient also has high cholesterol levels which could contribute to this diagnosis (total cholesterol: 235 mg/dL).[1] If this were to be a myocardial infarction, we'd expect higher troponin levels.10 This raises the question of when the serial troponin tests were conducted, as levels may have stabilized long after a potential myocardial infarction.

Answer to Question 2: Investigations that could be conducted to confirm this patient's diagnosis would be an echocardiogram, and a coronary computed tomography angiography (CCTA).[1] An echocardiogram is the most common procedural test to conduct when investigating coronary artery diseases in patients. This allows physicians to observe patients at intermediate pretest risk, who can exercise and have interpretable echocardiogram tests to conduct EKG stress tests.[1] A CCTA allows for anatomical testing, using this technique can reveal indeterminate information from EKG stress tests and potential plaque buildup in the coronary arteries and blood vessels supplying the heart.[1,11] In regards to this case study, this imaging revealed that the patient was experiencing 70% stenosis of the origin of the left anterior descending artery (LAD) and has approximately 4 mm of non-calcified plaque buildup.[1]

Answer to Question 3: Other investigations that can be used to characterize the risk stratification for this patient would be CCTA, fractional flow reverse computed tomography (FFR-TA), and cardiac catheterization. The CCTA revealed 70% stenosis of the LAD and non-calcified plaque buildup, while also revealing 40-50% stenosis of proximal ramus intermedius branch (variant coronary artery) secondary to mixed calcified and noncalcified plaque. With scattered noncalcified and calcified plaque along obtuse and circumflex marginal branches with luminal diameter stenosis of approximately 30-40%. FFR-TA would support the high likelihood of flow-limiting stenosis conditions.[1] The cardiac catheterization procedure would reveal that this patient was experiencing a 95% stenosis lesion of the LAD and **TIMI (Thrombolysis in Myocardial Infarction)** grade 2 blood flow – indicating incomplete filling of the distal coronary bed.1Altogether, diagnosing this patient with coronary heart disease.

- TIMI (Thrombolysis in Myocardial Infarction) is a method used for assessing coronary artery flow in acute coronary syndromes, below is the grading scale[13]:
    - Grade 0 – No flow
    - Grade 1 – Penetration without perfusion
    - Grade 2 – Partial perfusion
    - Grade 3 – Complete perfusion

Diagnosis [1]

- Coronary artery disease.

Treatment [1]

- Coronary artery bypass grafting (CABG).

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5.

CASE 3-2020: A 42-YEAR-OLD MAN WITH COUGH AND CHEST PAIN

Myocarditis presenting as typical acute myocardial infarction: A case report and review of the literature. World J Clin Cases 2020; 8(2): 415-424 [PMID: 32047794 DOI: 10.12998/wjcc.v8.i2.415]

Hou YM, Han PX, Wu X, Lin JR, Zheng F, Lin L, Xu R.

Case Summary [1]

A 42-year man is presented with a cough, chest pain and has a history of hypertension and smoking. Laboratory investigations of cardiac biomarkers ***troponin I****, troponin T, and CK-MB (creatine kinase-MB) were elevated. Electrocardiogram (ECG) also showed T-wave inversion. Coronary angiography showed normal results. Cardiovascular magnetic resonance imaging (CMR) was done which shows a thicker anterior wall and FST2WI (Fat Suppressed T2-Weighted Imaging) shows edema. Rubella virus* ***IgG*** *and* ***IgM*** *antibodies were also elevated.*

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Learning Objectives

- Investigating the clinical history of the patient and examinations to present a confirmatory diagnosis for cardiac disease.
- Identify and differentiate between the cardiac biomarkers required to assess acute myocardial infractions.
- Familiarizing and defining new medical terminology associated with cardiac disease.

Clinical History [1]

- Age: 42 years old
- Sex: Male

Medical History [1]

- Hypertension for 2 years. The patient has a history of smoking.

Symptoms [1]

- Chest pain for 2 days.
- Cough for 1 week.

Examinations (Clinical Assays/Tests/Imaging) [1]

Physical Examination [1]

- Temperature: 37.8^{o}C
- Blood pressure: 164/114 mmHg

Blood Investigations [1]

- Serum Tn I: 2.57 ng/mL (elevated)
- Troponin T: 34.34 pg/mL (elevated)
- Creatine kinase isozyme (CK-MB): 11.85 ng/mL (elevated)
- C-reactive protein: 4.95 mg/L (elevated)
- Erythrocyte sedimentation rate (ESR): 45 mm/h (elevated)

- **Brain natriuretic peptide**: 168 pg/mL (elevated)
- WBC: 3.30 × 109/L; neutrophil percentage, 0.735
- Platelet count: 312 × 109/L. (normal)
- Rubella virus IgG and IgM antibody were elevated.

** Please check reference ranges at the back

Electrocardiogram [1]

- After admission, ECG was done and that showed T inversions on lead II, III, and aVF.

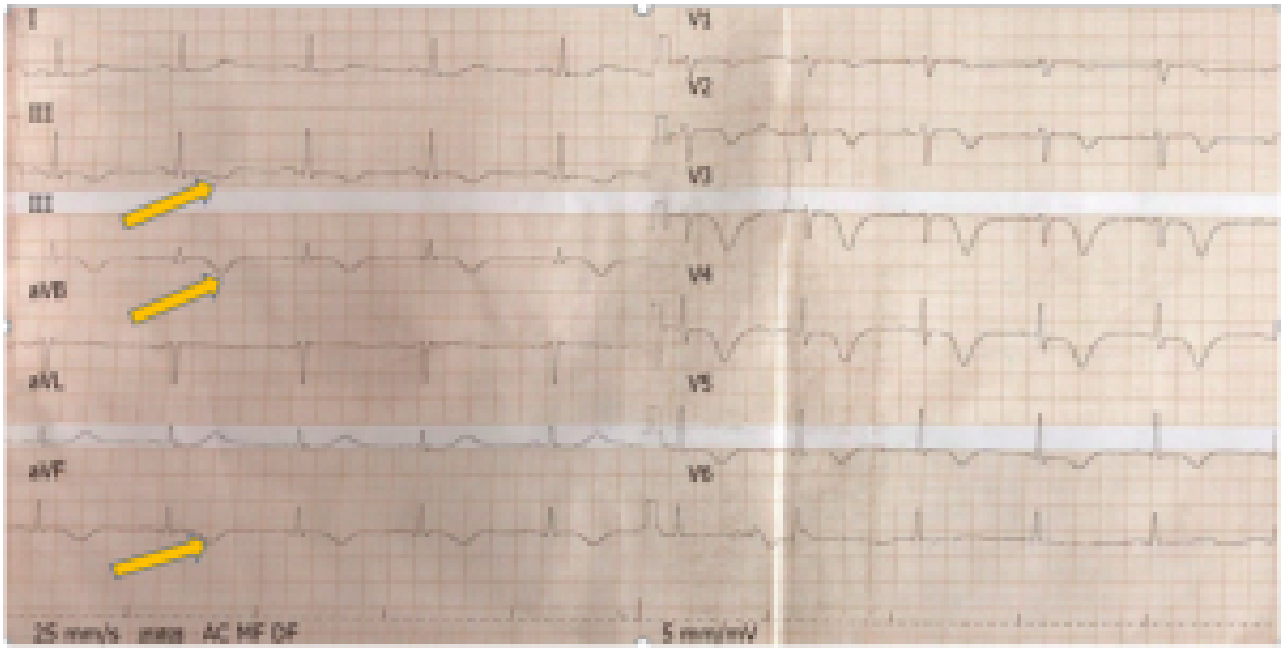

Figure 1: ECG shows T inversion (yellow arrows) in lead II, III, and aVF1.[1]

Coronary Angiography [1]

- Normal (at day 5).

Cardiac Magnetic Resonance Imaging (MRI) [1]

- Wall motion abnormalities (mid septal, apical septal, and apical anterior), and the anterior walls were obviously thicker than the normal walls (Figure 2A), with the thickest part of the ventricular wall being approximately 20 mm.
- FST2WI (Fat Suppressed T2-Weighted Imaging -Figure 2B) – Edema of the mid septal, apical septal,

and apical anterior walls (Figure 2B). **T1 mapping** (Figure 2C) depicts more specifically myocardial edema.

- **Late gadolinium enhancement (LGE)** (Figure 2D): shows enhancement in the endocardium and middle myocardium of the mid septal and apical septal walls.

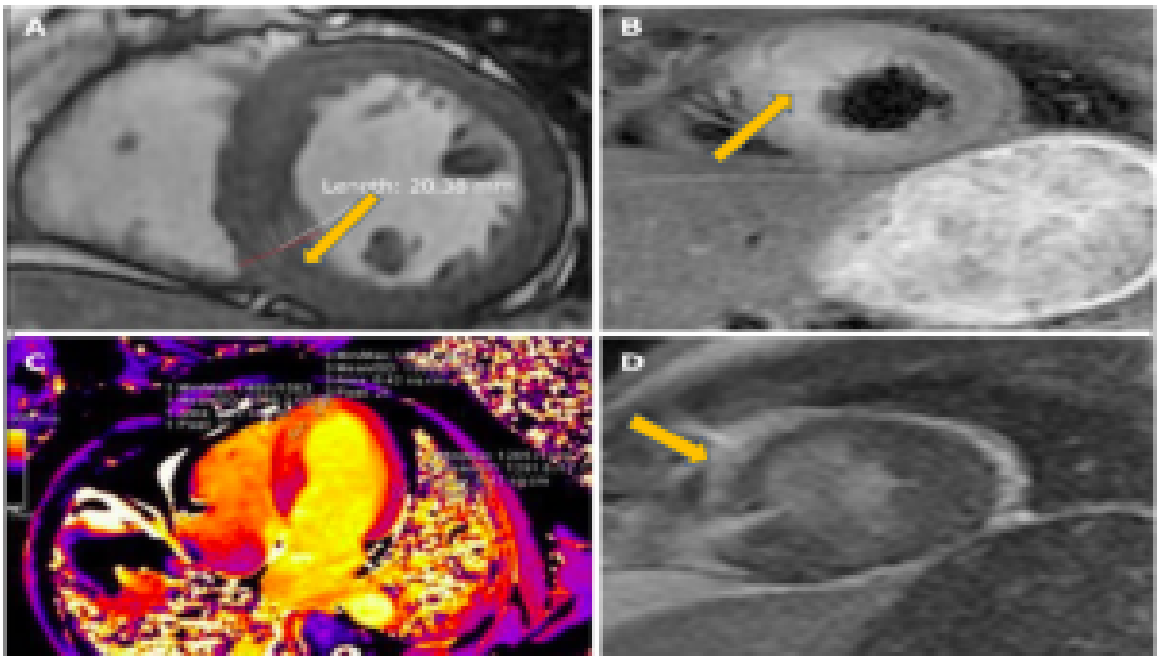

Figure 2: Cardiovascular magnetic resonance imaging. A: In the [pb_glossary id="526"]CINE[/pb_glossary] sequence at the left ventricular end-diastolic phase, the ventricular wall (yellow arrow) was 20.38 mm (normal 12 mm). B: FS-T2WI showed obvious edema (yellow arrow); C: The T1 mapping showed that the T1 value of the walls was obviously higher than that of the normal walls (1586.3 ms vs 1291.6 ms) in the interventricular septum in the first cardiovascular magnetic resonance. D: Late gadolinium enhancement (yellow arrow) of the endocardium and middle myocardium of the middle and apical septal walls.[1]

Question & Answers Leading to Diagnosis:

Question 1: Based on the ECG, what cardiac biomarkers should we examine for this patient? What would they tell us?

Question 2: What is the purpose of IgG and IgM antibody analysis?

Question 3: Which tests were performed to confirm the diagnosis? How can we interpret these results?

** For answers please check the next chapter.

Medical terminology/Abbreviations:

- TnI (Troponin I) – Cardiac bio marker. Cardiac troponin T (cTnT) and troponin I (cTnI) are cardiac regulatory proteins that control the calcium-mediated interaction between actin and myosin.[12]
- IgG – Immunoglobulin G-antibody. IgG is synthesized mostly in the secondary immune response to pathogens. [13]
- IgM – Immunoglobulin M-antibody. It is mainly produced in the primary immune response to infectious agents or antigens.[13]
- Brain natriuretic peptide (BNP) – Peptide hormone that is released in response to volume expansion and the increased wall stress of cardiac myocytes.[2]
- CMR imaging – Cardiovascular magnetic resonance imaging.[6]
- Cine CMR – Consists in the acquisition of the same slice position at different phases of the cardiac cycle. [6]
- FST2WI – Fat Suppressed T2-Weighted Imaging.4 FST2WI fusion technology improves signal differences with surrounding structures and facilitates the better evaluation of disease. [4]
- Late gadolinium enhancement – Gadolinium is a chemical agent used as a contrast, administered intravenously to achieve optimum contrast between normal and infarcted myocardium.[3]
- T1 mapping – It is a cardiac magnetic resonance (CMR) imaging technique, which shows early clinical promise particularly in the setting of diffuse fibrosis.[7]

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Further Reading

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6.

CASE 3-2020: ANSWERS TO THE QUESTIONS

Answer to Question 1: The patient is hypertensive and ECG shows T inversion in lead II, III, and aVF so, we should look for cardiac biomarker troponin I, Troponin T, CK-MB. These markers were elevated in the patient.

- Serum Tn I: 2.57 ng/mL (normal range: 0-0.034 ng/mL),
- Troponin T: 34.34 pg/mL (normal range : 3-14 pg/mL).
- Creatine kinase isozyme (CK-MB): 11.85 ng/mL (normal range: 0.1-4.94 ng/mL)

Considering the patient's symptoms of chest pain, elevated cardiac biomarker (troponin T and I), and ECG findings (T inversion), all these findings indicate myocardial infarction.[5]

Answer to Question 2: Lab investigations had revealed elevated C-reactive protein of 4.95 mg/L (normal range 0-2.87 mg/L)[1] and an erythrocyte sedimentation rate (ESR) of 45mm/h, together, indicative of infection.

- Further analysis would reveal elevated levels of IgG and IgM antibodies. In the literature, IgM antibodies have been linked to recent infections, while IgG antibodies reveal the presence of recent or previous infections.[11]

Answer to Question 3:

- To confirm the diagnosis, cardiovascular resonance imaging was used to reveal an anterior ventricular wall thickness of 20.38mm (normal walls 12mm), while FS-T2WI results showed edema. Rubella IgG and IgM antibody levels were elevated. Based on these results, the confirmatory diagnosis is viral myocarditis. [1]

Diagnosis [1]

- Patient symptoms and elevated cardiac biomarker with ECG findings indicate myocardial infarction.
- Based on CMR imaging findings and elevated rubella IgG and IgM antibody confirmatory diagnosis is viral myocarditis.

Treatment and Prognosis[1]

- Treatment: Aspirin, clopidogrel, acyclovir(antiviral), levofloxacin (antibiotic).
- Prognosis:
  - 10 months later: The patient was asymptomatic. ECG: normal, echocardiography: normal with patchy enhancement in the ventricular septal wall. CMR: edema disappears ventricular wall thickness 14mm (as the patient is hypertensive so high BP leads to ventricular hypertrophy).

7.

CASE 4-2020: A 65-YEAR-OLD WOMAN CHEST TIGHTNESS, NAUSEA, VOMITING DURING BRONCHOSCOPY

Diagnosis and prognosis of myocardial infarction in a patient without obstructive coronary artery disease during bronchoscopy: a case study and literature review. BMC Cardiovasc Disord 20, 185 (2020). https://doi.org/10.1186/s12872-020-01458-5

Li, M., Liu, Y. & Wang, H.

Case Summary [1]

A 65-year-old woman was hospitalized with the main complaint of chest tightness, nausea, and vomiting for 30 min during ***bronchoscopy*** *under local anesthesia. Immediate electrocardiogram (****ECG****) showed ST-segments elevation in leads V2–6 compared with those at admission, and the further evolvement of leads V2–3 into pathological Q wave. Serum cardiac biomarkers revealed an increase of* ***high-sensitive cardiac troponin T*** *(hs-cTnT) levels. Emergency* ***coronary angiography (CAG)*** *showed only approximately 30% stenosis in the left anterior descending (LAD) ostium and 40% stenosis in the first diagonal branch(D1), with a quantitative flow ratio (QFR) value for LAD of 0.96. Moreover, her echocardiographic examination presented new significant abnormal wall motion (anterior ventricular wall) with an estimated left ventricular ejection fraction (LVEF) of 62.1% after the cardiac attack. Thoracic enhanced CT scanning indicated no obvious sign of pulmonary embolism. This patient was diagnosed with* ***MINOCA*** *(Myocardial infarction with nonobstructive coronary arteries) based on her atypical angina symptoms, dynamic changes of ECGs, and elevated cardiac biomarker with CAG revealing no significant obstruction of coronary arteries. She was treated accordingly and had a good prognosis during a 14-month follow-up.*

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Learning Objectives

- Understanding emergency cardiac conditions.
- Investigating cardiac cases based on the patient's history and presenting symptoms.
- Determine the required lab investigations and their role in the diagnosis.
- Familiarizing and defining new medical terminology associated with the disease.

Clinical History [1]

- Age: 65 years old
- Sex: Female
- Ethnicity: Not mentioned.

Medical History [1]

- The patient underwent right upper lung **adenocarcinoma** resection 4 months back and was found to have an elevated **carcinoembryonic antigen (CEA)**, 2 days before admission. A bronchoscopy examination was scheduled to determine local recurrence.
- History of hypertension for 1 year but no history of taking any anti-hypertensive medication.
- No history of other chronic diseases such as diabetes, coronary artery disease (CAD), or stroke, and no history of cigarettes, alcohol, or substance abuse.

Symptoms [1]

- Sudden onset of chest tightness, nausea, and vomiting for half an hour during the scheduled bronchoscopy procedure.

Examinations (Clinical Assays/Tests/Imaging) [1]

Physical Examination [1]

- Blood pressure: 166/94 mmHg
- BMI: 22.73 kg/m^2 (normal)

Laboratory Investigations [1]

Investigation name	Result	Reference range
High-sensitive cardiac troponin T (hs-cTnT)	20.12 ng/L and 674.6 ng/L at the peak	0-14 ng/L
Total cholesterol	6.70 mmol/L	3.00–5.70 mmol/L
Low-density-lipoprotein cholesterol (LDL-C)	4.18 mmol/L	2.60–4.10 mmol/L
Routine complete blood count, urine test, glucose levels, renal and liver function, coagulation factors, hemoglobin A1c, thyroid function and autoimmune indicators were within the normal ranges.		

Immediate Electrocardiogram [1]

- Showed ST-segments elevation in leads V2–6 compared with those at admission, then the further evolvement of leads V2–3 into pathological Q wave.

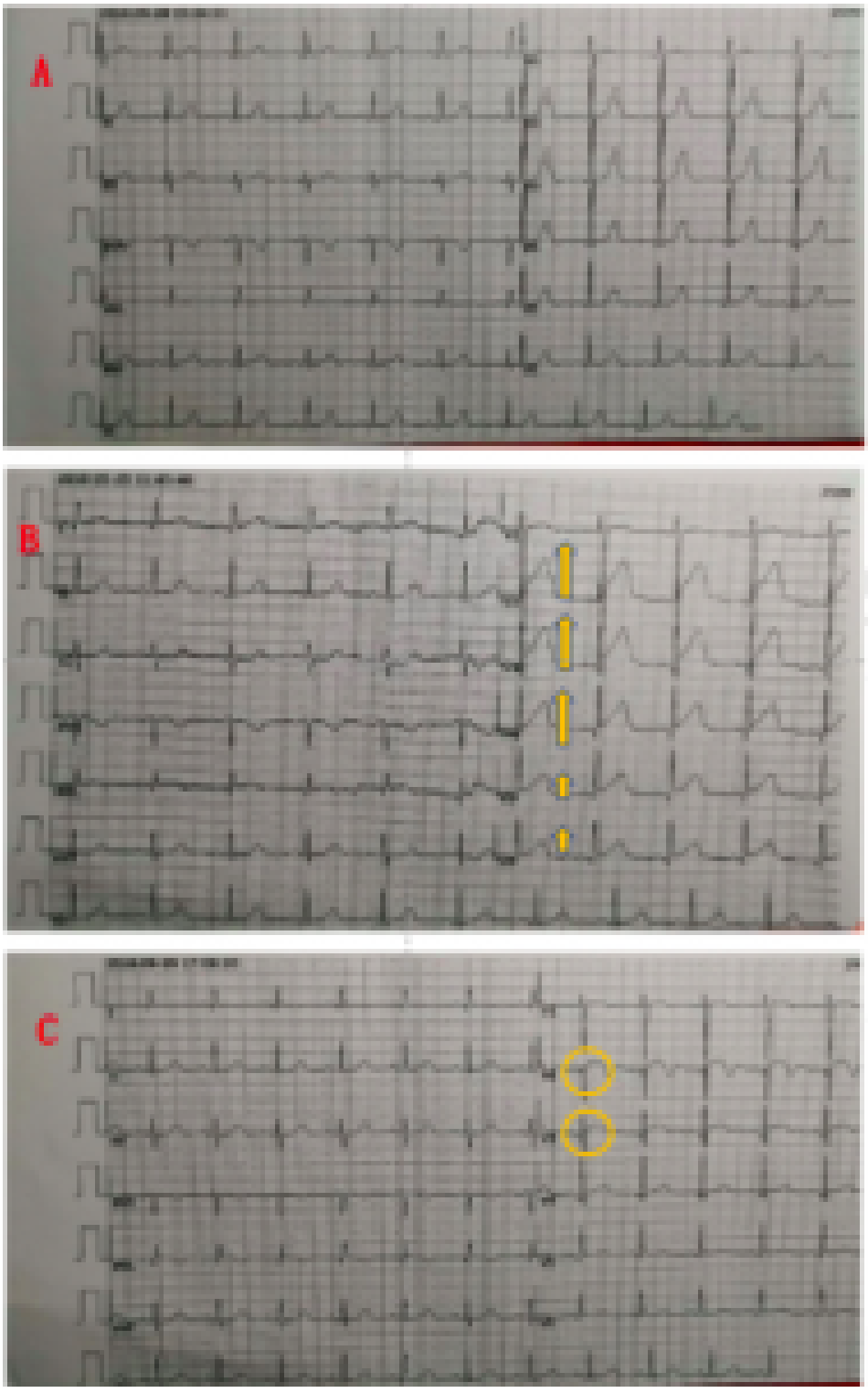

Figure 1: Dynamic changes in electrocardiography during acute myocardial infarction. (a) Sinus rhythm, normal ECG. (b) ST-segments elevation in leads V2–6 during the sudden onset of cardiac attack (yellow arrows). (c) Pathological Q waves in leads V2–3 (yellow circles), ST-segments elevation in leads V1–4, T-waves inverted in lead V1–3 and aVL.[1]

Thoracic Enhanced Computed Tomography (CT) Scan [1]

- No obvious sign of pulmonary embolism.

Echocardiogram [1]

- New significant abnormal wall motion (anterior ventricular wall) with an estimated left ventricular ejection fraction (LVEF) of 62.1%.

Emergency CAG (Coronary Angiography)[1]

- Approximate 30% stenosis in the left anterior descending (LAD) ostium and 40% stenosis in the first diagonal branch, functional quantitative flow ratio (QFR) value for LAD was 0.96.

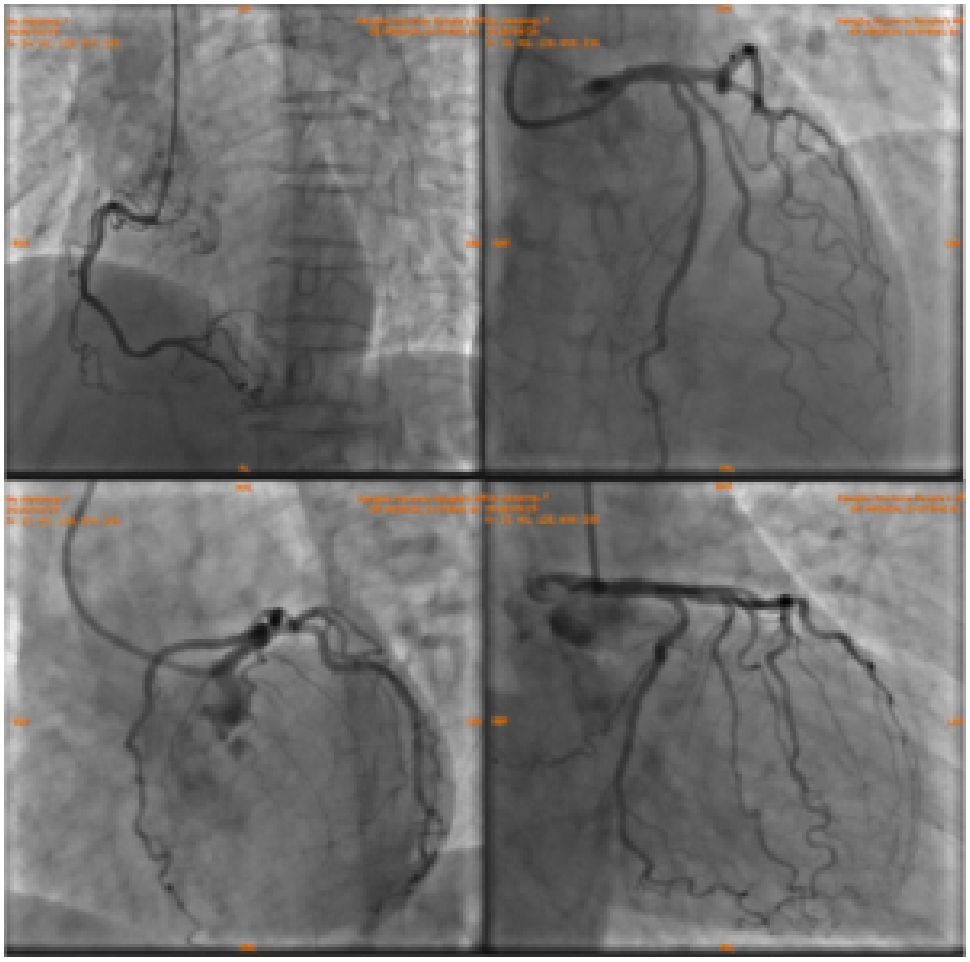

Figure 2: Images of coronary angiography. Approximate 30% stenosis in the left anterior descending (LAD) ostium and 40% stenosis in the first diagonal branch (D1).[1]

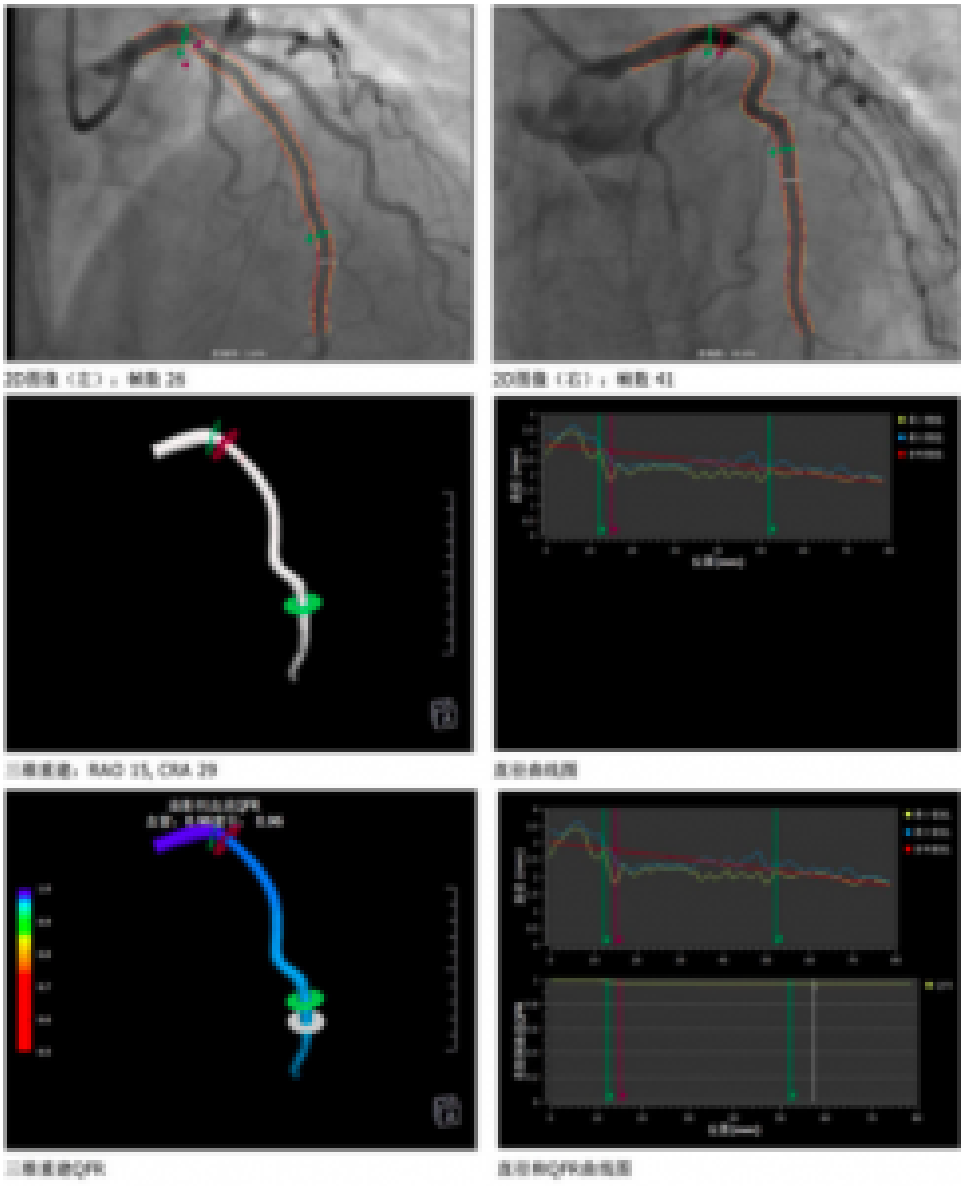

Figure 3: QFR value of left anterior descending (LAD). Based on the three-dimensional images from CAG and principles of fluid dynamics, the QFR value of the target vessel – LAD was 0.96.[1]

Question & Answers Leading to Diagnosis:

Question 1: Based on clinical history and lab investigations result what diagnosis can we make for this patient?

Question 2: What does the ST elevation in ECG indicate?

Question 3: Based on the symptoms present, how can we recognize emergency cardiac conditions?

** For answers please check the next chapter.

Medical terminology/Abbreviations:

- Adenocarcinoma – Adenocarcinoma is a type of cancer that starts in mucus-producing glandular cells of the body.[5]
- Bronchoscopy – Bronchoscopy is a procedure that looks inside the lung airways. It can detect tumors, signs of infection, excess mucus in the airways, bleeding, or blockages in the lungs.[7]
- CEA – A carcinoembryonic antigen (CEA) test is a blood test used to help diagnose and manage certain types of cancers.[6]
- Coronary Angiography – Coronary angiography is a procedure that uses a special dye (contrast material) and x-rays to see how blood flows through the arteries in the heart.[11]
- ECG – An electrocardiogram or ECG is a test to record the electrical signals in the heart.[9]
- Echocardiogram – An echocardiogram (echo) is a graphic outline of the heart's movement done by ultrasound.[10]
- High-sensitive cardiac troponin T – Cardiac troponin is the preferred biomarker for the diagnosis of acute myocardial infarction and high-sensitive cardiac troponin T (hs-cTnT) assay permits detection of very low levels of cTnT.[8]
- MINOCA – Myocardial infarction with nonobstructive coronary arteries (MINOCA) is clinically defined by the presence of the universal acute myocardial infarction (AMI) criteria, absence of obstructive coronary artery disease (≥50% stenosis), and no overt cause for the clinical presentation at the time of angiography.[2]

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Further Reading

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8.

CASE 4-2020: ANSWERS TO THE QUESTIONS

Answer to Question 1:

From the literature Mendis et. Al., 2010, the clinical presentation of MI varies from a minor coronary event to life-threatening clinical situations or sudden death.

The WHO European Myocardial Infarction registry criteria are based on clinical history, findings on the electrocardiogram (ECG), enzyme measurements in blood, and postmortem findings. MI is diagnosed in the presence of one of the following:

- (i) ECG showing unequivocal pathological Q waves and/or ST-segment elevation or depression in serial recordings;
- (ii) history of typical or atypical angina pectoris, together with equivocal changes on the ECG and elevated enzymes;
- (iii) history of typical angina pectoris and elevated enzymes with no changes on the ECG or not available;
- (iv) fatal cases, whether sudden or not, with naked-eye appearances of fresh MI and/or recent coronary occlusion at necropsy (antemortem thrombus, hemorrhage into an atheromatous plaque or embolism).[12]

In the given case, the patient demonstrated chest tightness along with nausea and vomiting, which coincides with the symptom of angina pectoris and as per the WHO criteria outlined above.[1]

- Her ECG also showed ST-segments elevation in leads V2–6 and then the further evolvement of leads V2–3 into pathological Q wave.[1]
- Laboratory result revealed high-sensitive cardiac troponin T (hs-cTnT) levels of20.12 ng/L and 674.6 ng/L at the peak (normal range 0-14 ng/L).[1]
- Overall, according to the WHO definition of MI, a diagnosis of acute myocardial infarction

was made for this patient.

Answer to Question 2:

- The ST-segment elevation is an abnormality detected on the 12-lead ECG due to a serious type of heart attack.[3]
- ST-Elevation Myocardial Infarction (STEMI) is a very serious type of heart attack during which one of the heart's major arteries (one of the arteries that supply oxygen and nutrient-rich blood to the heart muscle) is blocked.[13]

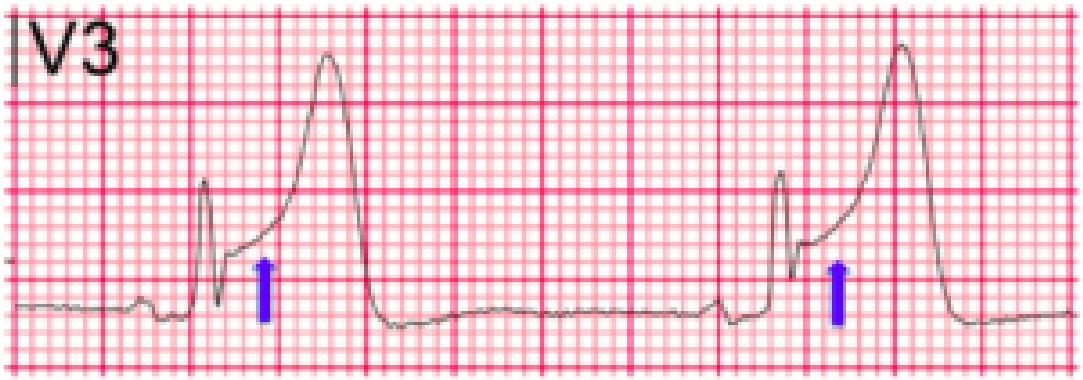

Figure: ECG with ST-segment elevated.[13]

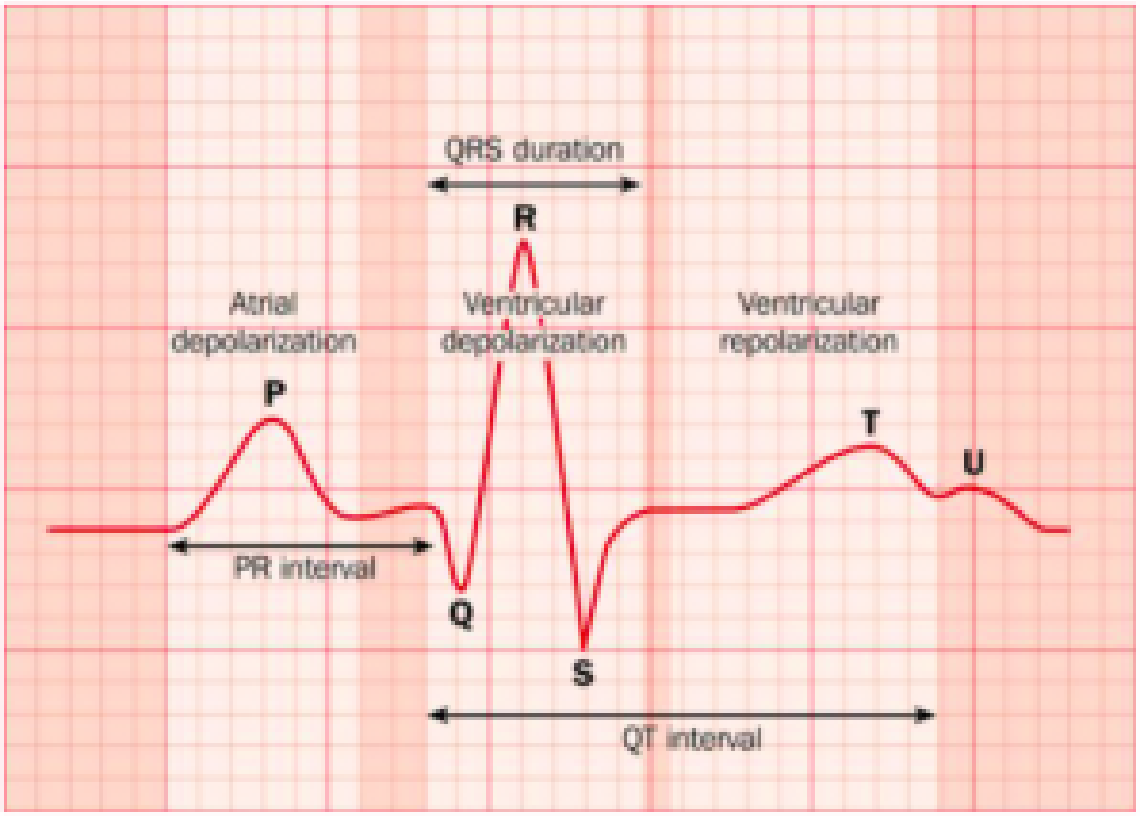

Figure: Basic of 12 lead ECG14

Answer to Question 3: Emergency cardiac conditions can be recognized by the following symptoms-

- chest discomfort (pressure, squeezing, fullness or pain, burning or heaviness),
- sweating,
- upper body discomfort (neck, jaw, shoulder, arms, back),
- nausea,
- shortness of breath,
- light-headedness. [4]

Diagnosis [1]

- MINOCA (Myocardial infarction with nonobstructive coronary arteries). The diagnosis was made as the patient had atypical angina symptoms, dynamic changes of ECGs, and elevated cardiac biomarkers but CAG revealed no significant obstruction of coronary arteries.

Treatment [1]

- The patient received dual anti-platelet therapy with daily low-dose aspirin for life and clopidogrel for 1 year.
- Statin and cholesterol absorption inhibitors were given for hyperlipidemia. Calcium channel blocker (CCB) and nitrites were given to control coronary artery spasm.
- Angiotensin receptor antagonist (ARB) was also prescribed for her uncontrolled blood pressure.

Prognosis [1]

- An echocardiogram was performed during her follow-up visit, which revealed a normal ventricular wall motion and the estimated LVEF had risen to 69.4%.

PART II

COVID-19 CASE STUDIES

Coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus.

Most people infected with the virus will experience mild to moderate respiratory illness and recover without requiring special treatment. However, some will become seriously ill and require medical attention. Older people and those with underlying medical conditions like cardiovascular disease, diabetes, chronic respiratory disease, or cancer are more likely to develop serious illnesses. Anyone can get sick with COVID-19 and become seriously ill or die at any age.

The virus can spread from an infected person's mouth or nose in small liquid particles when they cough, sneeze, speak, sing or breathe. These particles range from larger respiratory droplets to smaller aerosols.[1]

Symptoms[1]

COVID-19 affects different people in different ways. Most infected people will develop mild to moderate illness and recover without hospitalization.

Most common symptoms:[1]

- fever
- cough
- tiredness
- loss of taste or smell.

Less common symptoms:[1]

- sore throat
- headache
- aches and pains
- diarrhea
- a rash on the skin, or discoloration of fingers or toes
- red or irritated eyes.

Serious symptoms:[1]

- difficulty breathing or shortness of breath

- loss of speech or mobility, or confusion
- chest pain.

Reference:

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9.

CASE 1-2020: A 53-YEAR-OLD MALE FEVER, SORE THROAT AND DYSPNEA WITH CONTACT HISTORY

Case Study: A Patient with Asthma, COVID-19 Pneumonia and Cytokine Release Syndrome Treated with Corticosteroids and Tocilizumab. Wits J. Clin. Med. 2, 47 (2020)

Schleicher, G. K., Lowman, W. & Richards, G. A.

Case Summary [1]

A 53-year-old male is presented with a fever, sore throat, dry cough, severe wheezing, and worsening ***dyspnea****. He had a history of asthma and had come in contact with a COVID-19 positive patient. A COVID–19 PCR test was conducted and had been negative, however, his condition had worsened. A CT scan showed a bilateral ground-glass appearance in the lower zone of the lungs. His oxygen saturation was 86% and the lab investigations had shown a significant decrease in white blood cell count (****lymphopenia****), increased C-reactive protein, pro-B-type natriuretic peptide (****Pro-BNP****), lactate dehydrogenase (LDH),* ***D-dimer****s, and ferritin. His* ***hypoxemia*** *(decreased oxygen levels in blood) worsened and increased bilateral chest infiltrates were shown on a follow-up chest X-ray.*

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://ecampusontario.pressbooks.pub/clinicalcases/?p=77#audio-77-1

Learning Objectives

- Investigating the clinical history of the patient and selecting appropriate examinations needed to diagnosis of COVID-19.
- Understanding the typical symptoms of COVID-19 and identifying those presented in the patient.
- Discuss the common clinical laboratory tests used to assess and monitor COVID-19.

Clinical History [1]

- Age: 52 years old
- Sex: Male

Medical History [1]

- History of asthma.
- History of contact with a COVID-19 positive patient.

Drug History [1]

- Low dose inhaled corticosteroid.

Symptoms [1]

- Fever
- Sore throat, dry cough
- Severe wheezing
- Worsening dyspnea

Examinations (Clinical Assays/Tests/Imaging) [1]

Physical Examination [1]

- Oxygen saturation: 86% on room air.

Blood Investigations [1]

Chart 1

	Date								
	2020-03-16	2020-03-17	2020-03-21	2020-03-23	2020-03-24	2020-03-25	2020-03-26	2020-03-27	2020-03-31
Laboratory marker									
White cell count (4–10 × 10^9/L)	7.0	6.1	9.8	7.8	9.5	8.1	6.3	6.6	8.0
Neutrophils abs (2–7 × 10^9/L)	5.8	4.2	8.8	7.3	8.4	6.4	4.3	4.6	6.9
Lymphocytes abs (1–3 × 10^9/L)	0.6	1.2	0.4	0.2	0.8	1.1	1.3	1.2	1.4
Neutrophil: Lymphocyte ratio	8.6	3.5	22.3	38.5	14.8	5.8	3.3	3.8	5.1
CRP (0–10 mg/L)	58	73	88	169	84	43	22	12	4
PCT (0–0.05 ng/L)			0.05	0.04	0.03	0.02		0.04	
Ferritin (21–275 µg/L				1900	1851	1384			
LDH (125–220 U/L)	185	181	340		259	215			
D-Dimer (0–0.215 mg/L)		0.37	1.31	0.85	0.88	0.68			
Pro-BNP (<125 ng/L)			338	297	173	115		98	
SARS-CoV-2	Detected								Not detected
				↑	↑				
				Tocilizumab	Tocilizumab				

Chest X-ray [1]

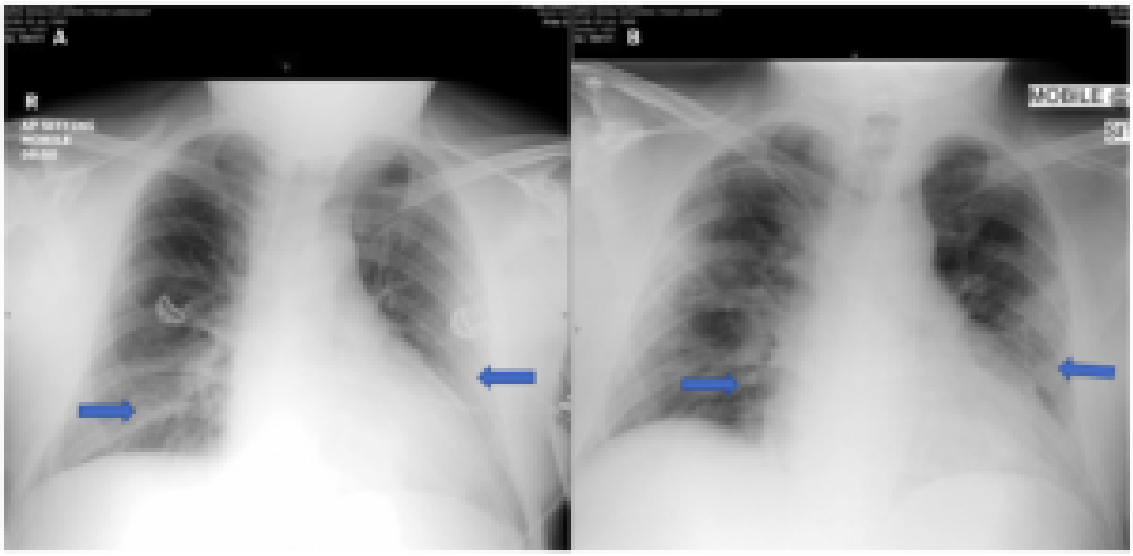

Figure 1: A – Chest X-ray on 17 March – bilateral infiltration (blue arrows) in the lower zone of lung. B – Chest X-ray on 20 March showed progressive bilateral infiltration in the lower zone.[1]

High-resolution Computed Tomography (CT) Scan of Chest [1]

- Bilateral asymmetrical peripheral ground-glass infiltrates in a subsegmental distribution, particularly in the lower zone. Transthoracic Echocardiography (TTE) [1]

Question & Answers Leading to Diagnosis:

Question 1: Based on the patient's symptoms and contact with a COVID-19 positive individual, what will be the possible diagnosis? What investigation(s) can confirm this diagnosis?

Question 2: Considering the initial RT-PCR results were negative, what investigations can be done to further support this patient's diagnosis?

Question 3: What biomarkers could be used for monitoring this patient's treatment efficacy and disease prognosis?

** For answers please check the next chapter.

Medical terminology/Abbreviations:

- Lymphopenia – Reduced leukocytes count.[3]
- Dyspnea – Dyspnea means difficulty in breathing, breathlessness, or a feeling of suffocation.[6]
- Hypoxemia – Hypoxemia refers to a decrease in the partial pressure of oxygen (PaO2) or oxygen saturation in the blood.[7]
- CRS – Cytokine Release Syndrome. CRS is a systemic inflammatory response due to massive T cell stimulation that can be triggered by a variety of factors such as infections, and certain drugs.[2]
    - The COVID-19 virus binds to alveolar epithelial cells, activating the innate and adaptive immune

systems resulting in the release of pro-inflammatory cytokines. This can lead to the CRS which is characterized by a hyperinflammatory state with raised inflammatory cytokines and biomarkers such as interleukin (IL)-2, IL-6, IL-7, granulocyte-colony stimulating factor, macrophage inflammatory protein 1-α, tumor necrosis factor-α, CRP, ferritin, Pro-BNP, and D-dimer. [1]

- ARDS – acute respiratory distress syndrome.[10]
- Pro-BNP – Pro-B-type natriuretic peptide is a hormone produced by the heart.[4]
- PCT (procalcitonin) – A peptide precursor of the hormone calcitonin. serum PCT concentrations remain normal in uncomplicated cases of COVID-19 and inflated values may indicate bacterial co-infection in severe cases.[8]
- D-dimers – It is a small protein fragment present in the blood after the degradation of a blood clot. D-dimer concentration help to diagnose thrombosis and intravascular coagulation.[5]
- Tocilizumab – Interleukin-6 antagonist used for CRS treatment. Tocilizumab binds specifically to both soluble and membrane-bound IL-6 receptors. [1]

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Further Reading

10.

CASE 1-2020: ANSWERS TO THE QUESTIONS

Answer to Question 1:

- Based on presented symptoms, fever, sore throat, dry cough, severe wheezing, worsening dyspnea, contact with a COVID-19 positive individual, and on blood profile showing high CRP and reduced WBC (white blood cell) count, the possible diagnosis is COVID-19.
- To confirm the diagnosis, RT-PCR, CT-scan of chest and chest X-ray can be done.

Answer to Question 2: The initial COVID-19 RT-PCR results were negative, however as the patient's symptoms worsened, a chest x-ray and CT scan were done to further support the diagnosis. The chest X-ray showed bilateral infiltration in the lower zone indicating lung infection. The chest CT scan showed bilateral asymmetrical peripheral ground-glass infiltrates in the lower zone of lungs which is a hallmark of the COVID-19 infection.[9]

Answer to Question 3: C-reactive protein (inflammation), D–dimer (increased after blood clot formation to assess thrombosis or intravascular coagulation)**,** ferritin, PCT (procalcitonin, used as an infection marker) these biomarkers are used to monitor treatment efficacy and disease prognosis of COVID-19.[5, 8]

Diagnosis [1]

- COVID-19 hyperinflammatory syndrome, Cytokine Release Syndrome (CRS), and ARDS.

11.

CASE 2-2020: A 32-YEAR-OLD MALE WITH FEVER, RHINORRHEA AND MYALGIA

A COVID-19 patient with multiple negative results for PCR assays outside Wuhan, China: a case report. BMC Infectious Diseases, 20(1). 2020. doi: 10.1186/s12879-020-05245-7

Chen, L., Li, H., Ye, Y., Wu, Z., Huang, Y., Zhang, W., & Lin, L.

Case Summary [1]

A 32-year-old male was admitted with an unexplained fever for six days, nasal congestion, ***rhinorrhea****, fatigue, and* ***myalgia****. He had no cough, hemoptysis, headache, sore throat, shortness of breath, nausea, or diarrhea. He had a travel history of Wuhan city 10 days before admission. Five days before admission, no abnormalities were noted in leucocyte and lymphocyte count, chest radiography. Nasopharyngeal swab test for the SARS-CoV-2 nucleic acid was found negative. Six days after the onset of fever, the patient was admitted, and chest computed tomography showed multiple ground-glass opacities in the right lower lung field. The patient's laboratory results revealed reduced leucocyte and white blood cell counts, and elevated alanine aminotransferase (ALT), aspartate aminotransferase (AST), γ-glutamyl transpeptidase (GGT), and high-sensitivity C-reactive protein (hs-CRP). Three (Jan 29, Jan 30, and Feb 1, 2020) nasopharyngeal swab specimens were collected after admission. However, none of the specimens were positive for COVID-19. This was followed by another, nasopharyngeal swab specimen on Feb 2, 2020, with a positive mild COVID-19 finding using a cycle threshold value (Ct-value) less than 37 for polymerase chain reaction (PCR), and the patient was finally diagnosed as COVID –19.*

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://ecampusontario.pressbooks.pub/clinicalcases/?p=79#audio-79-1

Learning Objectives

- Investigating the clinical history of the patient and selecting appropriate examinations needed to diagnosis of COVID-19.
- Understanding the typical symptoms of COVID-19 and identifying those presented in the patient.
- Discuss reasons for potential false-positive and false-negative RT-PCR results for COVID-19.

Clinical History [1]

- Age: 32 years old
- Sex: Male

Medical History [1]

- No underlying medical condition.

Travel History [1]

- History of travel to Wuhan city 10 days back.

Symptoms [1]

- Fever
- Nasal congestion, rhinorrhea
- Fatigue
- Myalgia

Examinations (Clinical Assays/Tests/Imaging) [1]

Physical Examination [1]

- Body temperature: 38.4oC (normal oral temperature 35.7-37.7oC) 8
- Respiratory rate: 22 breaths/min (normal range 12 to 20 breaths/min)9
- Blood pressure: 124/82 mmHg.
- Pulse rate: 113 beats/min (normal range 60-100 beats/min)10
- Physical examination of lungs: Normal.

Blood Investigations [1]

		Leukocyte count, cells/mm^3	Lymphocyte count, cells/mm^3	Creatinine, umol/L	ALT, U/L	AST, U/L	GGT,U/L	Hs-CRP, mg/L	SARS-CoV-2 nucleic acid assay
Reference Range		4000–10,000	800–4000	40–133	5–42	1–40	5–40	0–3	–
January 24	5 days before admission	8150	1580	–	–	–	–	34.1	Negative
January 29	Admission day	5760	1270	82.8	46.8	31.6	45	–	Negative
January 30	Day 2	5170	690	–	–	–	–	23.7	Negative
February 1	Day 4	–	–	–	–	–	–	–	Negative
February 2	Day 5	–	–	–	–	–	–	–	Positive
February 4	Day 7	8020	1500	75.9	35	20.9	30.2	31.9	–
February 7	Day 10	–	–	–	–	–	–	–	Negative
February 8	Day 11	6600	1410	60.4	39.3	29.8	29.0	3.07	–
February 10	Day 13	–	–	–	–	–	–	–	Negative
February 12	Day 15	6020	3240	–	–	–	–	–	–
February 13	Day 16	–	–	–	–	–	–	–	Negative

Chest X-ray [1]

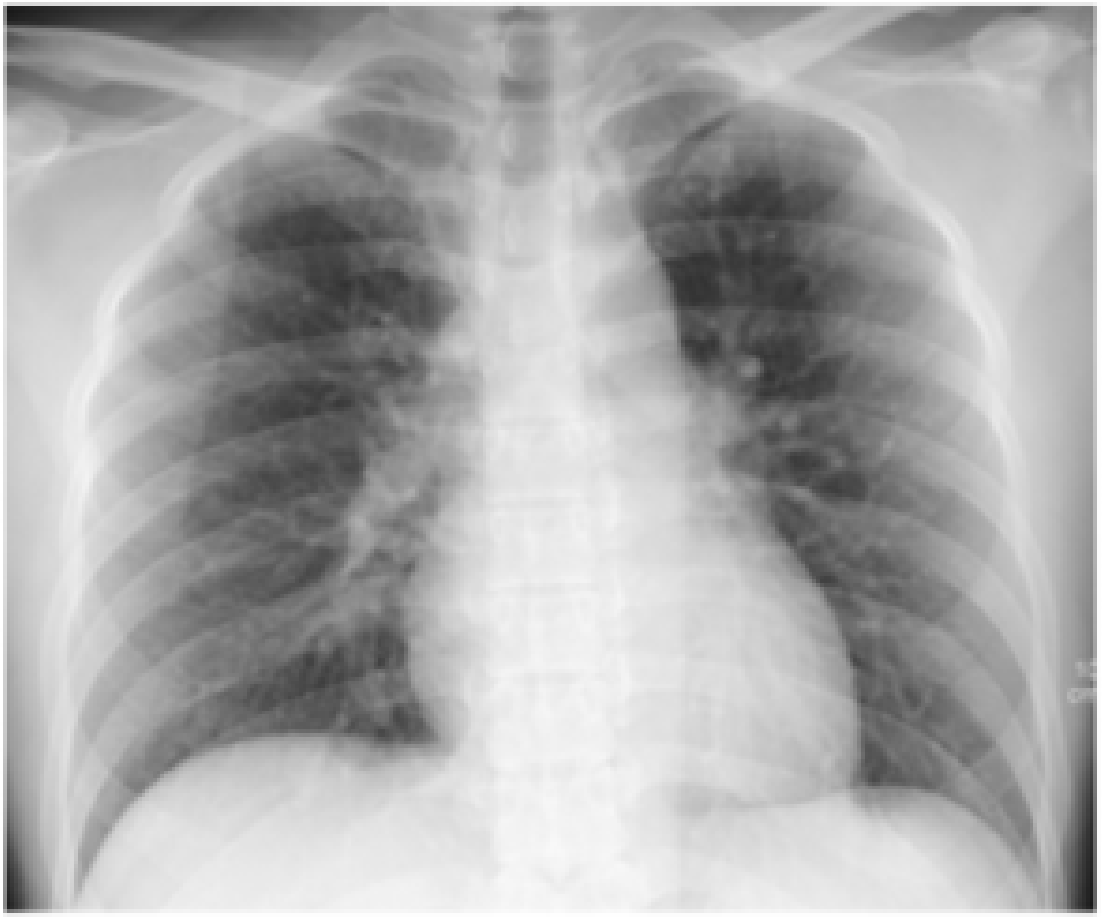

Figure 1: Chest X-ray 5 days before admission showed no abnormality. [1]

High-Resolution CT (computed tomography) Scan [1]

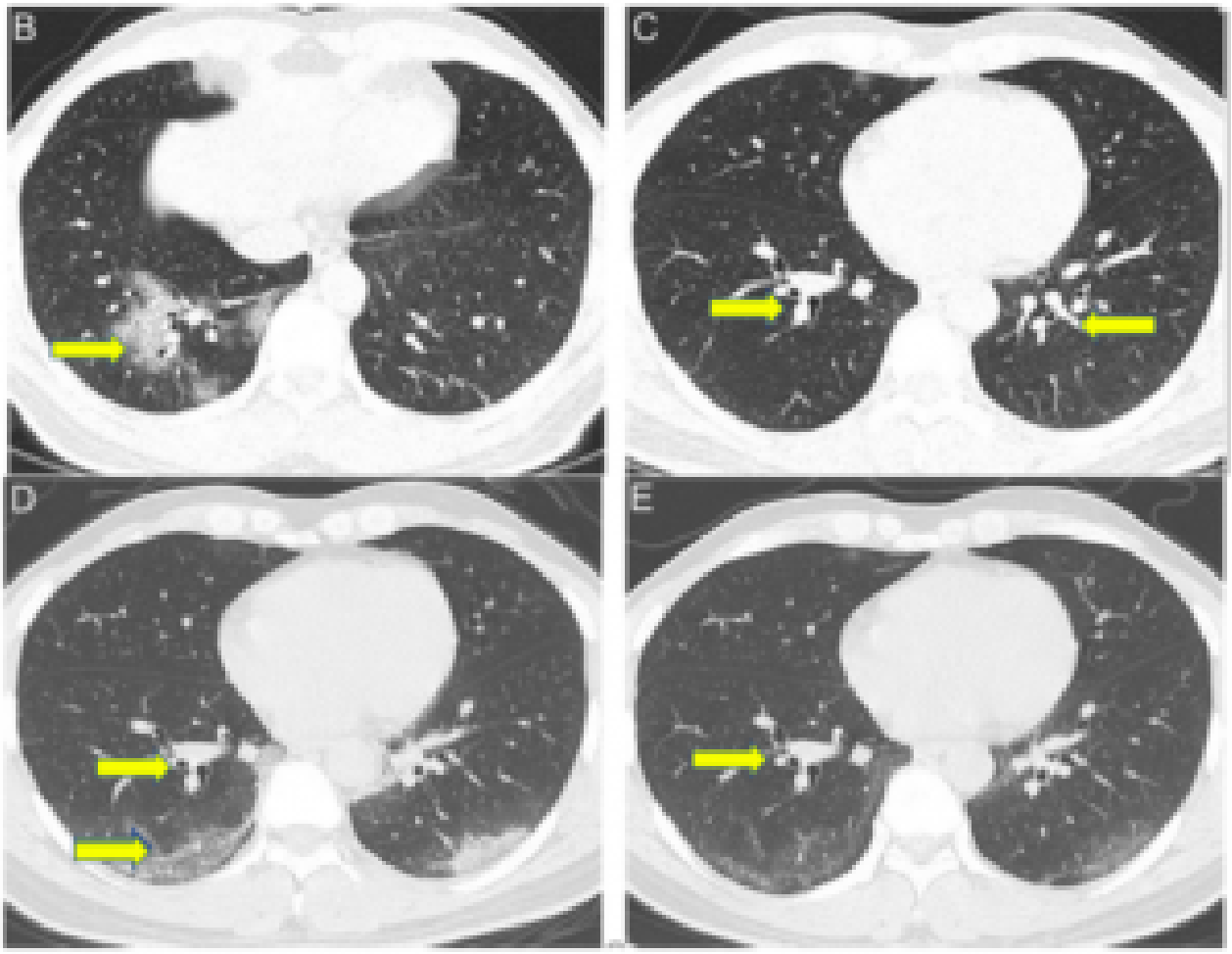

Figure 3: B and C- Chest CT showed multiple ground-glass infiltrates (yellow arrows) in right lower lung field (admission day). D- Repeat chest CT displayed larger areas of ground-glass opacities (yellow arrows) in both lower lungs with a peripheral distribution (day 8). E- Repeat chest CT showed remission of lung lesions, with reduced density of ground-glass opacities (day 17). [1]

Question & Answers Leading to Diagnosis:

Question 1: Based on the patient's symptoms and travel history what will be the possible diagnosis? What investigation(s) can confirm this diagnosis?

Question 2: Considering the initial RT-PCR results were negative and normal chest X-ray findings, what investigations can be done to further support this patient's diagnosis?

Question 3: What is indicative of the elevated alanine aminotransferase, aspartate aminotransferase and y-glutamine transpeptidase?

Question 4: Why does the repeated initial RT- PCR show negative results?

** For answers please check the next chapter.

Medical terminology/Abbreviations:

- Lymphopenia – Reduced leukocytes count.[5]
- Leukopenia – A low white blood cell count.[5]
- Rhinorrhea – Rhinorrhea refers to a thin, mostly clear nasal discharge.[6]
- Myalgia – Myalgia describes muscle aches and pain, which can involve ligaments, tendons, and fascia, the soft tissues that connect muscles, bones, and organs.[7]

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Further Reading

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12.

CASE 2-2020: ANSWERS TO THE QUESTIONS

Answer to Question 1:

- Based on presented symptoms, fever, rhinorrhea, nasal congestion, fatigue, myalgia. and recently traveled to an epidemic area in Wuhan city of China, the possible diagnosis is COVID-19.
- To confirm the diagnosis, RT-PCR, chest X-ray, and CT-scan of the chest can be done.

Answer to Question 2:

- The initial COVID-19 RT-PCR results were negative and the chest x-ray showed normal findings. Chest CT scans were done to further support the diagnosis. The chest CT scan showed bilateral asymmetrical peripheral ground-glass infiltrates in the lower zone of the lungs which is a hallmark of the COVID-19 infection.[4]
- The RT-PCR could be repeated for further investigation.

Answer to Question 3: Serum alanine aminotransferase, aspartate aminotransferase, and y-glutamine transpeptidase are the biomarkers for liver function tests.

Elevated liver enzyme indicates liver injury. Also, it is reported by Guan et al.that 21.3% of the included patients 33.7% had an elevation of alanine aminotransferase. [11]

Answer to Question 4:

- Several reasons may account for the false-negative RT-PCR results.
    - Firstly, the body's viral load is a vital factor affecting detection. Viral load is associated with disease severity and disease course. Also, a study found that about 5–6 days of symptom onset the viral loads in throat swab and sputum samples peaked.[2]
    - Secondly, viral load varies in different samples. It is suggested that sputum samples had higher viral loads than throat swab samples.[2]
    - Thirdly, the sensitivity and specificity of RT-PCR test.[12]
    - Lastly, other factors such as kit performance, sample collection, sample transportation and storage condition, standardized operation, results interpretation, and quality control can affect test results.[3]

Diagnosis [1]

- The patient was diagnosed as COVID-19.

13.

CASE 3-2021: A 53-YEAR-OLD MALE WITH HEADACHE AND BIZARRE BEHAVIOR

Presentation of COVID-19 infection with bizarre behavior and encephalopathy: a case report. Journal Of Medical Case Reports, 15(1). 2021. https://doi.org/10.1186/s13256-021-02851-0

Teimouri-Jervekani, Z., & Salmasi, M.

Case Summary [1]

A 53-year-old man presented to the emergency department with symptoms of severe headache and bizarre behavior. Symptom onset occurred 2 weeks before admission with fever and ***myalgia****. The fever lasted 3 days, and then cough and dyspnea appeared, the patient experienced some episodes of severe generalized headache which became progressively worse, and on the day of his admission, he exhibited bizarre behavior with* ***dysarthria*** *(slurring) and for example, he undressed, removing his shirt and trousers, in front of his family and also tried to urinate in the room. He had no specific family or social history. On physical exam, except for dysarthria, he had normal vital signs, no sign of hypoxia, and a normal neurological exam. The patient was alert and oriented to time, place, and person. No neck stiffness,* ***Kernig's sign****, or Brudzinski's sign was detected. Routine laboratory tests and chest and brain computed tomography (CT) were performed. Laboratory test results were normal except for raised ESR and c-reactive protein. Chest CT revealed bilateral peripheral ground-glass opacities suggestive of COVID-19 infection and then the RT-PCR for COVID-19 came out positive. The patient was then treated accordingly.*

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://ecampusontario.pressbooks.pub/clinicalcases/?p=81#audio-81-1

Learning Objectives

- Identify atypical presentations of COVID-19 and how standard diagnostic practices for COVID-19 should be inclusive of neurological assessments.
- Investigate and understand the neurological symptoms unique to COVID-19 patients.
- Discuss the lab and medical imaging investigations for atypical COVID-19 cases.

Clinical History [1]

- Age: 53 years old
- Sex: Male
- Ethnicity: Iranian

Medical History [1]

- Nothing significant.

Drug History [1]

- Not applicable.

Symptoms [1]

- Severe headache and bizarre behavior (during admission, he undressed, removing his shirt and trousers, in front of his family and also tried to urinate in the room.)
- History of fever and myalgia for 3days which was followed by cough, dyspnea and progressive headaches.
- Dysarthria for 1 day.

Examinations (Clinical Assays/Tests/Imaging) [1]

Physical Examination [1]

- General appearance: Dysarthria present, but the patient was alert and oriented to time, place, and person.
- Vital signs: Pulse, BP, respiratory rate was normal.
- Neurological examination: Normal, no neck stiffness, Kernig's sign, or Brudzinski's sign was detected.

Laboratory Investigations [1]

- The lab investigations revealed high ESR, high c-reactive protein along with positive RT-PCR for COVID 19.

Table 1 Laboratory tests

White blood cells/μL	8,100	4000–10800
Hemoglobin g/dl	14.6	14–18
Platelets/μL	353 × 10^3	150–450 × 10^3
Lymphocytes %	11.1	
Neutrophils %	81	
Erythrocyte sedimentation rate mm/hour	67	0–12
C-reactive protein mg/dl	12	0–6
Blood urea nitrogen mg/dl	34	8.4–21.7
Creatinine mg/dl	0.81	0.7–1.4
Sodium mEq/L	144	135–145
Potassium mEq/L	4	3.6–5
Magnesium mEq/L	2.2	1.8–2.6
Calcium mg/dl	8.56	8.6–11
Phosphorous mg/dl	3.86	2.8–4.6
Albumin g/dl	4.3	3.5–5.2
Aspartate aminotransferase U/L	37	0–38
Alanine aminotransferase U/L	16	0–41
Alkaline phosphatase U/L	124	80–306
pH	7.33	
PCO_2, arterial	37.2	
HCO_3 mEq/L	19.6	
Creatine phosphokinase IU/L	100	21–232
Glucose mg/dl	90	70–115
COVID-19 RT-PCR	Positive	
Blood culture	Negative	
Toxin panel	Negative for opioids, amphetamine and methamphetamine, tricyclic antidepressants, benzodiazepine	
Urinalysis	Normal	

PCO_2, partial pressure of carbon dioxide; HCO_3, bicarbonate; RT-PCR reverse transcription polymerase chain reaction

Chest Computed Tomography (CT) Scan [1]

- Chest CT revealed bilateral peripheral ground-glass opacities suggestive of COVID-19 infection.

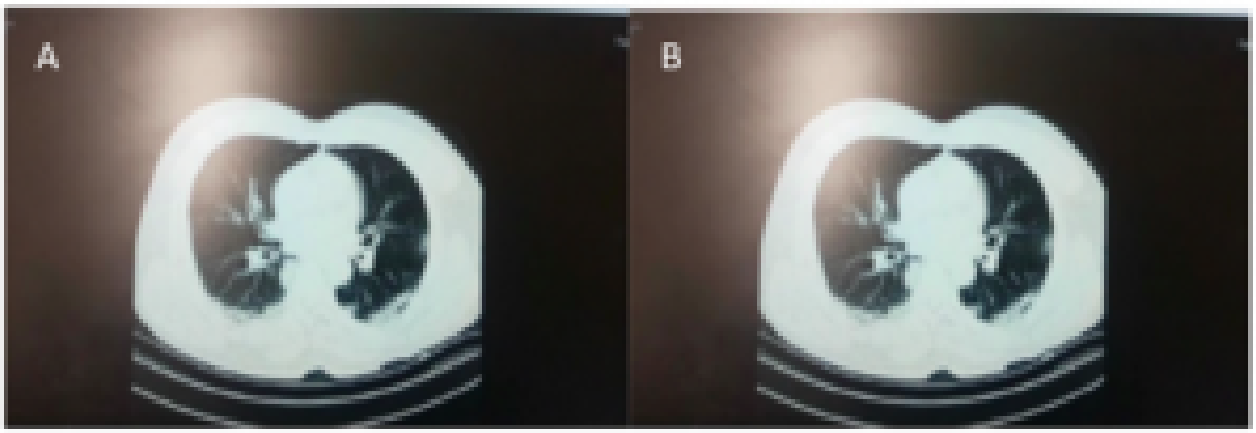

Figure 1: Lung high-resolution computed tomography.[1]

Brain MRI [1]

- Due to normal brain CT results, brain magnetic resonance imaging (MRI) was performed to evaluate the cause of dysarthria and bizarre behavior. The brain MRI results were normal.

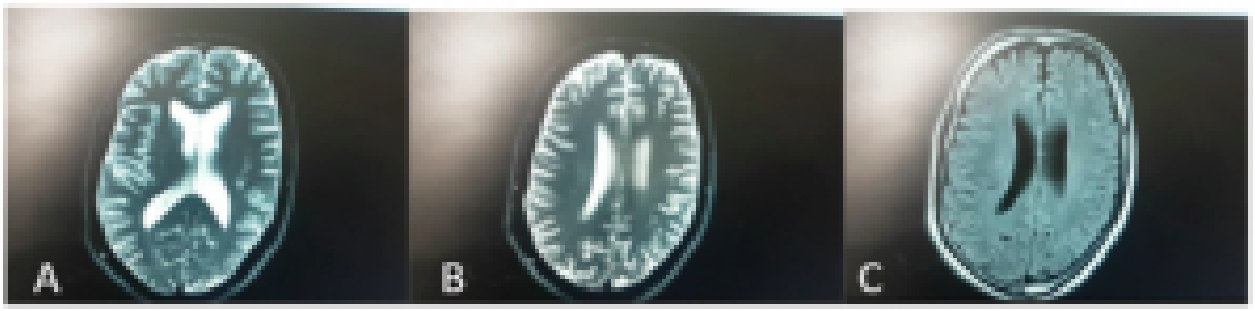

Figure 2: Brain magnetic resonance imaging with diffusion-weighted imaging.[1]

Question & Answers Leading to Diagnosis:

Question 1: Based on the clinical history of disease progression and physical examinations of the patient, which disease can we suspect initially and why?

Question 2: What investigations should we plan to confirm and understand the diagnosis?

Question 3: How can we correlate the neurological symptoms with COVID-19 disease?

Question 4: What are the atypical presentations of COVID-19 disease?

** For answers please check the next chapter.

Medical terminology/Abbreviations:

- Myalgia – Myalgia describes muscle aches and pain, which can involve ligaments, tendons, and fascia, the soft tissues that connect muscles, bones, and organs. Injuries, trauma, overuse, tension, certain drugs, and illnesses can all bring about myalgia.[3]
- Dysarthria – Dysarthria is a motor speech disorder in which the muscles that are used to produce speech are damaged, paralyzed, or weakened. The person with dysarthria cannot control their tongue or voice box and may slur words.[4]
- Kernig's sign – Kernig's sign is one of the physically demonstrable symptoms of meningitis. Severe stiffness of the hamstrings causes an inability to straighten the leg when the hip is flexed to 90 degrees. (Figure 3) It is used to diagnose meningitis.[5]

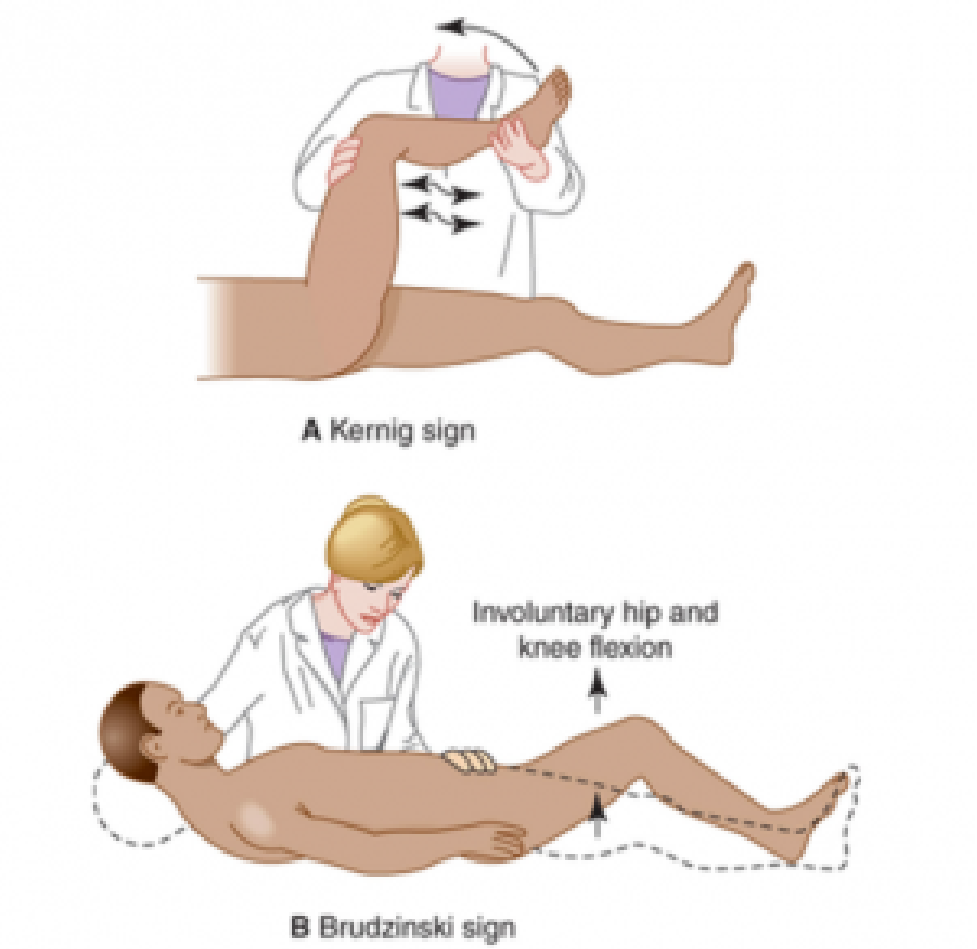

Figure 3: Kernig sign and Brudzinski sign[6]

- Brudzinski's sign – Brudzinski's sign is one of the physically demonstrable symptoms of meningitis. Severe neck stiffness causes a patient's hips and knees to flex when the neck is flexed. (Figure 3) It is used to diagnose meningitis.[7]
- Ground-glass opacities – According to Dr. Cortopassi, Ground glass opacities are a pattern that can be seen when the lungs are sick, while normal lung CT scans appear black, an abnormal chest CT with GGOs will show lighter-colored or gray patches. Those lighter patches don't completely obscure the other structures in the lungs. There is haziness seen overlying an area of the lung, but the underlying structures of the lung (airways, blood vessels, lung tissue) can still be identified. It resembles ground glass or glass that is still transparent but has a matte finish.[8]

    - GGOs aren't specific to COVID-19 and can be seen in so many different settings. GGOs in chest CT scans can also indicate congestive heart failure, inflammatory interstitial lung diseases, and diffuse alveolar hemorrhage (bleeding into the airspaces of the lungs), among other issues. But one of the most common diagnoses for GGOs is viral pneumonias, most often caused by respiratory syncytial virus (RSV), cytomegalovirus, herpes simplex virus, and coronavirus.[8]
    - In terms of COVID-19, Dr. Cortopassi explains GGOs on a CT scan are indicative of COVID-19-related pneumonia, or lung inflammation caused by the viral infection.[8]
    - A study published in the journal Radiology found that, among 51 Chinese patients with confirmed COVID-19 pneumonia, GGOs showed up in the chest CT scans of 77% of patients. And original research from scientists in China, also published in Radiology, found that CT scans were able to find 97% of COVID-19 infections overall, while blood tests were only able to correctly identify 59% of cases.[8]

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Further Reading

14.

CASE 3-2021: ANSWERS TO THE QUESTIONS

Answer to Question 1:

- Based on the clinical history of a 3-day fever and myalgia followed by cough, dyspnea, generalized headache, and bizarre behavior of the patient and- a suspicion of encephalopathy arises.[1]
- The absence of neck stiffness, Kernig's sign, or Brudzinski's sign rules out the possibility of meningitis here.[1]

Answer to Question 2:

- To understand the patient's condition and confirm the diagnosis routine blood tests along with chest CT scan and brain MRI should be done.[1]
- In this given case, though the MRI brain was normal, the CT scan revealed ground-glass opacity suggestive of COVID-19 disease.[1]
- To confirm the cause of the disease, RT-PCR COVID-19 was done, and it came out positive confirming the diagnosis of COVID-19 encephalopathy.[1]

Answer to Question 3:

- Common neurological manifestations reported for COVID-19 are acute stroke, impaired consciousness, and muscle injury. Patients with severe cases and older patients are more susceptible to these complications.[1]
- The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) invades the brain by various routes, such as binding to the ACE2 receptor on neurons and endothelial cells, through the olfactory system and spread across the cribriform plate, and by crossing the blood-brain barrier via infected leukocyte migration by a Trojan horse mechanism.[1]
- The etiology of encephalopathy or possible encephalitis in COVID-19 or other coronaviruses remains poorly understood and could be due to misdirected host immune responses. Neurological manifestations of COVID-19 derive from both direct invasion and indirect effects due to hyperinflammation and encephalopathy.[1]

Answer to Question 4:

- COVID-19 exhibits a diverse range of clinical presentations. Whilst classical respiratory symptoms of a dry cough have been underscored, these may be preceded by atypical respiratory symptoms such as hemoptysis.[2]
- Additionally, progressive gastrointestinal symptoms (diarrhea, vomiting, abdominal pain) may be the index presentation, even occurring in the absence of other features.[2]
- More recently, isolated anosmia or hyposmia has been widely reported as a primary symptom.[2]
- Ocular manifestations, primarily conjunctivitis, have also been pinpointed in case series, and the possibility of tear transmission has been broached.[2]
- In critically ill patients, evidence of raised inflammatory markers suggests that cytokine storm syndrome occurs in COVID-19 and may underlie some atypical presentations.[2]
- Cytokines have also been attributed to certain neurologic symptoms: a patient presenting with fever, cough, and altered mental status eventually developed acute necrotizing hemorrhagic encephalopathy. Other atypical neurologic presentations include acute cerebrovascular disease and muscle injuries.[2]

Diagnosis [1]

- Based on the respiratory problem and positive polymerase chain reaction (PCR) test for COVID-19, the final diagnosis was COVID-19.

Treatment and Prognosis [1]

- The patient was treated with hydroxychloroquine (200 mg twice daily for 5 days). After 2 days, dysarthria and abnormal behavior were resolved completely. The patient was discharged on day 4, with a resolution of respiratory and neurological signs and symptoms.

15.

CASE 4-2019: A 33-YEAR-OLD PREGNANT WOMAN WITH PNEUMONIA

"A case report of a pregnant woman infected with coronavirus disease 2019 pneumonia". (2020).

Peng, J., Li, R., Yin, H., Tang, F., Xie, H., Li, M., & Zhao, Y

Case Summary [1]

A 33-year-old pregnant woman was admitted to hospital at her 38+5 weeks of pregnancy with vaginal bleeding. She had a history of contact with COVID-19 case during her ***second trimester*** *and had symptoms of cough, expectoration and fever. Initially, she was misdiagnosed as common pneumonia and treated accordingly. But later as her symptoms didn't improve, and the Chest CT showed scattered consolidation and ground glass shadow in both lungs – she was clinically diagnosed with COVID-19 pneumonia during her 30 weeks of gestation and was quarantined. Her condition got improved with nebulization and antibiotic treatment. Later at 34+4 weeks of gestational period, her pharyngeal swab was tested for COVID-19 but came out negative. During her hospital admission on 38+5 weeks, her temperature was 36.4°C, heart rate was 78 bpm, respiratory rate was 20 bpm, blood pressure was 111/61 mmHg with no abnormalities on cardiopulmonary auscultation. She underwent a cesarean section and gave birth to a healthy newborn. COVID-19 Colloidal Gold method for both mother and baby were positive for IgG and negative for IgM and the baby's pharyngeal swab came out negative. During the hospitalization period, she developed no fever, cough or other symptoms. Five days after cesarean delivery, she was discharged.*

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://ecampusontario.pressbooks.pub/clinicalcases/?p=385#audio-385-1

Learning Objectives

- Identify the presentations of COVID-19 during pregnancy.
- Investigate and understand the differential diagnosis for COVID-19 pneumonia.
- Discuss the importance of medical imaging investigations for the diagnosis and prognosis of COVID-19 cases.
- Recognize the role of COVID-19 antibody tests along with their interpretation.

Clinical History [1]

- Age: 33 years old
- Sex: Female

Medical History [1]

- History of contact with diagnosed COVID-19 positive patient during her second trimester (middle phase of pregnancy, 4th to 6th month) on January 23, 2020.
- Record of developing cough and expectoration on January 26 and fever on January 27, 2020, with temperatures fluctuating in between 37.5°C and 37.8°C.
- Common pneumonia was diagnosed, and antibiotics were given for 3days in the community hospital.
- After that, based on the criteria of COVID-19 pneumonia in the New Coronavirus Prevention and Control Program (5th edition), she was diagnosed as a clinically confirmed case of COVID-19, and was

quarantined with nebulized inhalation and oral cephalosporin as part of treatment.

- Five days later (30 weeks gestation), her body temperature returned to normal and the symptoms such as cough and expectoration disappeared.

Drug History [1]

- History of antibiotics administration (Cephalosporine) during her second trimester.

Obstetric History [1]

- L.M.P (first day of last menstrual period) was on July 9, 2019.
- History of smooth uneventful early pregnancy.
- History of one previous cesarean delivery in 2015.

Symptoms [1]

- On April 5, 2020, at the gestational age of 38 weeks and 5days, she was admitted to the hospital with complaints of small amount of vaginal bleeding.

Examinations (Clinical Assays/Tests/Imaging) [1]

Physical Examination [1]

- Temperature: 36.4 °C
- Heart rate: 78 beats per minute.
- Respiratory rate: 20 beats per minute.
- Blood pressure: 111/61 mmHg
- No abnormalities were heard on cardiopulmonary auscultation.

Laboratory Investigations [1]

Blood Investigations on January 30, 2020 (29+2 weeks gestation)[1]:

Test	Result
Hemoglobin	115 gm/L
White blood cell count	8.15 x 109/L
Neutrophil ratio	78.6%
Lymphocyte count	1.08 x 109/L
Lymphocyte ratio	13.3%
C-reactive protein	99.67 mg/L
Influenza A and B virus antigens,	Negative
Test for Mycoplasma pneumoniae and Chlamydia pneumoniae	Negative

Pharyngeal swab test of SARS-CoV-2 [1]:

- It revealed twice negative at a community hospital on March 5 and March 7, 2020 (34+4 weeks of gestation).
- Again, the repeat tests conducted on April 6, 2020 (the first day after delivery) and April 7, 2020 (the second day after delivery) showed negative SARS-CoV-2 results.
- On April 7, 2020, the pharyngeal swab test for the newborn revealed negative.

Chest Computed Tomography (CT) Scan:

On January 30, 2020 (29+2 weeks of gestation) [1]:

- Chest CT showed scattered consolidation and ground-glass shadow of both lungs.

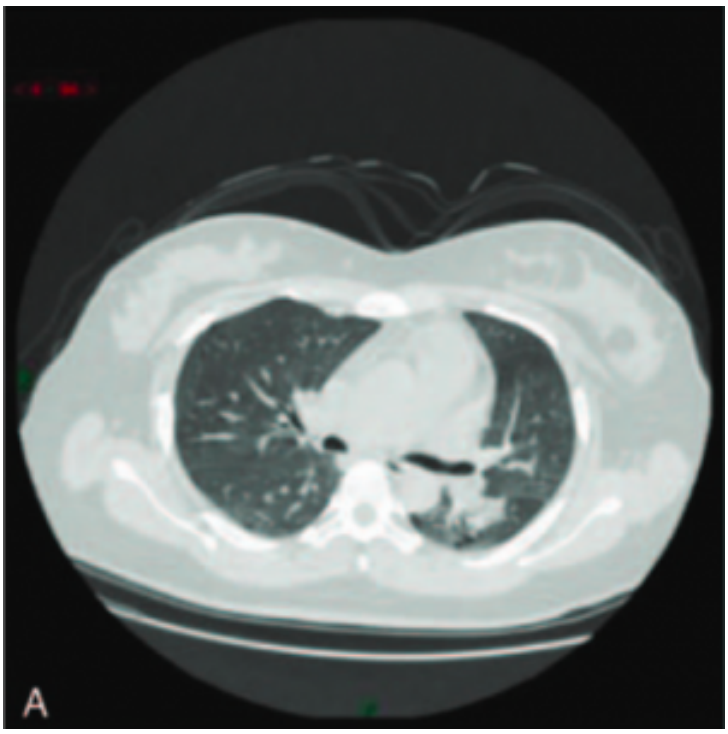

Figure 1: January 30, 2020, CT: scattered consolidation of both lungs and ground glass shadow. [1]

On March 24, 2020 (37 weeks of gestation) [1]:

- The pulmonary CT revealed that most of the lung lesions were absorbed.

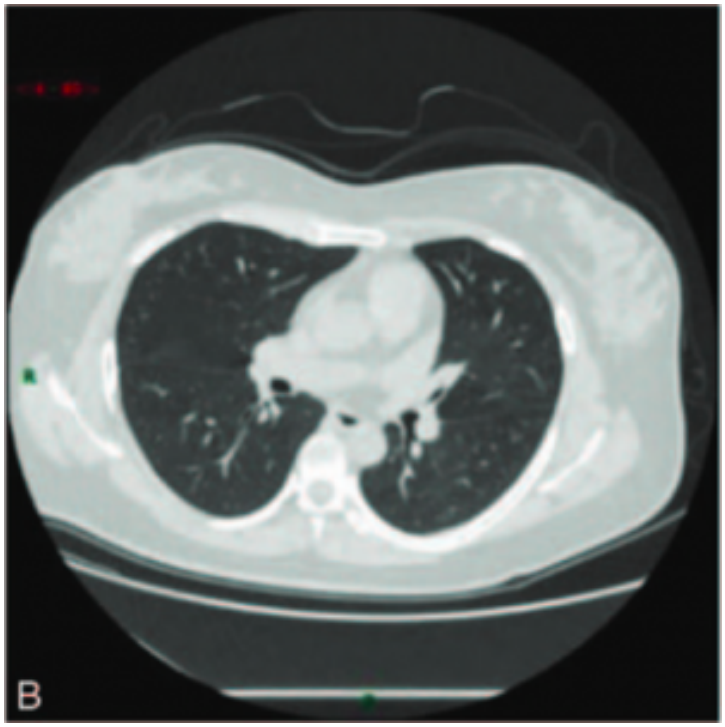

Figure 2: Mar 24, 2020, CT: most of the lung lesions are absorbed. [1]

On April 5, 2020 (38+8 weeks of gestation) [1]:

- The pulmonary CT scan revealed further absorption of the lung lesions.

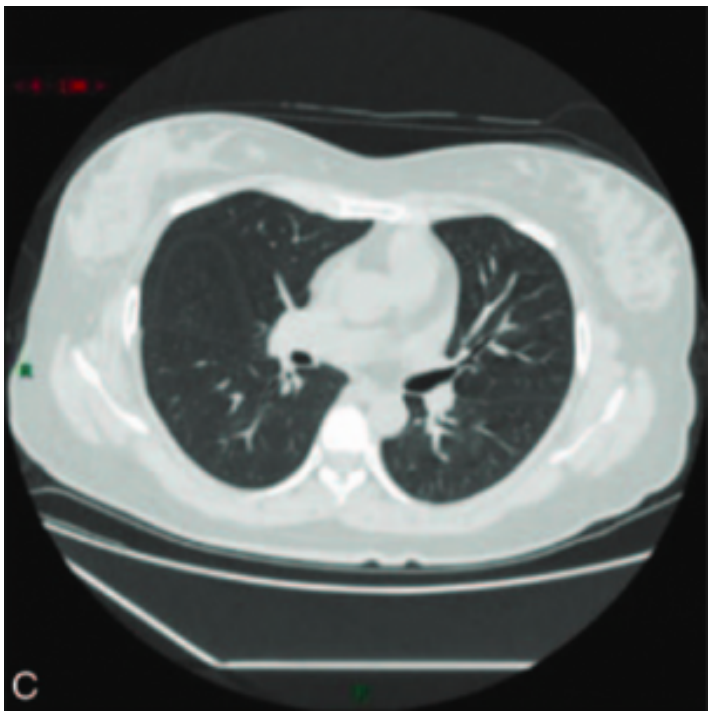

Figure 3: April 5, 2020, CT: further absorption of the lung lesions. [1]

Question & Answers Leading to Diagnosis:

Question 1: Despite being misdiagnosed initially as a common pneumonia case, how was the final diagnosis made in the given case?

Question 2: What could be the differential diagnosis/(s) for COVID-19 pneumonia and how can we differentiate them based on radiology?

Question 3: What are the risks of COVID-19 infection during pregnancy?

** For answers please check the next chapter.

Medical terminology/Abbreviations:

Trimester of pregnancy– A pregnancy is divided into trimesters:

- the first trimester is from week 1 to the end of week 12
- the second trimester is from week 13 to the end of week 26
- the third trimester is from week 27 to the end of the pregnancy.[4]

Ground-glass opacities – According to Dr. Cortopassi, Ground glass opacities are a pattern that can be seen when the lungs are sick, while normal lung CT scans appear black, an abnormal chest CT with GGOs will show lighter-colored or gray patches. Those lighter patches don't completely obscure the other structures in the lungs. There is haziness seen overlying an area of the lung, but the underlying structures of the lung (airways, blood vessels, lung tissue) can still be identified. It resembles, ground glass, or glass that is still transparent but has a matte finish.[5]

- GGOs aren't specific to COVID-19 and can be seen in so many different settings. GGOs in chest CT scans can also indicate congestive heart failure, inflammatory interstitial lung diseases, and diffuse alveolar hemorrhage (bleeding into the airspaces of the lungs), among other issues. But one of the most common diagnosis for GGOs is viral pneumonias, most often caused by respiratory syncytial virus (RSV), cytomegalovirus, herpes simplex virus, and coronavirus.[5]
- In terms of COVID-19, Dr. Cortopassi explains GGOs on a CT scan are indicative of COVID-19-related pneumonia, or lung inflammation caused by the viral infection.[5]
- A study published in the journal Radiology found that, among 51 Chinese patients with confirmed COVID-19 pneumonia, GGOs showed up in the chest CT scans of 77% of patients. And original research from scientists in China, also published in Radiology, found that CT scans were able to find 97% of COVID-19 infections overall, while blood tests were only able to correctly identify 59% of cases.[5]

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Further Reading

16.

CASE 4-2019: ANSWERS TO THE QUESTIONS

Answer to Question 1:

- In this given case based on her symptoms of fever, cough and expectoration, she was diagnosed as common pneumonia initially and was treated accordingly. But her condition didn't improve.[1]
- Additionally, her chest CT showed scattered consolidation and ground-glass shadow of both lungs. [1]
- She also had a close contact with a confirmed COVID-19 pneumonia case within 14 days of onset but did not accept throat swab nucleic acid test for SARS-CoV-2 at first.[1]
- Though later her pharyngeal swab test revealed negative for nucleic acid, she was diagnosed clinically as a case of COVID-19 pneumonia based on her symptoms and CT findings.[1]
- Moreover, she and her baby were also tested positive for COVID-19 IgG and negative for IgM during hospitalization, which further supported the diagnosis.[1]

Answer to Question 2:

- There is a wide spectrum of possible differential diagnoses for COVID-19 pneumonia, and it is always necessary to consider a triptych of clinical, laboratory and radiological data to reach the correct diagnosis.[2]

Table 1: Differential diagnosis of COVID-19 pneumonia with their radiological features[2]

Pathogenesis of differential diagnosis	Ground glass	Crazy paving	Consolidation
Bacterial pneumonia	R (ATYPICAL)	OD/A	C (TYPICAL)
Viral pneumonia	C	OD/A	R
Fungal: pneumocystis jiroveci pneumonia	C	R	R
Fungal: angioinvasive aspergillosis	(HALO)	OD/A	C
Acute pulmonary oedema	C (INTERSTITIAL)	C (INTERSTITIAL)	C (INTERSTITIAL)
Acute pulmonary embolism and infarctions	C	C	C
Vasculitis	C (HAEMORRAGE)	C (REABSORPTION)	C (MASSIVE HAEMORRAGE)
Hypersensitivity pneumonia	C	OD/A	R
Simple pulmonary eosinophilia	C	OD/A	C
Acute eosinophilic pneumonia	C	C	R
Chronic eosinophilic pneumonia	R	R	C
Fluid-related ab ingestis pneumonia	C	OD/A	C
Chronic lipoid pneumonia	C	C	C
Alveolar proteinosis	OD/A	C	R

(Analysed pathologies usually share at least one radiological feature, among ground-glass areas, crazy paving opacities and consolidations, with COVID-19 pneumonia. These findings may be either common or rare presentation of pathologies or be occasionally described/absent. The timing of these features' presentation frequently varies with respect to COVID-19 pneumonia characteristic phases. C, common; R, rare; OD/A, occasionally described/absent)[2]

Answer to Question 3:

- The overall risk of COVID-19 to pregnant women is low. However, pregnancy increases the risk for severe illness and death with COVID-19. Pregnant women who have COVID-19 appear more likely to develop respiratory complications requiring intensive care than women who aren't pregnant, according to the Centers for Disease Control and Prevention (CDC). Pregnant women are also more likely to be placed on a ventilator.[3]
- Pregnant women who have underlying medical conditions, such as diabetes, also might be at even higher risk of severe illness due to COVID-19.[3]
- Some research suggests that pregnant women with COVID-19 are also more likely to have a premature birth and cesarean delivery, and their babies are more likely to be admitted to a neonatal unit.[3]

Diagnosis [1]

- This is a case of pregnancy with clinically confirmed COVID-19 pneumonia.

Management [1]**:**

- Initially, the patient was mistreated for common pneumonia but later she was placed in quarantine and treated accordingly for COVID-19 pneumonia. Her condition gradually improved and the rest of her pregnancy period was uneventful. Then on her 38+5 weeks of gestational period, she underwent cesarean section and gave birth to a healthy newborn of 3100 gm and APGAR score 10 on both 1-min and 5-min assessment.

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PART III

CRITICAL CARE MEDICINE CASE STUDIES

Intensive care medicine also called critical care medicine, is a medical specialty that deals with seriously or critically ill patients who have, are at risk of, or are recovering from conditions that may be life-threatening.[1]

Patients are admitted to the intensive care unit if their medical needs are greater than what the general hospital ward can provide. Indications for the ICU include blood pressure support for cardiovascular instability (hypertension/hypotension), sepsis, or certain cardiac arrhythmias. Other ICU needs include airway or ventilator support due to respiratory compromise. The cumulative effects of multiple organ failure, more commonly referred to as multiple organ dysfunction syndrome, also require advanced care.[2]

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17.

CASE 1-2020: A 29-YEAR-OLD MALE WITH HIGH GRADE FEVER

Value of dynamic plasma cell-free DNA monitoring in septic shock syndrome: A case report. World Journal of Clinical Cases. 2020;8(1):200-207.

Liu J, Zhang S, Pan S.

Case Summary [1]

A 29-year-old male was brought to the hospital with a history of high fever, gum pain, and swelling for 1 day along with intermittent upper abdominal pain, nausea, and retching. His physical examination revealed a temperature of 39.8 °C, very low BP (80/50mmHg), rapid pulse rate (130 beats/min), and abdominal palpation manifested tender right upper abdomen with positive ***Murphy's sign*** *and liver percussion pain. Laboratory investigation showed signs of sepsis in CBC with elevated CRP, liver enzymes,* ***procalcitonin****, and metabolic acidosis with hypokalemia and hypocalcemia. Blood culture was positive for Gram-negative bacilli. An abdominal CT scan revealed liver and gall bladder involvement with cardiac dysfunction and pulmonary edema. The patient was treated in ICU and initial investigations were repeated for monitoring purposes. Cell-free DNA (****CfDNA****) level was also measured as a marker of sepsis. Unfortunately, the patient expired on the 9th day of his admission due to septic shock.*

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Learning Objectives

- Identifying the signs of suspected septic shock.
- Recognize the clinical and laboratory findings associated with sepsis.
- Understand the rationale of newer biomarkers such as the cfDNA test (cell free DNA).
- Familiarizing and defining new medical terminology associated with septic shock.

Clinical History [1]

- Age: 29 years old
- Sex: Male

Medical History [1]

- History of a left lateral malleolus fracture subluxation 6 years ago.
- Allergies to penicillin and amoxicillin.
- No history of smoking, drinking, hyperlipemia, and chronic diseases, such as coronary heart disease, hypertension and diabetes.

Drug History [1]

- Not applicable.

Symptoms [1]

- Pain and bilateral gum swelling for 1 day.
- Sudden chill and a high fever with a peak of 39.8 °C on the morning of admission on July 27, 2017.
- Also presented intermittent right upper quadrant pain, accompanied by nausea and retching.

Examinations (Clinical Assays/Tests/Imaging) [1]

Physical Examination [1]

- Temperature: 39.8 °C
- Blood pressure: 80/50 mmHg
- Pulse: 130 beats/min.
- On abdominal examination:
    - Prominent right upper abdomen which was tender at palpation without guarding and rebound tenderness.
    - Presence of positive Murphy's sign and liver percussion pain.

Laboratory Investigations [1]

- Laboratory tests showed leukocytopenia (2.38 × 109/L), a high percentage of neutrophils (83.2%), mild thrombocytopenia (68 × 109/L), abnormal blood coagulation function, a reduced international normalized ratio, hypokalemia, hyperbilirubinemia, elevated liver enzymes (both hepatocellular and cholestatic enzymes), an elevated procalcitonin (PCT) concentration (35.30 ng/mL), metabolic acidosis, and hyperlactatemia, suggesting progressive sepsis.

Chart 1: Laboratory parameters[1]

Parameter	Normal range	On admission 27 July	HD 2, 28 July	HD 3, 29 July	HD 4, 30 July	HD 5, 31 July	HD 6, 1 August	HD 7, 2 August	HD 8, 3 August
Hemoglobin (g/L)	130-175	131	123	113	93	101	94	104	93
RBC (× 10^{12}/L)	4.30-5.80	4.78	3.91	3.62	2.95	3.25	3.06	3.32	2.94
WBC (× 10^{9}/L)	3.50-9.50	2.58	14.97	29.40	12.33	10.21	8.34	5.09	6.43
NEUT (%)	40.0-75.0	85.2	96.6	97.6	86.3	73.7	11.5	61.0	2.4
LYMPH (%)	20.0-50.0	14.8	3.5	3.62	3.2	15.9	82.0	25.0	86.0
Platelets (× 10^{9}/L)	125-350	68	44	42	51	43	48	21	16
Glucose (mmol/L)	3.9-6.1	/	7.3	10.9	/	6.5	6.3	4.7	/
Sodium (mmol/L)	137-147	138.9	148.3	150.5	148.7	148.7	149.8	155.0	155.5
Potassium (mmol/L)	3.5-5.3	3.2	2.6	4.6	3.3	3.8	3.8	3.4	2.9
Calcium (mmol/L)	2.20-2.65	2.08	2.10	2.04	1.94	2.35	2.35	2.09	1.99
Total bilirubin (μmol/L)	0.0-22.0	41.0	47.9	65.6	/	69.1	98.3	95.9	51.3
AST (IU/L)	0-45	97.2	198.5	165.8	62	65.5	118.1	229.5	55.5
ALT (IU/L)	13-69	62.5	72.7	56.2	39.8	33.8	55.6	62.7	25.4
GGT (IU/L)	8-78	255	530.4	285.9	/	144.1	124	162.9	72.0
Alkaline phosphatase (IU/L)	38-126	88	63.0	88	/	107.4	99	182.6	97.2
LDH (IU/L)	140-271	433	626	559	/	402	/	437	295
Albumin (g/L)	40.0-55.0	/	39.5	41.1	/	47.5	/	47.6	44.0
Globulin (g/L)	20.0-40.0	/	34.1	22.9	/	20.8	/	28.0	35.0
Urea (mmol/L)	2.10-7.20	5.91	10.00	12.50	/	13.81	15.64	17.29	12.79
Creatinine (μmol/L)	44.0-132.0	110.8	143.3	147.3	/	80.6	84.4	74.8	110.8
Lactate (mmol/L)	0.5-1.6	8.8	3.8	2.9	/	3.9	8.3	4.1	> 18
Procalcitonin (ng/mL)	0-0.05	35.50	96.50	18.74	2.82	3.22	0.99	2.15	8.12
C-reactive protein (mg/L)	0-10	/	> 96.00	/	> 96.00	/	/	/	> 96.00

Bold face numbers denote figures out of the normal range. ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; GGT: Gamma glutamyl transferase; HD: Day of hospitalization; LDH: Lactate dehydrogenase; RBC: Red blood cells; WBC: White blood cells.

Microscopic Examinations [1]

- On light microscopy, the peripheral blood smear showed a left shift of neutrophil nuclei, prominent **toxic granulations** and vacuolation in the neutrophil cytoplasm (Figure 1).
- Gram-negative bacilli were isolated from blood cultures.

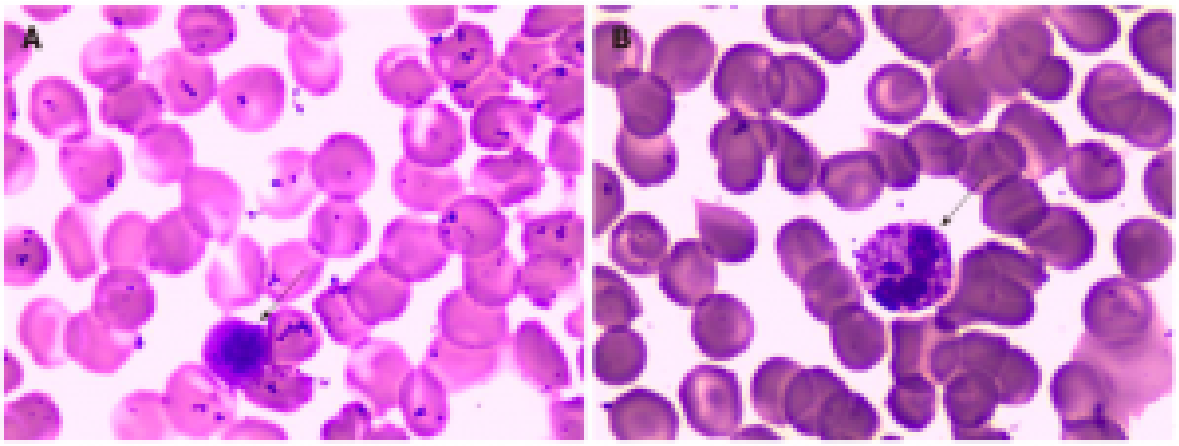

Figure 1: The peripheral blood smear showed a left shift of neutrophil nuclei, prominent toxic granulations, and vacuolation in the neutrophil cytoplasm (see black arrows) (Wright stain ×1000).[1]

Head Computed Tomography (CT) Scan [1]

- No abnormality was reported.

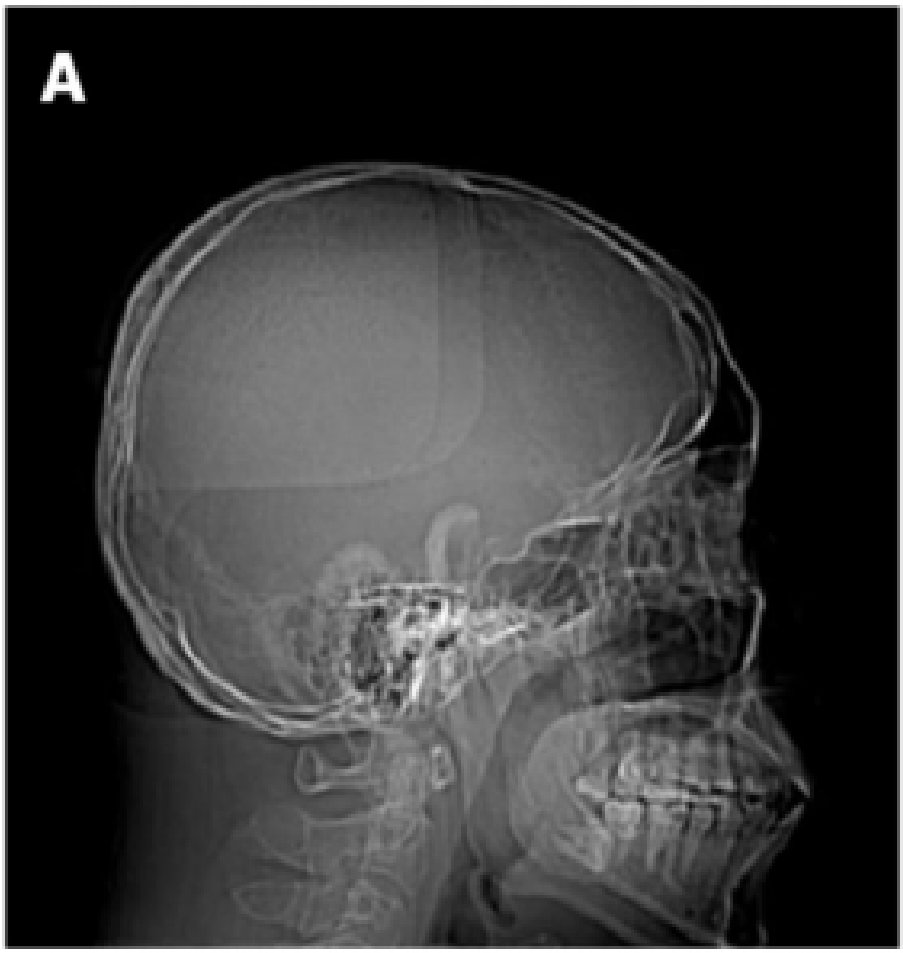

Figure 2: A. Head computed tomography (CT) scan.[1]

Chest Computed Tomography (CT) Scan [1]

- Showed little interstitial change in the lower lung. (yellow arrows pointing to the lower lung).

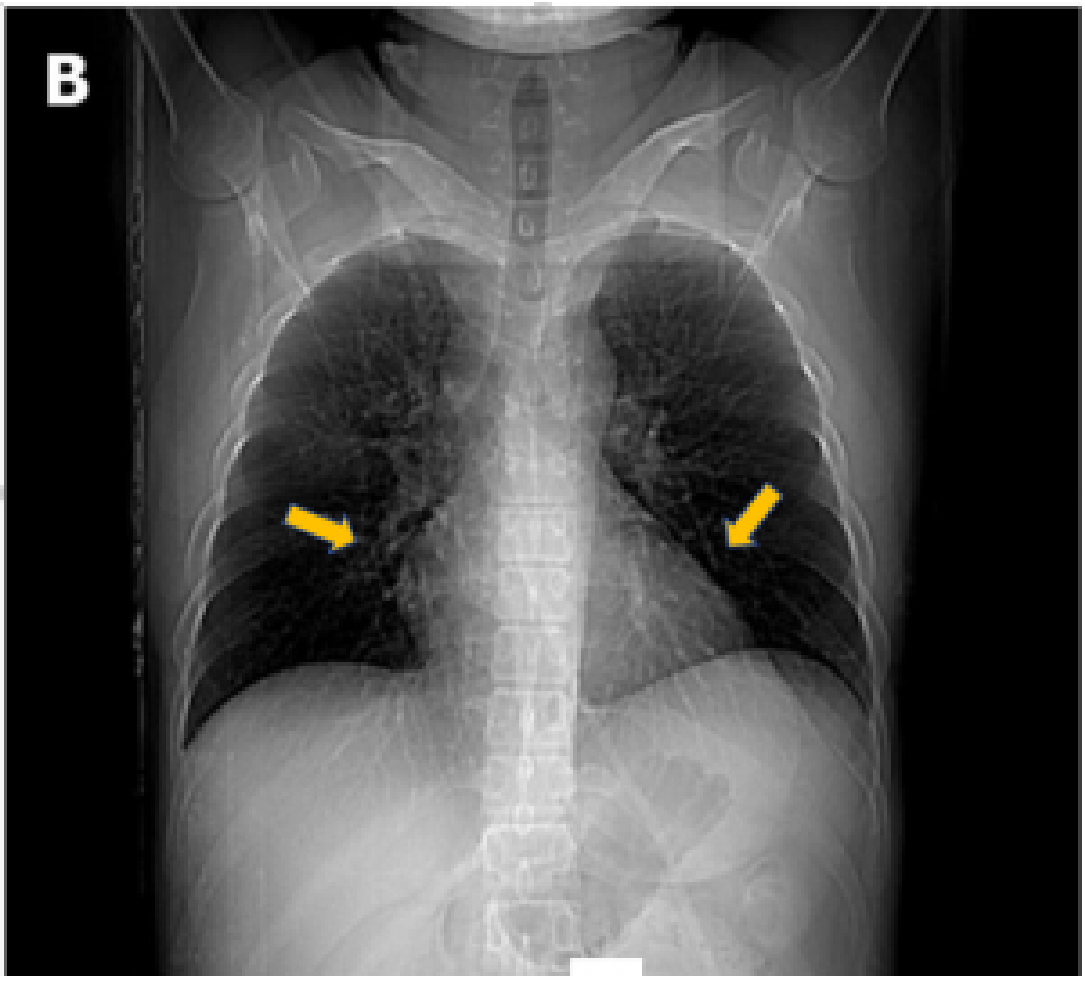

Figure 3: B. Multislice CT chest scan, showing little interstitial change (yellow arrows) in the lower lung.[1]

Abdominal Computed Tomography (CT) Scan [1]

- Scanning of the abdomen showed gallbladder wall edema with increased gallbladder density, swelling of the kidneys, and an enlarged pancreas. There was interlobular septal thickening on both sides and bilateral pleural effusion with lower lung insufficiency of both longs, suggesting cardiac dysfunction with pulmonary edema.

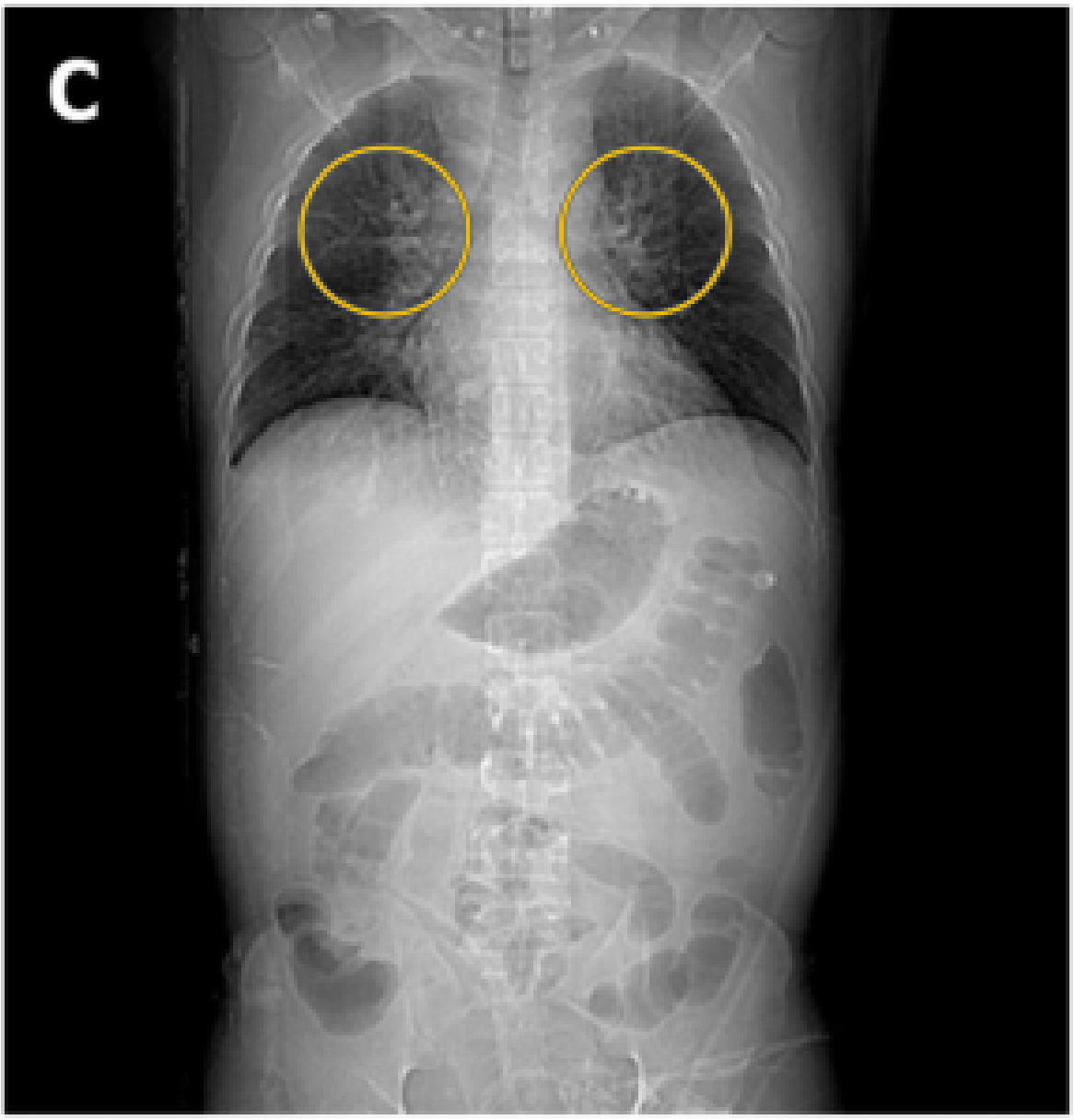

Figure 4: C. An abdominal CT scan suggested cardiac dysfunction with pulmonary edema.[1] *(Yellow circle showing batwing sign of pulmonary edema.*[6]*)*

Plasma Cell-Free DNA Levels [1]

- cfDNA levels were measured by a duplex real-time PCR assay with internal control, which was developed as a novel method for the accurate quantification of plasma cfDNA. Within the 95% confidence interval, the normal reference intervals were 0-52.5 ng/mL for males and 0-45.8 ng/mL for females. However, plasma cfDNA levels were constantly high, peaking at 1366.40 ng/mL (Figure 5).

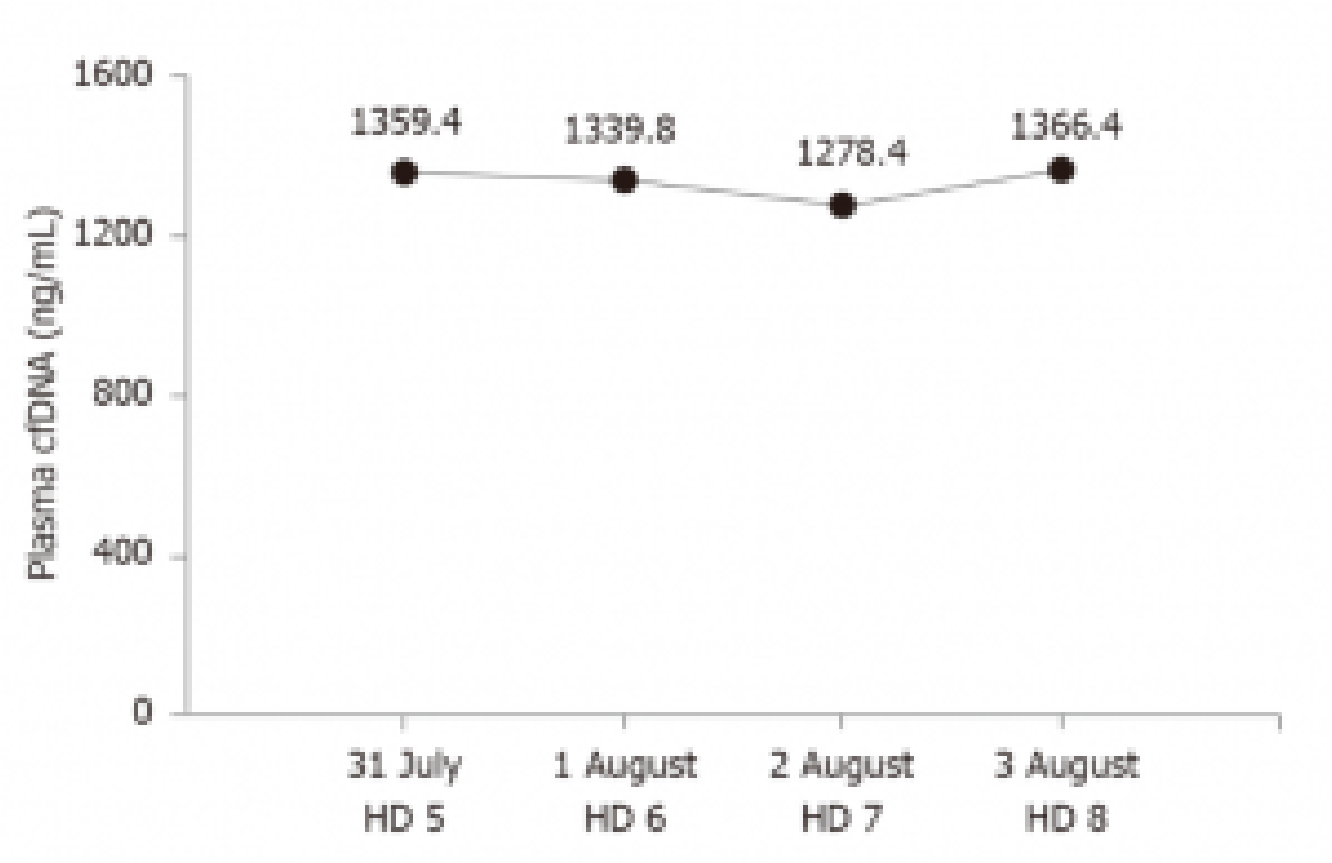

Figure 5: Plasma cell-free DNA concentrations. cfDNA: Cell-free DNA; HD: Day of hospitalization. [1]

Peripheral Blood Smear and Bone Marrow Examination [1]

- On the 7th day, Peripheral blood and bone marrow examinations showed granulocyte maturation disorders, which may have been caused by infection (figure 6).

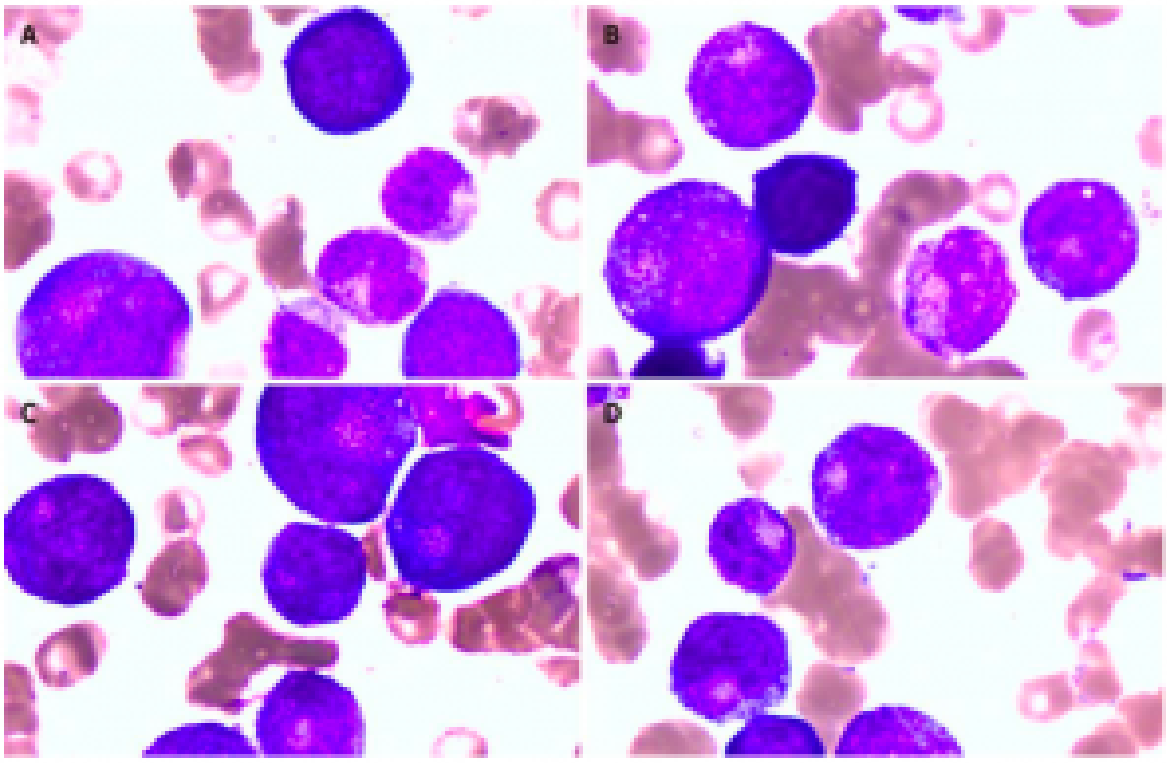

Figure 6: The bone marrow smear showed granulocyte maturation disorders. A-D: Bone marrow smear. Wright stain ×1000.[1]

Question & Answers Leading to Diagnosis:

Question 1: Based on chief complaints, medical history, physical examination, what initial diagnosis can we suspect?

Question 2: Which lab investigations should be done to confirm the diagnosis and what finding are confirmatory to reach the final diagnosis in this case study?

Question 3: What investigations can be suggested to monitor the condition of this patient? Is there any specific biomarker which can be useful in this regard?

** For answers please check the next chapter.

Medical terminology/Abbreviations:

- Murphy's sign – Murphy's sign is elicited in patients with acute cholecystitis by asking the patient to take in and hold a deep breath while palpating the right subcostal area. If pain occurs on inspiration, when the inflamed gallbladder meets the examiner's hand, Murphy's sign is positive.[2] A positive Murphy's sign is seen in acute cholecystitis.
- Procalcitonin – Procalcitonin is a substance produced by many types of cells in the body, often in response to bacterial infections but also in response to tissue injury. The level of procalcitonin in the blood can increase significantly in systemic bacterial infections and sepsis. This test measures the level of procalcitonin in the blood.[3]
- Toxic granulations – Toxic granulations are purple or dark-blue staining azurophilic granules in the cytoplasm of neutrophils, bands, and metamyelocytes resulting from an abnormality in the maturation of the primary granules with consequent retention of their azurophilic property, while toxic vacuolizations are vacuoles representing phagocytosis and depletion of toxic granules.[4]
- Interstitial change in the lung – When these interstitial changes occur, your physician may see "increased interstitial markings" on your chest x-ray or CT scan because the inflammation, swelling, or scarring of the interstitium makes the tissue denser so that it is now visible as white "interstitial markings" on the x-ray or scan.[5]
- CfDNA – In addition to the classic biomarkers, cfDNA was first described in 1948, has the potential to be a useful marker in septic shock. CfDNA is released into the circulation through cell lysis, necrosis, apoptosis, and active DNA release, resulting in higher concentrations of cfDNA in patients with microbial infections, trauma, cancer, and other clinical conditions. Although elevated levels of cfDNA are not specific to a single disease, elevated cfDNA has been shown to be an extremely sensitive and promising prognostic marker in septic shock. This observation may be associated with the shorter half-life of cfDNA than that of PCT and CRP. According to Ahmed, cfDNA is a good prognostic predictor for patients in the ICU and, to a lesser extent, is a good marker of septic shock. However, the inevitable loss of cfDNA during extraction has become a considerable detriment, hindering its clinical applications. We previously developed a duplex real-time PCR assay with an internal control as a novel

method for the accurate quantification of plasma cfDNA, which can eliminate preanalytical errors and increase precision and accuracy. Our previous studies showed the clinical value of plasma cfDNA levels, as measured by this novel method, in several conditions. CfDNA levels can be useful not only in evaluating chemotherapy effects and guiding treatment in advanced lung cancer patients but also in assessing liver injury in hepatitis B patients. In this case, cfDNA remained high until the patient died, suggesting that cfDNA could be used to monitor disease progression more effectively than PCT.[1]

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Further Reading

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18.

CASE 1-2020: ANSWERS TO THE QUESTIONS

Answer to Question 1:

- The suspected diagnosis is septic shock. Points in favor of the diagnosis are as follows-
    - From the symptoms, patient presented with gum pain and swelling associated with high fever which indicates a focal point of infection.[1]
    - Patient also complained of abdominal pain with positive findings in examinations like positive Murphy's sign (Murphy's sign is elicited in patients with acute cholecystitis by asking the patient to take in and hold a deep breath while palpating the right subcostal area.[2]) and pain in liver percussion which indicates the involvement of gall bladder and liver respectively.[1]
    - On examination, patient was hemodynamically unstable with very low blood pressure (80/50 mmHg) and high pulse rate 130 beats/min, which indicates that patient in in shock.
    - Therefore, considering sudden onset of shock which coincides with the gum infection, the initial suspected diagnosis is septic shock. [1]

Answer to Question 2:

- To confirm the diagnosis several lab investigations like complete blood count, liver function test, serum electrolytes, blood microscopy, blood culture, and imaging investigations like CT chest and abdomen should be done.[1]
- In our case study, lab investigation findings that support the diagnosis of septic shock are

given below-

- In complete blood count, features of acute infections are present such as leukocytopenia (2.38 × 109/L), a high percentage of neutrophils (83.2%), mild thrombocytopenia (68 × 109/L)
- Electrolyte analysis showed, hypokalemia and hypocalcemia with progressing metabolic acidosis.
- Liver function test manifested hyperbilirubinemia, elevated liver enzymes (both hepatocellular and cholestatic enzymes), an elevated procalcitonin (PCT) concentration (35.30 ng/mL).
- Blood culture revealed Gram negative bacilli which supports the diagnosis of sepsis.
- Abdominal CT scans exhibited the gallbladder wall edema with increased gallbladder density, swelling of the kidneys, and an enlarged pancreas. There was interlobular septal thickening on both sides and bilateral pleural effusion with lower lung insufficiency of both longs, suggesting cardiac dysfunction with pulmonary edema.
- All above features from investigations supports that the patient was having a septic shock involving multiorgan.[1]

Answer to Question 3:

- To monitor the condition of the patient, all blood investigations which were done initially should be repeated in a specific interval. Complete blood count, CRP level, liver function tests, serum creatinine level, serum electrolyte level, serum lactate, and pro-calcitonin level should be conducted at regular intervals to monitor the patient's condition. [1]
- In case of septic shock, a newer biomarker like cell-free DNA (cfDNA) level can be useful for monitoring the patient. CfDNA is released into the circulation through cell lysis, necrosis, apoptosis, and active DNA release, resulting in higher concentrations of cfDNA in patients with microbial infections, trauma, cancer, and other clinical conditions. Although elevated levels of cfDNA are not specific to a single disease, elevated cfDNA has been shown to be an extremely sensitive and promising prognostic marker in septic shock. This

observation may be associated with the shorter half-life of cfDNA than that of PCT and CRP. According to Ahmed, cfDNA is a good prognostic predictor for patients in the ICU and, to a lesser extent, is a good marker of septic shock. [1]

Diagnosis [1]

- Septic shock.

PART IV

ENDOCRINOLOGY CASE STUDIES

Endocrinology is the branch of medicine dealing with the conditions of endocrine glands and their secreted hormones. There are several endocrine glands in the human body namely, the Pituitary, Hypothalamus, Thyroid, Parathyroid, Thymus, Pancreas, Adrenal glands, Testis, and Ovary.

Common endocrine diseases

1. Diabetes type 1 & 2
2. Hyperthyroidism and Hypothyroidism
3. Addison's disease
4. Cushing syndrome
5. Osteoporosis
6. Obesity
7. Hypopituitarism and Hyperpituiterism.
8. Acromegaly etc.

Common signs and symptoms

1. Unexplained weight loss or gain
2. Infertility
3. Fatigue
4. Nausea & vomiting
5. Headache
6. Diarrhea or constipation
7. High or low blood pressure
8. High or low blood sugar
9. Heat or cold intolerance
10. Goiter
11. Menstrual abnormality etc.

Common investigations

1. Serum hormone levels
2. Ultrasonogram
3. CT scan
4. MRI scan
5. Positron emission tomography or PET scan
6. Scintigraphy
7. FNAC
8. Biopsy

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19.

CASE 2-2012: A 38-YEAR-OLD FEMALE WITH WEIGH LOSS, LEG EDEMA AND HAND TREMOR

Unilateral pitting edema of the leg as a manifestation of Graves' disease: a case report. Journal Of Medical Case Reports, 2012,6(1). doi: 10.1186/1752-1947-6-258

Volke, V., & Matjus, S.

Case Summary [1]

A 38-year-old Caucasian female had been experiencing symptoms of ***hyperthyroidism*** *for five months and had developed pitting edema of the left leg four months prior to. The patient had lost approximately 3 kilograms and had mild hand tremors. The patient's physical examinations revealed* ***tachycardia*** *(95 beats per minute) and a smooth thyroid – with a slightly increased volume. Laboratory investigations revealed normal* ***D-dimer*** *levels and suppressed* ***thyroid-stimulating hormone*** *levels (less than 0.001 mIU/L, local reference of 0.4 mIU/L to 4 mIU/L).*

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://ecampusontario.pressbooks.pub/clinicalcases/?p=91#audio-91-1

Learning Objectives

- Investigating the clinical history of the patient with symptoms of hyperthyroidism and selecting appropriate examinations for further analysis and diagnosis.
- Familiarizing and defining new medical terminology associated with the endocrinological disease while understanding the purpose of each lab investigation.
- Extrapolating key lifestyle factors that have contributed to the disease and correlating the diagnosis to the laboratory results.

Clinical History [1]

- Age: 38 years old
- Sex: Female
- Ethnicity: Caucasian

Medical History [1]

- No history of taking oral contraceptive pills.

Symptoms [1]

- Symptoms of hyperthyroidism lasting for ~five months.
  - Weight loss (3 kg)
  - Irritability
  - Mild hand tremor
- She developed painless pitting edema of the left leg four months before
- No history of trauma

Examinations (Clinical Assays/Tests/Imaging) [1]

Physical Examination [1]

- Signs of **thyrotoxicosis** were moderate: hand tremor, tachycardia (95 beats per minute)
- Warm skin was apparent.
- Thyroid was smooth, slightly increased volume, and was not tender on palpation.
- No eye involvement except mild **periorbital edema** of her left eye
- The skin of both legs was of normal color and the pitting edema on her left leg was of a diffuse nature and spread to two-thirds of her leg.
- The skin surface was smooth and had no elevations or discoloration, whereas her right leg appeared normal.

Laboratory Investigations [1]

- Thyroid-stimulating hormone level (less than 0.001 mlU/L, local reference of 0.4 to 4).
- Free T4 (75 pmol/L, local reference of 10.3 to 24.5)
- **Anti-thyroid receptor antibodies** (13.5 U/L, local reference of less than one and a half)
- Antithyroid peroxisomal antibodies are normal (26 IU/L, local reference of less than 35).
- Normal D-dimer levels.

Doppler Ultrasound [1]

- Had normal findings of her leg veins.

Question & Answers Leading to Diagnosis:

Question 1: Based on the patient physicals symptoms, such as mild hand tremors, weight loss and edema, what lab investigations should be conducted to determine the diagnosis?

Question 2: Thyroid-stimulating hormones levels were low while free T4 levels were high, what immediate diagnosis could be suggested?

Question 3: Hyperthyroidism can be the by-product of difference illnesses; what lab investigations would support a specific diagnosis and what is that diagnosis?

Question 4: How could we correlate this diagnosis with the patient's demographic?

** For answers please check the next chapter.

Medical terminology/Abbreviations:

- Anti-thyroid peroxisomal antibodies – Antibodies that are associated with a thyroid disease due to an autoimmune disorder.[9]
- Anti-thyroid receptor antibodies – Antibodies responsible for blocking, neutralizing, and activating thyroid receptors, associated with autoimmune thyrotoxicosis. [10, 11]
- Congestive heart failure – A condition where the heart muscles don't pump blood as efficiently as they should. [5]
- D-dimer – Small protein fragment found in the blood post blood clot degradation by fibrinolysis. [12]
- Hyperthyroidism – An overactive thyroid, occurring when the thyroid gland produces an excess amount of hormone thyroxine.[2]
- Periorbital edema – Swelling around the eye. [13]
- Pretibial myxedema – Describes localized lesions of the skin due to the deposition of hyaluronic acid, a rare thyroid disease. [4]
- Tachycardia – A condition where a pulse exceeds 100 beats per minute. [8]
- Thyroid acropachy – A rare autoimmune thyroid disease. [3]
- Thyroid dermopathy – Thickening of the skin usually in the pretibial area, a symptom of hyperthyroidism. [14]
- Thyroid-stimulating hormone – A hormone made in the pituitary gland to regulate your weight, body temperature, muscle strength, and mood. 7
- Thyrotoxicosis – Excess thyroid hormone in the body. [6]

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Further Reading

20.

CASE 2-2012: ANSWERS TO THE QUESTIONS

Answer to Question 1: Based on the patient's physical symptoms and diagnosis of edema, physicians should request lab investigations inclusive of thyroid function hormones. According to the literature, symptoms of hand tremors and weight loss are common in patients with hyperthyroidism.1 The literature would further support that pitting edema without heart failure has been cited in the context of hyperthyroidism. As such, a thyroid function test should be conducted to investigate levels of thyroid-stimulating hormone (high levels – too much hormone, low levels – lack of hormone) and thyroxine-free T4 (unbound hormone, high levels – overactive thyroid, low levels – underactive thyroid) in the blood.[1,18]

Answer to Question 2: Low thyroid-stimulating hormone levels would support that the thyroid is making too much of the hormone, while high levels of T4 support an overactive thyroid.[1,15,16] With or without the consideration of this patient's symptoms, she could be diagnosed with hyperthyroidism.[15,16]

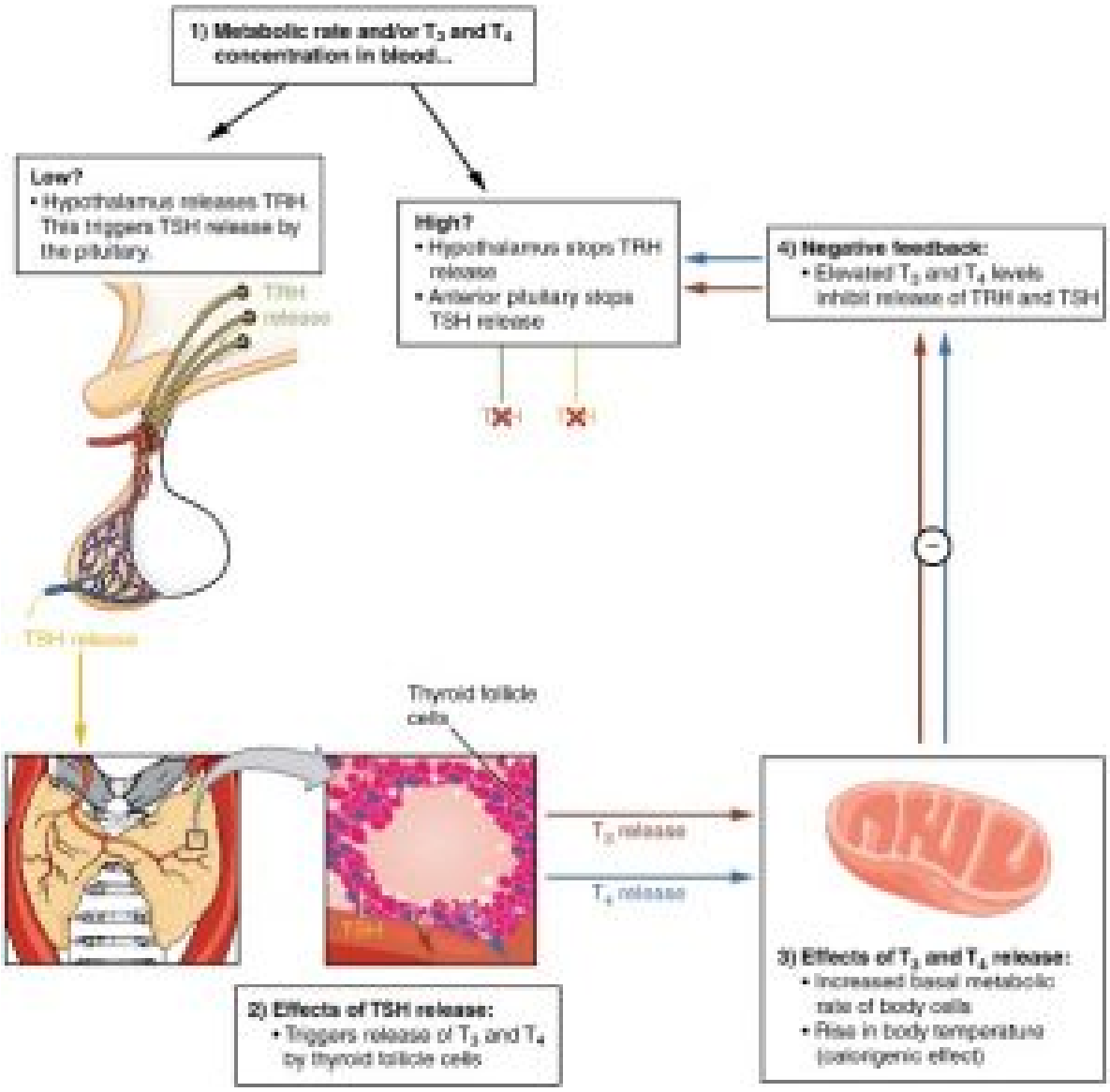

Figure 1: Negative Feedback Loop showing the regulation of the thyroid hormone levels.[20]

Answer to Question 3:

- Laboratory investigations revealed high levels of anti-thyroid receptor antibodies (13.5 U/

L, local reference of less than one and a half). The presence of these antibodies has been used to test for autoimmune thyroid diseases. These antibodies are imperative in the detection of Grave's disease and Hashimoto thyroiditis.[10]

- Grave's disease is when there's an overproduction of thyroid hormones, it is one of the most common diseases of hyperthyroidism.[1]
- Hashimoto's disease is leading to an underactive thyroid gland and is one of the common causes of hypothyroidism.19

- With consideration of the patient's symptoms, inclusive of hand tremors, irritability, weight loss, and the overproduction of the anti-thyroid receptor antibodies would support the diagnosis of Grave's disease.[1]

Answer to Question 4: Grave's disease is ~8 times more common in women than men, usually affecting people between the ages of 30-50 or reproductive years. This patient falls within both these categories where autoimmune diseases are more likely to occur.[17]

Diagnosis [1]

- Pitting edema of the leg as a manifestation of Graves' disease.

Treatment [1]

- Treatment of 10 mg of thiamazole three times a day was started.
- During the treatment course of 12 months, free T4 levels were normalized, and edema was completely cleared.

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21.

CASE 3-2017: A 40-YEAR-OLD FEMALE WITH EPIGASTRIC PAIN, NAUSEA AND VOMITING

Acute Pancreatitis: An Atypical Presentation. Case reports in gastroenterology, 2017, 11(2), 359–363. https://doi.org/10.1159/000475920

Nadhem, O., & Salh, O.

Case Summary [1]

A 40-year-old woman is presented with severe, sharp ***epigastric*** *pain radiating to the back with symptoms of nausea and vomiting. She has a medical history of hypertension and* ***cholecystectomy*** *three years prior to this hospital admission. Upon examination epigastric tenderness was present. Lab investigations showed whole blood cell counts were high (22.1 × 103/μL with neutrophils 87%) while serum amylase and lipase level were normal. To exclude further diagnosis an abdominal computed tomography (CT) scan was done which showed fat stranding in the pancreatic head.*

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://ecampusontario.pressbooks.pub/clinicalcases/?p=93#audio-93-1

Learning Objectives

- Investigating the clinical history of the patient and selecting appropriate examinations for the diagnosis of **acute pancreatitis**.
- Understanding the atypical presentation of acute pancreatitis and identifying those presented in the patient.
- Familiarizing and defining new medical terminology associated with acute pancreatitis.

Clinical History [1]

- Age: 40 years old
- Sex: Female

Medical History [1]

- Hypertension
- Bipolar disorder
- Cholecystectomy (three years prior to this hospital admission)

Symptoms [1]

- Severe, sharp epigastric abdominal pain radiating to the back.
- Nausea and vomiting.

Examinations (Clinical Assays/Tests/Imaging) [1]

Physical Examination [1]

- Heart rate – 105 beats/min
- Blood pressure – 132/84 mm Hg
- Severe epigastric tenderness- present.

Blood Investigations [1]

- WBC: 22.1 × 103/μL with neutrophils 87%, (normal range: 4000-10,000/μL, 45%-75% neutrophils)[6]
- Hemoglobin: 14.0 g/dL (normal range:12.0-15.5g/dl)[8]
- Platelets: 380 × 103/μL. (normal range:150×109-400×109/L)[7]
- Potassium level: 2.7 mEq/L (normal range: 3.5-5.5 mEq/L)[2]
- Triglyceride level: 53 mg/dL (normal range: <150 mg/dL)[3]
- Serum amylase: 31 IU/L (normal range: 20–160)[1]
- Serum lipase: 14 IU/L (normal range: 8–78)[1]

Abdominal Computed Tomography (CT) Scan [1]

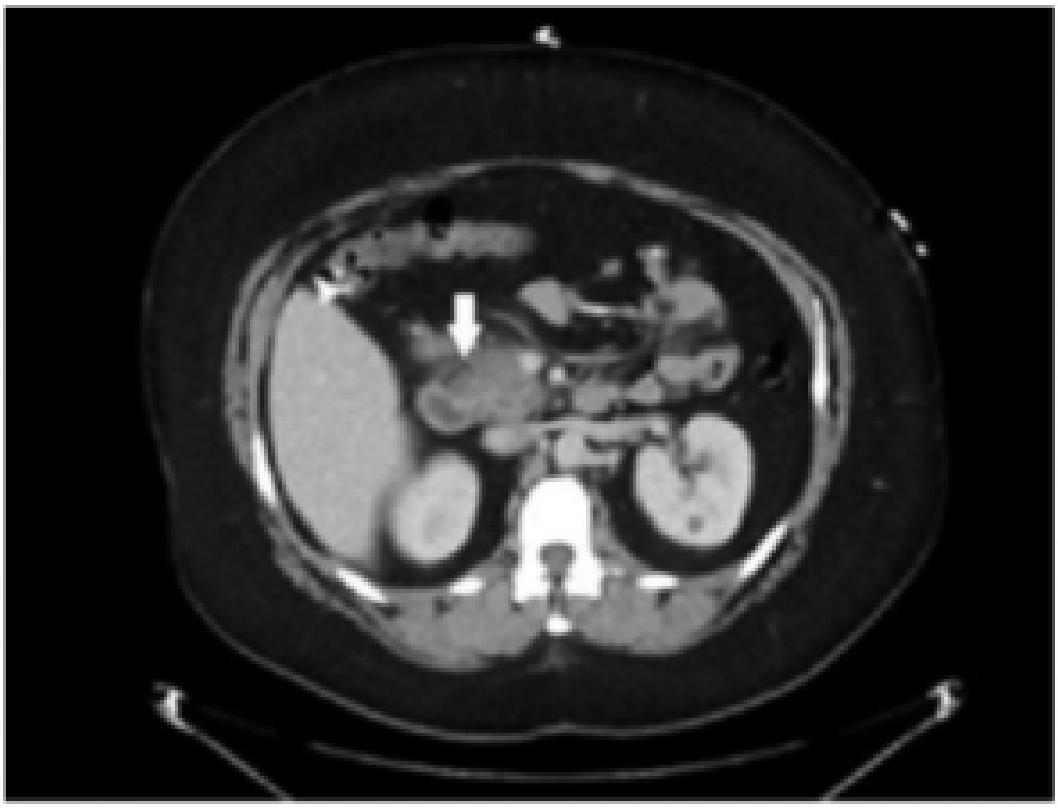

Figure 1: Abdominal CT scan with intravenous contrast- white arrows in the figure shows fat stranding in the pancreatic head consistent with pancreatitis and reactive thickening in the duodenum.[1]

Question & Answers Leading to Diagnosis:

Question 1: Based on the physical, imaging and laboratory investigations, what results would support this patient's diagnosis? Does she meet all the criteria for this diagnosis?

Question 2: If this were a clear acute pancreatitis case, what lab results would we expect to see?

Question 3: What factors would lead to normal amylase and lipase levels in acute pancreatitis?

** For answers please check the next chapter.

Medical terminology/Abbreviations:

- AP (Acute pancreatitis) – Acute pancreatitis means inflammation of the pancreas that develops quickly.[10]
- CT scan – Computerized Tomography scan. (CT) scan combines a series of X-ray images taken from different angles around your body and uses computer processing to create cross-sectional images (slices) of the bones, blood vessels, and soft tissues inside your body. [11]
- Cholecystectomy – Cholecystectomy is a surgical procedure to remove the gallbladder. [4]
- Epigastric region – Epigastric region is the upper central region of the abdomen.[5]

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Further Reading

22.

CASE 3-2017: ANSWERS TO THE QUESTIONS

Answer to Question 1:

The diagnosis of acute pancreatitis requires the presence of 2 of the following 3 criteria as per Peter et al.,[9]

(1) Characteristic abdominal pain – Abdominal pain located in the epigastrium and radiated to the back. The onset may be swift with pain reaching maximum intensity within 30 min, frequently unbearable, and characteristically persisting for more than 24 h without relief. The pain is often associated with nausea and/or vomiting.

(2) Serum amylase and/or lipase ≥3 times the upper limit of normal. Normal range of serum amylase is (20–160) IU/L, Serum lipase-(8–78) IU/L.

(3) CT scan finding showed fat stranding in the pancreatic head compatible with acute pancreatitis.

In her case, two characteristics namely pain and CT scan findings support this diagnosis. Serum amylase 31 IU/L and lipase 14 IU/L are within the normal range.

Answer to Question 2:

- If this were a typical case of acute pancreatitis, the WBC count for neutrophil, serum amylase, and lipase would be elevated.
- This patient only shows increased WBC count with raised neutrophils, and with normal serum amylase and lipase. Therefore, this is an excellent example of an atypical case of

acute pancreatitis.

Answer to Question 3:

It is well documented in the literature that several factors lead to normal serum lipase and amylase levels, such as:

- Hypertriglyceridemia.[1]
- Extensive pancreatic necrosis (acute fulminant or acute-on-chronic pancreatitis).[1]
- Very early pancreatitis when inflammation has not led to a lot of pancreatic acinar cell destruction yet.[1]

Diagnosis [1]

- Acute pancreatitis.

PART V

HEMATOLOGY CASE STUDIES

Hematology is a branch of internal medicine that deals with the physiology, pathology, etiology, diagnosis, treatment, prognosis, and prevention of blood-related disorders. Four major areas of study within hematology include hemoglobinopathy, hematological malignancies, anemia, and coagulopathy.[1]

Common hematological diseases

- Iron deficiency anemia
- Sickle cell anemia
- Thalassemia
- Leukemia
- Lymphoma
- Myeloma
- Bleeding disorders

Signs and symptoms

- Dizziness
- Fainting
- Jaundice
- Recurrent infection
- Spontaneous bleeding
- Easy bruising

Hematology tests[1]

One of the most common hematology tests is the complete blood count, or CBC. This test is often conducted during a routine exam and can detect anemia, clotting problems, blood cancers, immune system disorders and infections. Other hematology tests include:

- Blood chemistry test;
- Blood enzyme test; and
- Blood tests to assess heart disease risk.

Reference

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23.

CASE 1-2017: A NEWBORN BOY WITH POST-CIRCUMCISIONAL BLEEDING

A Case of Hemophilia A Presenting in a Neonate and a Review of the Literature. Global Pediatric Health, 2017, 4, 2333794X1769311. doi: 10.1177/2333794x17693110

Kisseih, E., Yerrapotu, N., Yadav, D., & February, M.

Case Summary [1]

A newborn boy was circumcised on his second day of life. Profuse bleeding occurred post ***circumcision*** *with* ***frenulum*** *tears. Bleeding worsened within 5 hours, leading to three changes of* ***pressure dressings*** *. During this time, the patient experienced prolonged bleeding from prior heel sticks. Lab investigations revealed prolonged* ***partial thromboplastin time****, lower* ***fibrinogen level****s of 3 mg/dL (186-486 mg/dL),* ***factor VIII*** *levels <1%,* ***Factor IX*** *level 9%. On further questioning of the family, it became apparent that the maternal grandfather had a similar bleeding disorder.*

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://ecampusontario.pressbooks.pub/clinicalcases/?p=95#audio-95-1

Learning Objectives

- Understanding the presentation of neonatal bleeding disorders and selecting appropriate investigations to suggest a diagnosis.
- Discuss the common clinical laboratory tests used to assess bleeding disorders.
- Familiarizing and defining new medical terminology associated with hereditary bleeding disorders.

Clinical History [1]

- Age: Neonate 2 days-old
- Sex: Male

Birth History [1]

- Vaginal delivery at 40 weeks gestation. Pregnancy was unremarkable.
- **APGAR** scores 9 at 1 and 5 minutes, with no complications.

Drug History [1]

- 1mg Vit K injection at birth.

Symptoms [1]

- Bleeding from post-circumcision frenulum tears.

Examinations (Clinical Assays/Tests/Imaging) [1]

Birth Parameters [1]

- Birth weight: 2.94 kg, the
- Birth length: 50 cm
- Head circumference: 34 cm
- "Examination revealed a small for gestational age (SGA) baby with caput succedaneum and an extra digit on the right hand".

Blood Investigations [1]

- White cell count: 11.5 k/mm^3 (normal ranges: 9,000 to 30,000/mm^3)[5]
- Hemoglobin: 21.7 gm/Dl (normal ranges: 14 to 24 g/dL)[6]
- **Hematocrit**: 61.3% (normal ranges: 55% to 68%)[7]
- Platelet count: 32 k/mm^3; on repeat, platelets-183 k/mm^3 (normal ranges: 150-450 k/mm3)[4]
- Blood Group: B positive.
- Partial thromboplastin time: >200 seconds (normal ranges: 23.1-33.1)[1]
- **D-dimer**: >35.2mg/L (normal ranges: 0.025-.5)[3]
- Fibrinogen level: 103 mg/dL (normal ranges: 186-486 mg/dL)[1]
- Factor VIII level: <1% (normal ranges: 50%-100%)[2]
- Factor IX activity: 9% (normal ranges: 50%-100%)[2]
- **Von Willebrand factor** activity level 134% (normal ranges: 43% to 138%)[1]
- Von Willebrand antigen:102% (normal ranges: 60% to 153%)[1]
- **Platelet function testing with screening epinephrine** : 119 seconds (normal ranges: 100-163)[1]
- Platelet factor ADP:78 seconds (normal ranges: 57-114)[1]

Question & Answers Leading to Diagnosis:

Question 1: Based on the infant's symptoms and family history, what investigation(s) would confirm the correct diagnosis?

Question 2: What are the potential differential diagnoses?Associate the lab results with each of differential diagnoses.

Question 3: How would the medical history of the maternal grandfather correlate to the patient's diagnosis? For which sex group is this disease most prominent?

** For answers please check the next chapter.

Medical terminology/Abbreviations:

- X-linked recessive – X-linked recessive inheritance refers to genetic conditions associated with mutations in genes on the X chromosome. A male carrying such a mutation will be affected because he carries only one X chromosome. A female carrying a mutation in one gene, with a normal gene on the other X chromosome, is generally unaffected.[19]
- Circumcision – Circumcision is the surgical removal of the skin covering the tip of the penis.[8]
- Frenulum – Elastic band of tissue under the glans penis.[9]
- APGAR score – The Apgar score is a scoring system that assesses newborn babies' well-being using five different factors: heart rate, breathing, muscle tone, reflexes, and skin colour. Apgar is a quick test performed on a baby at 1 and 5 minutes after birth. The 1-minute score determines how well the baby tolerated the birthing process. The 5-minute score tells the health care provider how well the baby is doing outside the mother's womb. score is based on a total score of 1 to 10. The higher the score, the better the baby is doing after birth. [10]
- Pressure dressing – it is a pressure bandage that's designed to apply pressure to a particular area of the body to prevent bleeding.[11]
- Hematocrit – The hematocrit is the proportion, by volume, of the blood that consists of red blood cells. For example, a hematocrit of 25% means that there are 25 milliliters of red blood cells in 100 milliliters of blood.[7]
- Partial thromboplastin time – Partial thromboplastin time (PTT) is a blood test that measures the time it takes blood to clot.[16]
- D-dimer – it is small protein fragment present in the blood after degradation of blood clot. D-dimer concentration help to diagnose thrombosis and intravascular coagulation.[13]
- Fibrinogen level – Fibrinogen is a plasma glycoprotein synthesized by the liver and is the major structural component of a clot.[17]
- Factor VIII – Essential clotting factor deficient in Hemophilia A.[15]
- Factor IX – Essential clotting factor deficient in Hemophilia B.[15]
- Von Willebrand factor – Von Willebrand factor is a glycoprotein that plays a key role in blood clotting.

Deficiency of this factor leading to Von Willebrand disease.14

- Platelet function testing with screening epinephrine – The PFA is a screening test for platelet dysfunction. The cartridge membrane is coated with collagen, and with one of two platelet agonists (epinephrine or ADP). The platelets adhere to the collagen and aggregate in response to the collagen and epinephrine (or ADP).[18]

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Further Reading

24.

CASE 1-2017: ANSWERS TO THE QUESTIONS

Answer to Question 1: Based on profuse bleeding after circumcision and genetic predisposition (maternal grandparents presenting similar disease conditions); factor VIII levels, factor IX activity, platelet function testing with screening epinephrine and Von Willebrand factor activity levels could be measured to confirm a diagnosis.[1]

Answer to Question 2:

The potential differential diagnosis would be Von Willebrand Disease, Hemophilia A or Hemophilia B, congenital platelet function defect.

Lab results with each differential diagnosis are given below-

- Von Willebrand disease – Von Willebrand factor activity and Von Willebrand antigen were 134% and 102% respectively. Results were within normal range.[1]
- Congenital platelet function defect and platelet function testing with screening epinephrine was done. The values obtained for platelet function testing were 119 seconds (100-163)[1] and platelet factor ADP:78 seconds (57-114)[1]
- Hemophilia A – factor VIII level analysis <1%, and for hemophilia B factor IX activity (9%). Normal ranges for factors VIII and IX are 50%-100% [2]. Both these clotting factor levels are found to be below normal. Factor VIII level is much lower than factor IX, so patient is diagnosed as Hemophilia A.

Answer to Question 3:

- Hemophilia is an X-linked recessive disorder that is well documented in the literature.[1] In this case, the patient's maternal grandfather had the disease and the patient mother was a carrier and not expressing the disease.
- Hemophilia is preponderance in males due to X-lined recessive inheritance. [12]

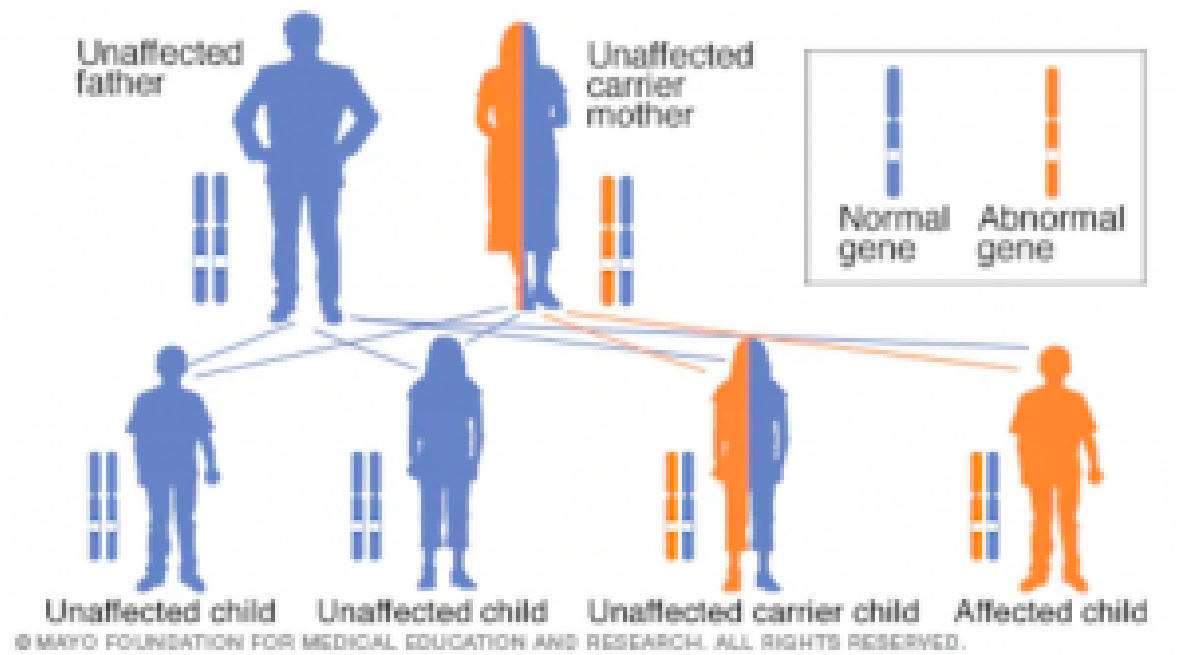

Figure 1: Showing unaffected carrier mother transmit disease to her son.[12]

Diagnosis [1]

- Hemophilia A.

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25.

CASE 2-2018: A 78-YEAR-OLD FEMALE WITH ANEMIA AND PURPLE BLOTCHES IN ORAL CAVITY

A case of acquired hemophilia A in an elderly female. Journal of community hospital internal medicine perspectives,2018, 8(4), 237-240. doi:10.1080/20009666.2018.1487246

Kaur, K. & Kalla, A.

Case Summary [1]

A 78-year-old African American woman presented with gradually worsening anemia with slurred speech, ***dysphagia****,* ***odynophagia*** *with purple blotches in her oral cavity. She gave a history of recurrent GI bleeding and spontaneous bruising in her body. She underwent endoscopies twice revealing a bleeding gastric ulcer. On physical examination, multiple ecchymoses (bruising) were found in her mouth, chest, and extremities. Laboratory investigations revealed a very low Hb level (6.7 g/dl), prolonged* ***aPTT*** *(Activated partial thromboplastin time), and low activity of factor VIII. She was treated according to the diagnosis and her condition gradually improved which reflected as normal aPTT, stable hemoglobin (10.7g/dL) after 6 months of treatment.*

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://ecampusontario.pressbooks.pub/clinicalcases/?p=97#audio-97-1

Learning Objectives

- Identify the clinical features of bleeding disorders.
- Describe the confirmatory tests for bleeding disorders.
- Discuss the outcome and prognosis of the treatment.
- Familiarizing and defining new medical terminology associated with bleeding disorders.

Clinical History [1]

- Age: 78 years old
- Sex: Female
- Ethnicity: African American

Medical History [1]

- History of two endoscopies that revealed bleeding gastric ulcer both times and treatment was done during the endoscopies.
- She also described having multiple spontaneous bruises and **ecchymosis** sporadically throughout her body over past few months.
- In addition to recurrent GI bleeding, past medical history was significant for chronic iron deficiency anemia, type 2 diabetes mellitus and multinodular goiter requiring thyroidectomy.
- She denied any history of a **bleeding diathesis** in the family.
- No history of heparin administration.

Symptoms [1]

- Slurred speech for 2 days which was suspected as stroke.
- She also complained of dysphagia, odynophagia, and having purple blotches inside her oral cavity.
- She also developed worsening anemia for the past few months and had needed three blood transfusions for symptomatic anemia within the past 2 months.

Examinations (Clinical Assays/Tests/Imaging) [1]

Physical Examination [1]

- The patient was hemodynamically stable.
- A large ecchymosis was found along the floor of the mouth, as well as on the ventral tongue, and the rest of the buccal mucosa was normal.
- Presence of multiple ecchymoses over the chest and upper extremities.

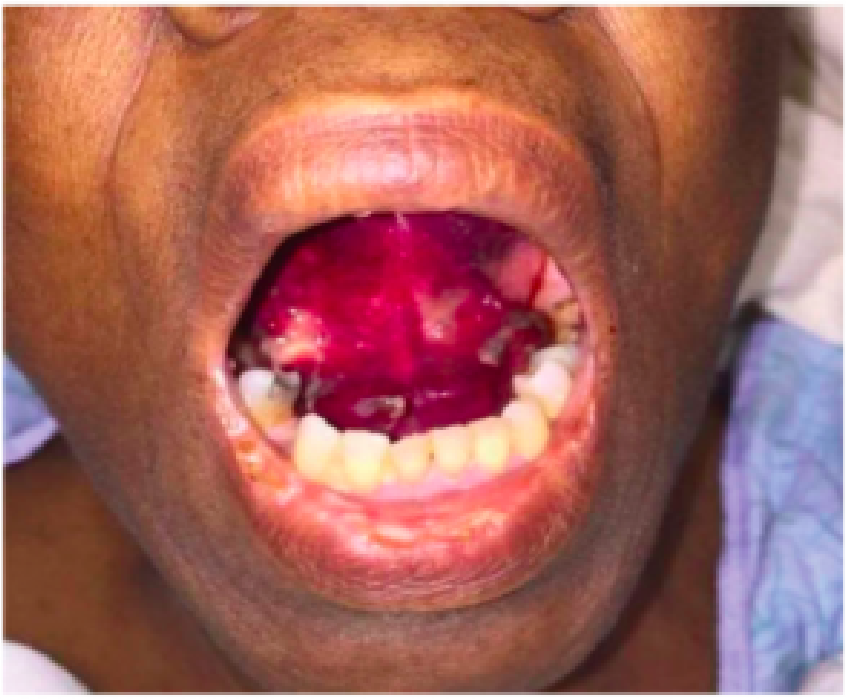

Figure 1: Demonstrating oral mucosal ecchymosis. [1]

Laboratory Investigations [1]

Investigation Name[1]	Result[1]	Reference Range[1]
Hemoglobin	6.7 g/dL	12.0-15.5 g/dL
aPTT	35-48 s	20-28s
PT	Normal	11.0-12.5s
Factor VIII activity	<1%	50-150%
Factor VIII inhibitor level	59.7 Bethesda units	</ = 0.50
Factor IX level	201%	78–184%
von Willebrand Factor	256%	52–214%

Question & Answers Leading to Diagnosis:

Question 1: Based on the clinical history and lab investigations, what diagnosis is suspected and why?

Question 2: What is the possible cause(s) of low hemoglobin in this patient?

Question 3: What are the manifestations of bleeding disorder?

** For answers please check the next chapter.

Medical terminology/Abbreviations:

- Ecchymosis – Medical term for common bruise caused by the impact of an injury.[3]
- Endoscopy – An endoscopy is a procedure in which your doctor uses specialized instruments to view and operate on the internal organs and vessels of your body.[4]
- Bleeding diathesis – In medicine (hematology), bleeding diathesis is an unusual susceptibility to bleed (hemorrhage) mostly due to hypocoagulability (a condition of irregular and slow blood clotting), in turn, caused by a coagulopathy (a defect in the system of coagulation).
- Dysphagia – Difficulty in swallowing. [5]
- Odynophagia – Painful swallowing.[6]
- APTT or PTT – The partial thromboplastin time (PTT; also known as activated partial thromboplastin time (aPTT)) is a screening test that helps evaluate a person's ability to appropriately form blood clots.[7]
- PT – Prothrombin time, a test to evaluate blood clotting.[8]
- Acquired Hemophilia A – Acquired Hemophilia A (AHA) is a rare bleeding disorder related to the formation of autoantibodies to Factor VIII.[1]

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Further Reading

CASE 2-2018: ANSWERS TO THE QUESTIONS

Answer to Question 1:

- In this given case, the patient presented with worsening anemia with signs of easy bruising and spontaneous bleeding, and her laboratory investigations revealed a very low Hb level (6.7 g/dl), prolonged aPTT (35-48 s), and low activity of factor VIII (<1%). Her blood reports also showed a high factor VIII inhibitor level (59.7 Bethesda units), a high factor IX level (201%), and a slightly high level of von Willebrand factor (256%).[1] Based on these clinical and lab findings, she was diagnosed as a case of hemophilia A which is due to factor VIII deficiency with elevated factor VIII inhibitor.[1]
- Furthermore, this diagnosis is considered an acquired case as the patient has started to have her symptoms in the late stage of her life with no family history of any bleeding disorders.
- Therefore, based on the clinical history, lab results, and considering the patient's age, acquired hemophilia A is diagnosed.

Answer to Question 2: This patient's hemoglobin level was low (6.7 g/dl) due to recurrent GI bleeding which was revealed in her prior endoscopies as bleeding gastric ulcer and spontaneous bleeding under the skin and oral mucosa manifested as ecchymoses.[1]

Answer to Question 3:

- The main manifestations of bleeding disorders are as follows-
    - Easy bruising,
    - Bleeding gums,
    - Heavy bleeding from small cuts or dental work,
    - Unexplained nosebleeds,
    - Heavy menstrual bleeding,
    - Bleeding into joints,
    - Excessive bleeding following surgery.[2]

Diagnosis [1]

- Acquired Hemophilia A considering patient's age and blood clotting factor levels.

Treatment [1]

- The patient was started on high-dose steroids (Methylprednisolone 60 mg IV twice a day) and monitored for any signs of bleeding.
- 1 unit of packed red blood cells was transfused due to symptomatic anemia.
- Prednisone was tapered off and she was switched to rituximab due to side effects of Prednisone.
- Four doses of rituximab 375 mg/m2 weekly were given and well-tolerated.

Prognosis [1]

- Factor VIII titers increased from <1% to 11% and inhibitor titer decreased from 59 BU to 2 BU immediately after four doses of rituximab were given.
- At 2 months after starting rituximab therapy, labs revealed a normal PT/PTT factor VIII level of 113%, and the Bethesda assay was not done due to the normal factor VIII level.
- At 6 months, she maintained a normal aPTT, stable hemoglobin (10.7 g/dL), and remained asymptomatic.
- The patient is being monitored every 3 months through complete blood count and aPTT.

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27.

CASE 3-2014: A 2.5-YEAR-OLD BOY WITH ANEMIA AND RECURRENT DIARRHEA

A two-and-a-half-year-old breastfed toddler presenting with anemia: a case report. BMC Research Notes, 2014, 7(1), 917. https://doi.org/10.1186/1756-0500-7-917

Bock, F., Borucki, K., Vorwerk, P., Biemann, R., & Isermann, B.

Case Summary [1]

*A 2.5-year-old Turkish boy presented with recurrent diarrhea and vomiting with a history of inadequate nutritional intake. On physical examination, he was weighted 11.5kg which is in between the 3rd and 10th percentile for his age. Anemia and mild dehydration were also present. On lab investigations, blood testing revealed decreased Hb, **MCV**, and **MCH** with increased reticulocyte count. His peripheral blood film showed increased **hypochromic RBC**. A low level of iron and ferritin were detected in the serum iron profile and **hemoglobin electrophoresis** came out normal. The child was diagnosed and treated accordingly. His condition gradually improved.*

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://ecampusontario.pressbooks.pub/clinicalcases/?p=99#audio-99-1

Learning Objectives

- Identifying the signs and causes of nutritional anemia in children.
- Recognize the clinical and laboratory findings associated with pediatric anemia.
- Discuss the findings of hemoglobin electrophoresis in thalassemia.
- Familiarizing and defining new medical terminology associated with pediatric anemia.

Clinical History [1]

- Age: 2.5 years old
- Sex: Male
- Ethnicity: Turkish

Medical History [1]

- No known medical issues.
- According to the information provided by the parents, the patient's sole source of nutrition was breast milk with a frequency of more than 6 breast-feeds a day and the boy did not receive any food supplements on a regular basis.

Drug History [1]

- Not applicable.

Symptoms [1]

- Recurrent diarrhea for the last 3 weeks following a family vacation accompanied by vomiting.

Examinations (Clinical Assays/Tests/Imaging) [1]

Physical Examination [1]

- Weight: 11.5kg
- Nutritional status: Reduced between the 3rd and 10th percentile and **carious dentition** were apparent.
- Temperature: 99.1F
- Anemia: Present

- Dehydration: Mild with reduced skin turgor but quick recapillarization.

Laboratory Investigations [1]

- Blood testing showed moderate-to-severe anemia: decreased Hb with 7.1 g/dl (10.8-12.7), MCV (mean corpuscular volume) of 48 Fl (73–101), MCH (mean corpuscular hemoglobin) of 0.71 fmol.(1.40-2.00), increased RBC count of 6.19×10^6 cells/µl (3.70-5.30) and increased red cell distribution width (**RDW**) of 20.3% (11.5-14.5), thrombocytosis of 754,000 cells/µl (140–360) and increased reticulocyte count of 316×10^9 cells/l (68–108) with reduced reticulocyte hemoglobin of 1.04 fmol (1.74-2.17).
- Peripheral blood film shows an increase of hypochromic RBCs (90%; Figure 1a)
- Serologic testing also revealed low values for serum-iron of 2 µM (5.7-18.6) and ferritin of 2 ng/ml (6–67) but normal CRP (C-reactive protein) (0.9 mg/l; <5), bilirubin (2.8 µM; <32) and **haptoglobin** (1.96 g/l; 0.30-2.00) were detected.
- The fecal occult blood test was negative and no pathogenic protozoa, helminths, shigella, yersinia, adeno-, noro-, rota-, astroviruses were found in co-proculture (stool culture).
- Hemoglobin electrophoresis is normal with 96.6% HbA1 (>96.3), 2.7% HbA2 (<3.2) and 0.4% HbF (<0.5).

Chart 1: Laboratory parameters[1]

Table 1

Selected laboratory test results of the patient at the time of initial presentation

Parameter (Unit)	Value	Reference range
Hemoglobin (g/l)	7.1	10.8-12.7
MCV (fl)	48	73-101
MCH (fmol)	0.71	1.40-2.00
RBC count (10^6 cells/µl)	6.19	3.70-5.30
WBC count (cells/nl)	7.6	5.0-12.0
Platelets (10^3 cells/µl)	754	140-360
Reticulocyte count (10^9 cells/l)	316	68-108
Retikulocyte hemoglobin (fmol)	1.04	1.74-2.17
Hypochromic RBCs (%)	90	<5
Ferritin (ng/ml)	2	6-67
RDW (%)	20.3	11.5-14.5
CRP (mg/l)	0.9	<5
Iron (µM)	2.0	5.7-18.6
Transferrin (g/l)	2.86	2.0-3.6
Transferrin-Saturation (%)	2.8	7-44
Haptoglobin (g/l)	1.96	0.30-2.00
Bilirubin (µM)	2.8	<32

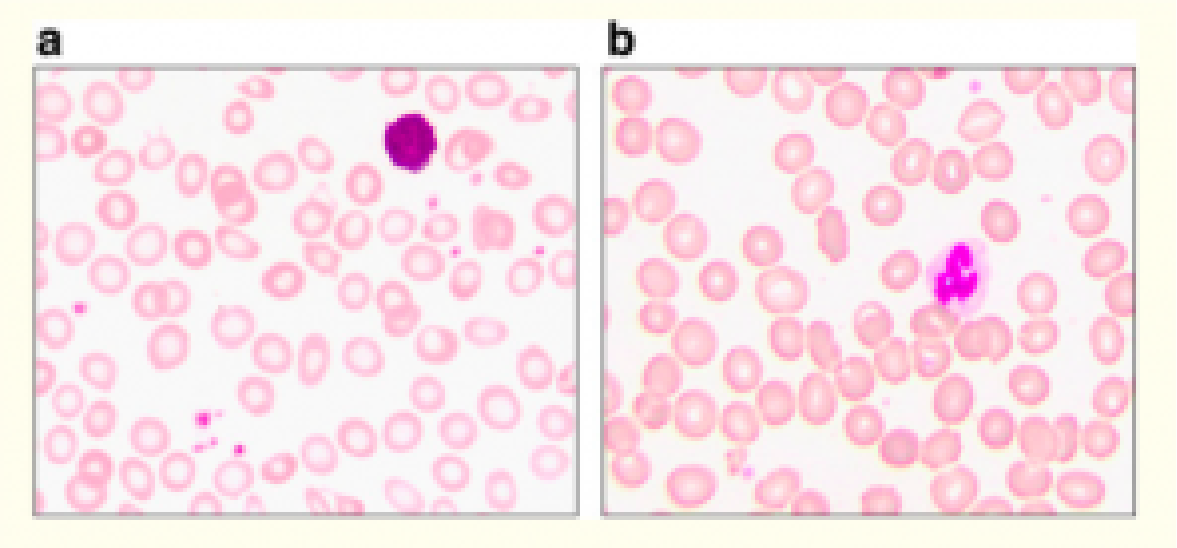

Figure 1: a,b: Peripheral blood smear from a two-and-a-half-years old breastfed patient. The blood smear is showing hypochromic red blood cells before therapy (a). Two months after therapy a decrease in hypochromic red blood cells was noted (b).[1]

Question & Answers Leading to Diagnosis:

Question 1: Based on chief complaints, medical history, physical examinations, what initial diagnosis can we suspect?

Question 2: Which findings in the above lab investigations are confirmatory to reach the final diagnosis?

Question 3: If this patient was experiencing thalassemia, what results would we expect from the hemoglobin electrophoresis?

** For answers please check the next chapter.

Medical terminology/Abbreviations:

- Carious dentition – Dental caries or cavities, more commonly known as tooth decay, are caused by a breakdown of the tooth enamel. This breakdown is the result of bacteria on teeth those breakdown foods and produces acid that destroys tooth enamel and results in tooth decay. [2]
- Hypochromic RBC – Hypochromia means that the red blood cells have less color than normal when examined under a microscope. This usually occurs when there is not enough of the pigment that carries oxygen (hemoglobin) in the red blood cells. [3]
- Haptoglobin – Haptoglobin is a protein produced by the liver that the body uses to clear free hemoglobin (found outside of red blood cells) from circulation. This test measures the amount of haptoglobin in the blood. [4]
- Hemoglobin electrophoresis – Hemoglobin electrophoresis is a test that measures the different types of hemoglobin in the blood. It also looks for abnormal types of hemoglobin. Normal types of hemoglobin include:

    - Hemoglobin (Hgb) A, the most common type of hemoglobin in healthy adults
    - Hemoglobin (Hgb) F, fetal hemoglobin. This type of hemoglobin is found in unborn babies and newborns. HgbF is replaced by HgbA shortly after birth.[5]
- MCH – MCH stands for "mean corpuscular hemoglobin." An MCH value refers to the average quantity of hemoglobin present in a single red blood cell.[8]
- MCV – MCV stands for mean corpuscular volume. There are three main types of corpuscles (blood cells) in your blood–red blood cells, white blood cells, and platelets. An MCV blood test measures the average size of your red blood cells, also known as erythrocytes. Red blood cells move oxygen from your lungs to every cell in your body. Your cells need oxygen to grow, reproduce and stay healthy. If your red blood cells are too small or too large, it could be a sign of a blood disorder such as anemia, a vitamin deficiency, or other medical condition.[7]
- RDW – The red cell distribution width (RDW) blood test measures the amount of red blood cell variation in volume and size. Normal red blood cells maintain a standard size of 6 to 8 micrometers (μm) in diameter.[6]

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Further Reading

28.

CASE 3-2014: ANSWERS TO THE QUESTIONS

Answer to Question 1:

- Based on the chief complaint of recurrent diarrhea and vomiting indicating recurrent infections and history of inadequate nutritional intake (because the baby was only getting breast milk without any other complementary foods) and physical examination findings like anemia, low body weight between the 3rd and 10th percentile for his age – we can suspect an initial diagnosis of nutritional anemia.
- Considering his age, attack of recurrent infection, and anemia, a differential diagnosis of thalassemia should be ruled out.

Answer to Question 2:

- To confirm the diagnosis routine blood tests, peripheral blood film, serum iron profile was done. Hb electrophoresis was conducted to rule out the differential diagnosis.
- In our given case, CBC revealed-
    - Decreased Hb with 7.1 g/dl (Normal range: 10.8-12.7),
    - Low MCV (mean corpuscular volume) of 48 Fl (Normal range: 73–101),
    - Low MCH (mean corpuscular hemoglobin) of 0.71 fmol.(Normal range: 1.40-2.00),
    - Increased RBC count of 6.19×10^6 cells/µl (Normal range: 3.70-5.30) and
    - Increased red cell distribution width (RDW) of 20.3% (Normal range: 11.5-14.5),
    - Thrombocytosis of 754,000 cells/µl (Normal range: 140–360) and
    - Increased reticulocyte count of 316×10^9 cells/l (Normal range: 68–108) with reduced

reticulocyte hemoglobin of 1.04 fmol (Normal range: 1.74-2.17).

- Peripheral blood film showed an increase of hypochromic RBCs (90%; Figure 1a)
- Serum iron profile revealed low serum-iron of 2 µM (Normal range: 5.7-18.6) and low ferritin of 2 ng/ml (6–67)
- Hemoglobin electrophoresis is normal with 96.6% HbA1 (>96.3), 2.7% HbA2 (<3.2) and 0.4% HbF (<0.5)
- Based on these lab reports, the final diagnosis of iron deficiency anemia was made.

Answer to Question 3:

- If this patient was experiencing thalassemia, then his hemoglobin electrophoresis would be abnormal.
- The following list corresponds to this image of alkaline hemoglobin electrophoresis.
    - Lanes 1 and 2: normal patient specimen
    - Hb A is over 98% with a small amount of Hb A2 visible
    - Lanes 3 and 4: Beta thalassemia minor
    - Hb A is decreased to 94%, Hb A2 is increased at 5%, and Hb F is 1%
    - Lanes 5 and 6: Delta-beta thalassemia major
    - No Hb A or A2 is present, Hb F is 100%
    - Lanes 7 & 8: Delta-beta thalassemia intermedia
    - Hb A is 8.5%, Hb A2 is 3.5% and Hb F is 88%
    - Lane 9: AF control
    - Lane 10: ASC control.[9]

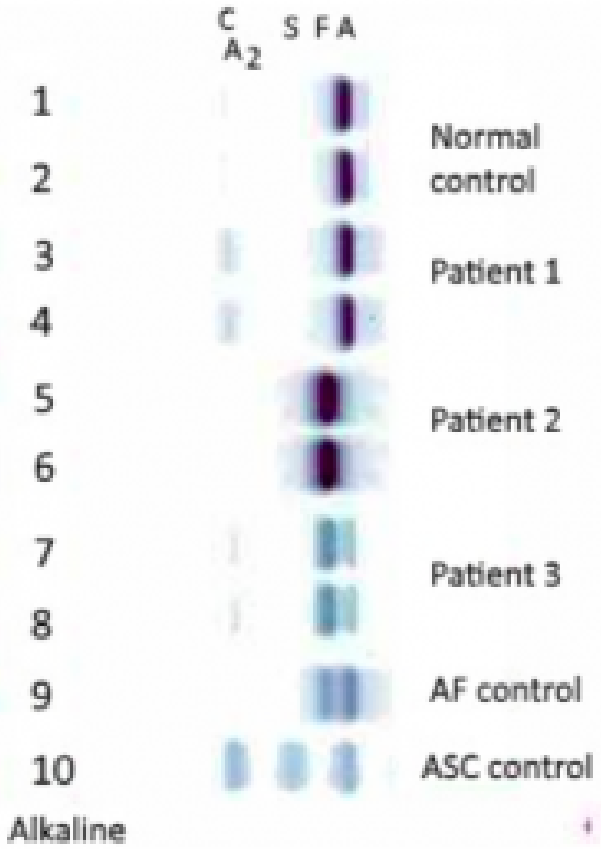

Figure 2: Hemoglobin electrophoresis patterns in beta thalassemia.[9]

Diagnosis [1]

- Given the nutritional status and the absence of enhanced hemolysis parameters the hypochromic microcytic anemia was attributed to nutritional iron deficiency.

Treatment and Prognosis [1]

- The parents were educated about the risks of under- and malnutrition, about the importance of a

healthy diet, taking the current WHO recommendations into account and about reducing the number of breastfeeds. Upon follow up visit the parents reported that the diet had been adopted accordingly. In addition, oral iron substitution was initiated. The Hb ameliorated (10.15 g/dl), hypochromic RBCs decreased to 15.7% and ferritin normalized (20.9 ng/ml) 2 months after discharge (Figure 1b).

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PART VI

HEPATOLOGY CASE STUDIES

29.

CASE 1-2016: A 12-YEAR-OLD BOY WITH FEVER AND RECURRENT ABDOMINAL PAIN

Wilson's Disease: A Rare Case Report in Western Maharashtra. Int J Sci Stud 2016;4(2):282-285

Pawar VS, Sontakke A, Sindal D, Patil S, Garud K.

Case Summary [1]

A 12-year-old boy hailing from rural India presents with chief complaints of abdominal pain with fever for 7 days. He had been having similar types of attacks every 3-4 months since he was 3 years of age and hasn't received any proper treatment. On examination, he was conscious and well-oriented while his abdominal palpation revealed an enlarged spleen. Lab investigations revealed an abnormality in blood counts, peripheral blood film, along with very low ceruloplasmin level with a high copper concentration in urine. His brain MRI also showed some hyperintensities in the midbrain. The patient was then treated according to the diagnosis and his condition improved gradually.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://ecampusontario.pressbooks.pub/clinicalcases/?p=101#audio-101-1

Learning Objectives

- Identifying the signs of suspected liver disease in children.
- Recognize the clinical and laboratory findings associated with liver disease.
- Describe the common clinical laboratory tests used to diagnose Wilson's disease.
- Familiarizing and defining new medical terminology associated with genetic metabolic disorders.

Clinical History [1]

- Age: 12 years old
- Sex: Male

Medical History [1]

- History of recurrent episodes of abdominal pain and fever every 3-4 months since his 3 years of age.
- He is a child of non-consanguineous (non-related) parents with normal developmental milestones.

Drug History [1]

- The patient was taken treatment for the same complaints (diagnosed as hepatitis), but details were not available.
- No history of blood transfusions.

Symptoms [1]

- Moderate fever for 7 days.
- Pain in left side of abdomen for same duration.
- No history of chills, rigor, vomiting, loose motion, rash, jaundice, joint pain, chest pain, hematemesis (blood vomiting), melena (altered blood in stool).

Examinations (Clinical Assays/Tests/Imaging) [1]

Physical Examination [1]

- The patient was conscious and well oriented.

- Vital signs (pulse, blood pressure, respiratory rate) were normal.
- Abdominal examination revealed a soft, non-tender spleen which was palpable 2cm below the left costal margin and hard in consistency with a smooth, regular surface. The liver was not palpable.
- Neurological and psychological examinations were normal.

Ophthalmic Examinations by Slit Lamp [1]

- Showed a rusty brown **Kayser-Fleischer (KF) ring** in Descemet's membrane of cornea near limbus of both eyes, no deposits seen on the lens.

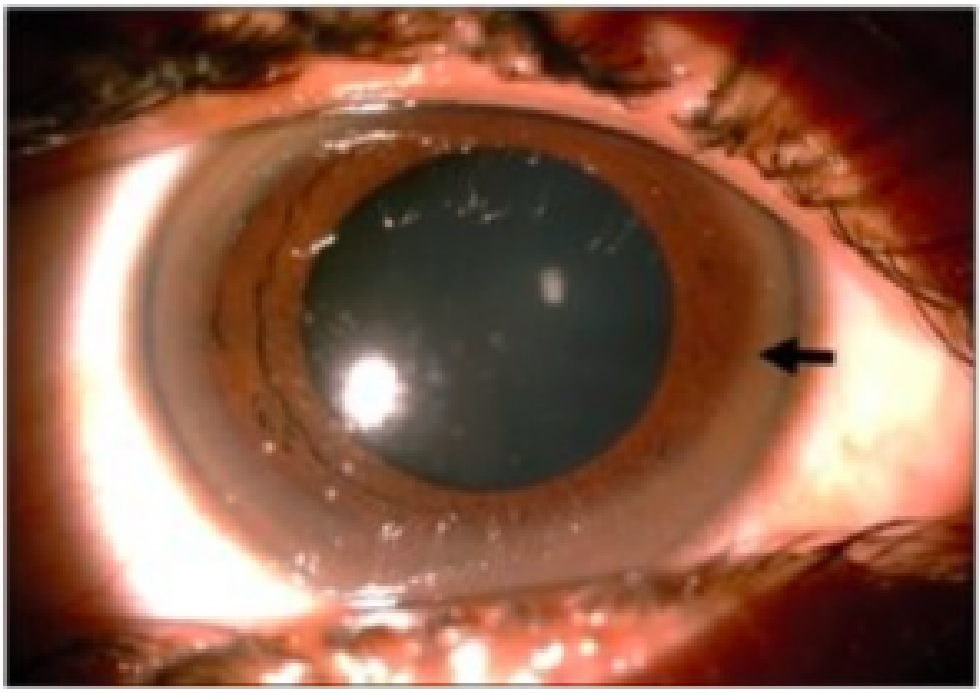

Figure 1: Slit-lamp examination showing KF ring (black arrow) [1]

Laboratory Investigations [1]

- Complete blood count with other blood investigations was done and the results are given below.

Chart 1: Laboratory parameters[1]

Investigation name	**Result**
Hb	10.1 g/dl
WBC count	2,340 cells/cumm
Platelets	90,000/cumm
Peripheral blood film	RBC showed anisopoikilocytes (various sizes of RBC), microcytes (small RBC).
Serum bilirubin	0.4 mg/dl
Serum creatinine	1.1 mg/dl
ALT	86 IU/L
AST	58 IU/L
ALP	165 IU/L
Serum total protein	6.2 g/dl
Serum albumin	4.0 g/dl
Serum globulin	2.2 g/dl
Serum ceruloplasmin	<0.08 g/L
24-hour urinary copper	660 µg/24 hour
Serum copper	30.3 µg/dl

- Serum sodium, potassium, iron, amylase, total iron-binding capacity, bleeding time, clotting time, and routine urine examination was normal.[1]

Brain Magnetic Nuclear Resonance (MRI) [1]

- On brain MRI, T2-weighted images revealed high signal hyperintensities in the bilateral ventrolateral

thalami and putamen region, midbrain, pons, cerebellum on the left side.

Question & Answers Leading to Diagnosis:

Question 1: Based on chief complaints, medical history, physical examinations, what differential diagnoses can we suspect? Give your explanation in favor of each diagnosis.

Question 2: To confirm the diagnosis what lab investigations should be done and how would you interpret the results to confirm the diagnosis in this given case?

Question 3: If this condition remains untreated, what complications might arise and how can we follow up this patient in future?

** For answers please check the next chapter.

Medical terminology/Abbreviations:

- Slit-lamp examination – A slit lamp is a microscope with a bright light used during an eye exam. It gives your ophthalmologist a closer look at the different structures at the front of the eye and inside the eye. It's a key tool in determining the health of your eyes and detecting eye disease. [2]
- Kayser-Fleischer (KF) ring – Kayser–Fleischer (KF) rings are a common ophthalmologic finding in patients with Wilson disease. Initially thought to be due to the accumulation of silver, they were first demonstrated to contain copper in 1934. KF rings are seen in most of the patients with neurologic involvement from Wilson disease. These rings are caused by the deposition of excess copper on the inner surface of the cornea in the Descemet membrane. A slit-lamp examination is mandatory to make a diagnosis of KF rings particularly in the early stages unless the rings are visible to the naked eye in conditions of severe copper overload. Kayser–Fleischer rings do not cause any impairment of vision but

disappear with treatment and reappear with disease progression. KF rings are not specific to Wilson disease alone, they are also seen in other chronic cholestatic disorders such as primary biliary cholangitis and children with neonatal cholestasis. [3]

- Ceruloplasmin test- Ceruloplasmin is a copper-containing enzyme that plays a role in the body's iron metabolism. This test measures the amount of ceruloplasmin in the blood. The liver binds copper to a protein to produce ceruloplasmin and then releases it into the bloodstream. About 95% of the copper in the blood is bound to ceruloplasmin. Because of this, the ceruloplasmin test can be used along with one or more copper tests to help diagnose Wilson disease, an inherited disorder that can lead to excess storage of copper in the eyes, liver, brain, and other organs. [4]
- Brain MRI in Wilson disease- MR imaging is a sensitive method to evaluate the brains of patients with neurologic WD. Whereas abnormalities in the putamen are the most common feature of neurologic WD, brain shrinkage is also frequently observed. [5]

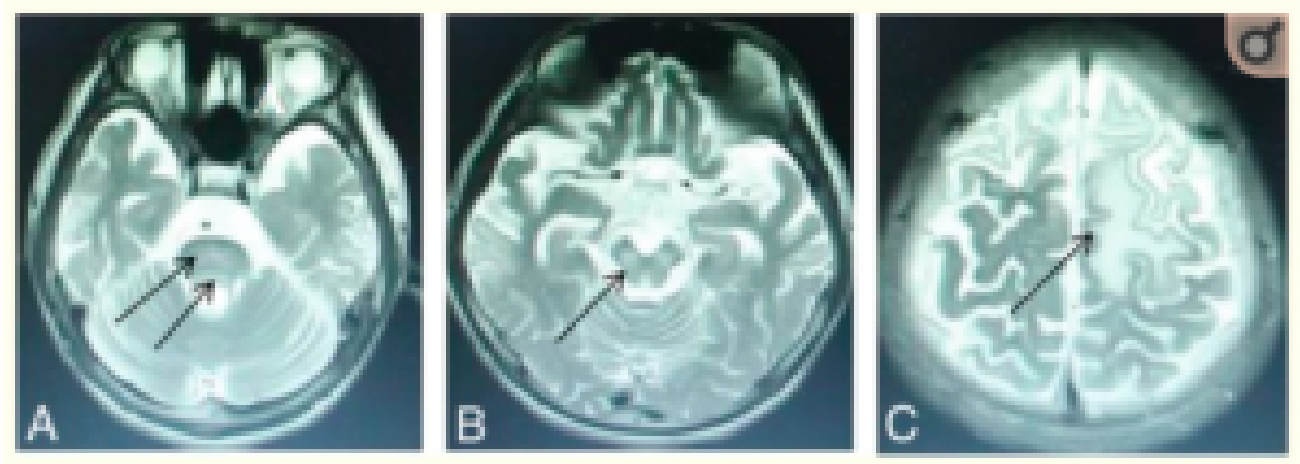

Figure 2: High signal intensity lesions on T2WI. Wilson disease in a 14-year-old girl with dystonia, with a diagnosis lag time 5 years (participant group >3 years) and abnormal signal in the pons (D), midbrain (E), and frontal and parietal lobes (F) (arrows).[5]

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Further Reading

30.

CASE 1-2016: ANSWERS TO THE QUESTIONS

Answer to Question 1:

- Based on the chief complaints of recurrent attack of upper abdominal pain and fever with the presence of enlarged spleen which was found in the physical examination- two differential diagnoses can be made in this case taking his age into consideration.
- The first differential diagnosis would be Thalassemia and the points in favor of this diagnosis are as follows-
    - Patient's young age
    - Repeating attack of hepatitis symptoms from 3 years of age
    - Presence of splenomegaly
    - But the patient gave no history of blood transfusions, and it conflicts with this diagnosis as thalassemia patients usually need repeated blood transfusions from an early age.
- The second differential diagnosis is Wilson disease and points in favor of this diagnosis are given below-
    - Patient's young age
    - Repeating attack of hepatitis symptoms from 3 years of age
    - Presence of splenomegaly
    - The most important finding is the presence of KF (Kayser-Fleischer) ring in the ophthalmic examination and it gives this diagnosis a strong foundation.

Answer to Question 2:

- To confirm the diagnosis, routine blood tests like complete blood count, liver function test along with iron profile, electrolyte level, and serum ceruloplasmin and urinary copper test should be performed.
- In this given case complete blood count revealed a low hemoglobin level (10.1 g/dl) with low WBC (2,340 cells/cumm) and platelet count (90,000/cumm). His peripheral blood film showed anisopoikilocytes (various size of RBC), microcytes (small RBC) – all of which indicates hemolytic anemia. [1]
- The liver function test was somewhat normal except for slightly raised alkaline phosphatase (165 IU/L) and slightly low serum globulin (2.2 g/dl). [1]
- His serum ceruloplasmin level was very low (0.08 g/L) while 24-hour urinary copper was very high (660 µg/24 hours). [1]
- After clinical and biochemical investigations, Wilson's disease was confirmed, and the diagnosis was mainly done based on the presence of KF ring and a low level of ceruloplasmin with elevated urinary copper. According to the Ferenci scoring system (chart 2), the score was 6. [1]

Chart 2: Ferenci scoring system for the diagnosis of Wilson's disease.6

The scoring system (Ferenci score) for the diagnosis of Wilson's disease developed at the 8th International Meeting on Wilson's Disease and Menkes Diseases, Leipzig 2002.

K–F rings	Present (2 points)	Absent (0 points)	
Neuropsychiatric symptoms suggest WD (or typical brain MRI)	Yes (2 points)	No (0 points)	
Coombs negative hemolytic anemia	Yes (1 point)	No (0 points)	
24 h urinary copper excretion (in the absence of acute hepatitis)	Normal (0 points)	1–2 × ULN (1 point)	>2 × ULN, or normal, but >5 × ULN after challenge with 2 × 0.5 g D-penicillamine (2 points)
Liver copper quantitative	Normal (−1 point)	<5 × ULN (1 point)	>5 × ULN (2 points)
Rhodamine-positive hepatocytes (only in case of lack of Cu quantitative assessment)	Absent (0 points)	Present (1 point)	
Serum ceruloplasmin (nephelometric assay, normal >20 mg/dL)	Normal (0 points)	10–20 mg/dL (1 point)	<10 mg/dL (2 points)
Mutation analysis	Disease causing mutations on both chromosomes (4 points)	Disease causing mutations on one chromosome (1 point)	No mutation detected (0 points)

Assessment of the WD diagnosis score:

≥4 points: diagnosis of WD highly likely.

2–3 points: diagnosis of WD probable, more investigations needed.

0–1 point: diagnosis of WD unlikely.

MRI, magnetic resonance imaging; ULN, upper limit of normal.

Answer to Question 3:

- Untreated, Wilson's disease can be fatal. Serious complications include:
    - Scarring of the liver (cirrhosis). As liver cells try to make repairs to damage done by excess copper, scar tissue forms in the liver, making it more difficult for the liver to function. It will lead to liver failure which can occur suddenly (acute liver failure), or it can develop slowly over years. [7]
    - Persistent neurological problems. Tremors, involuntary muscle movements, clumsy gait, and speech difficulties usually improve with treatment for Wilson's disease. However, some people have persistent neurological difficulty despite treatment. [7]
    - Kidney problems. Wilson's disease can damage the kidneys, leading to problems such as kidney stones and an abnormal number of amino acids excreted in the urine. [7]
    - Psychological problems. These might include personality changes, depression, irritability, bipolar disorder, or psychosis. [7]
    - Blood problems. These might include the destruction of red blood cells (hemolysis) leading to anemia and jaundice. [7]

Diagnosis [1]

- The patient was diagnosed with Wilson disease according to the Ferenci scoring system.

Treatment and Prognosis [1]

- The patient was started on penicillamine therapy to increase copper chelation and elimination.
- He was also advised to reduce intake of high copper-containing foods (nuts, chocolate, organ meats).
- After commencing the therapy his condition gradually improved.
- Treatment is lifelong and he will continue his treatment unless he gets a liver transplant in the future.

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PART VII

NEPHROLOGY CASE STUDIES

The renal system, in humans, organ system that includes the kidneys, where urine is produced, and the ureters, bladder, and urethra for the passage, storage, and voiding of urine.[1]

The system contains two kidneys, which control the electrolyte composition of the blood and eliminate dissolved waste products and excess amounts of other substances from the blood; the latter substances are excreted in the urine, which passes from the kidneys to the bladder by way of two thin muscular tubes called the ureters. The bladder is a sac that holds the urine until it is eliminated through the urethra.[1]

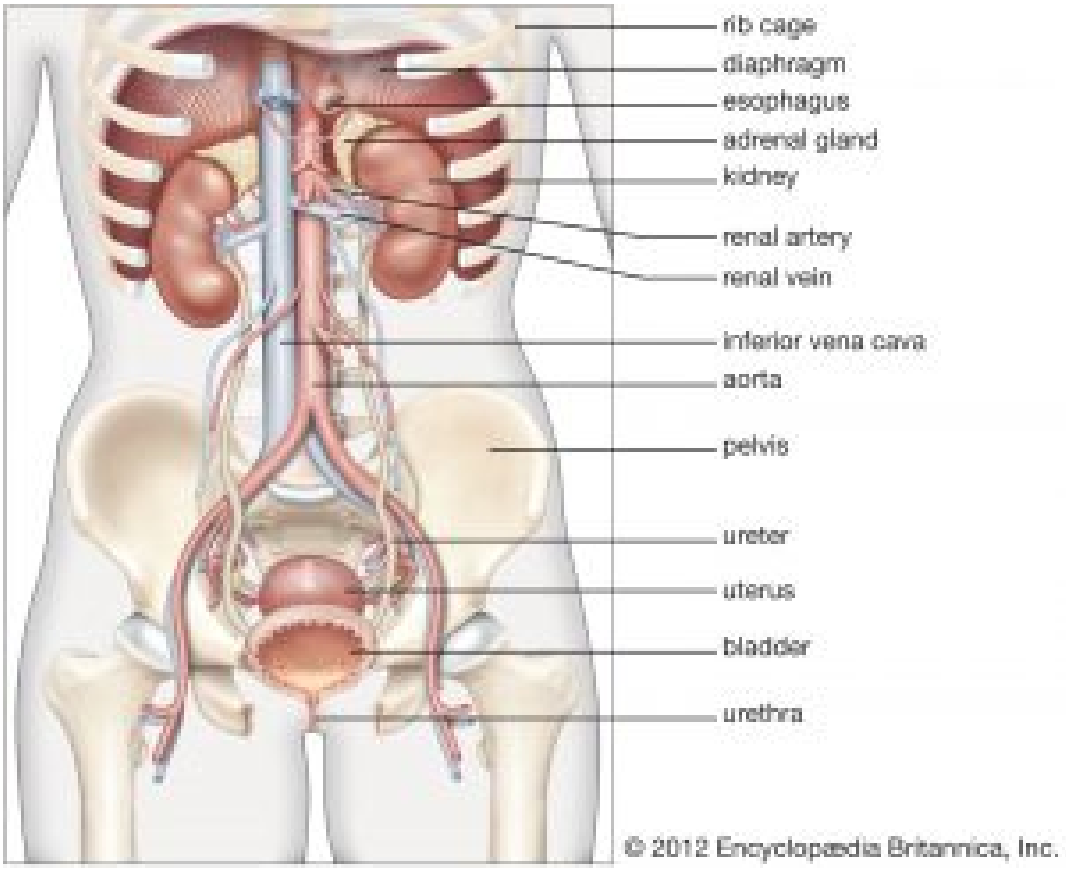

Figure 1: Female kidneys in situ.[1]

Nephrology is the subspecialty of internal medicine that focuses on the diagnosis and treatment of diseases of the kidney. Because the kidney performs so many critical functions, nephrologists maintain expertise in primary kidney disorders, but also the management of the systemic consequences of kidney dysfunction.

Renal system investigations[1]

- Renal Function Test
  - Glomerular Filtration Rate (GFR) and Creatinine Clearance
- Serum Creatinine
- Ultrasonogram
- X-ray
- CT scan
- MRI
- Renal biopsy

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31.

CASE 1-2020: A 2-YEAR-OLD BOY WITH FEVER, EDEMA AND OLIGURIA

Case Report on Pediatric Nephrotic Syndrome. EJIFCC, 2020, 31(2), 164–168.

Prince, S., Naresh, K., & Tulasi, R.

Case Summary [1]

A 2-year-old boy is presented with a high-grade continuous fever with chills and rigor, a wet cough, swelling over the face, and low urine output. Physical examinations revealed pitting edema found in both legs. Laboratory investigations showed proteinuria, decreased levels of C3 and albumin, prolonged APTT (activated partial thromboplastin time), high urine protein/creatinine ratios along hyperlipidemia. The patient was treated according to the diagnosis. His condition improved gradually.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://ecampusontario.pressbooks.pub/clinicalcases/?p=103#audio-103-1

Learning Objectives

- Identifying the signs of suspected renal disease in children.
- Recognize the clinical and laboratory findings associated with pediatric renal disease.
- Discuss the common clinical laboratory tests used to assess renal diseases.
- Familiarizing and defining new medical terminology associated with pediatric renal disease.

Clinical History [1]

- Age: 2 years old
- Sex: Male

Medical History [1]

- No medical issues.
- He was delivered by C-section and weighed 2.75 kg after birth.

Drug History [1]

- Not applicable.

Symptoms [1]

- High-grade continuous fever is associated with chills and rigor.
- Cough (wet cough more in amount) with whitish color sputum which was not foul-smelling.
- Swelling over the face was present which initially started around the peri-orbital (which is more during the morning) and gradually progressed to the face which decreases by evening.
- Decreased urine output (**oliguria**).

Examinations (Clinical Assays/Tests/Imaging) [1]

Physical Examination [1]

- Weight: 15 kg
- **Edema**: Present in lower limbs and face.

Laboratory Investigations [1]

- The urine dipstick indicated proteinuria (higher levels of proteins), no signs of hematuria (presence of blood in urine).
- Blood testing showed a significantly depressed C3 level of 0.638 g/L (reference interval 0.9-1.8 g/L) and hypoalbuminemia of 2.0 g/dL (reference interval 3.5-5.5 g/dL).
- The urine creatinine level was – 620 mg/L (reference interval 400-3000mg/L) and APTT (Activated partial thromboplastin time) was prolonged- 47.7 Sec (reference interval 24-30 Sec).
- Serologic testing for active infections: Anti-streptolysin-O titer was positive.
- The lipid profile showed markedly increased levels of total cholesterol, LDL cholesterol, triglycerides.
- The urine protein/creatinine ratio was found to be high (7.3).
- **Mantoux test** was done before administration of steroids which was negative.

Chart 1: Laboratory parameters[1]

Table 1 Laboratory parameters

Parameters	Result	References
Urine		
Creatinine	620 mg/L	400-3000 mg/L
Protein	4574 mg/L	< 100 mg/L
Protein Creatinine ratio	7.3	< 0.2
Serum electrolytes		
Serum Sodium	131 mmol/L	136-145 mmol/L
Serum Chloride	96 mmol/L	98-107 mmol/L
Serum Potassium	4.6 mmol/L	3.4-4.7 mmol/L
Serum lipid profile		
Total Cholesterol	342 mg/dL	< 170 mg/dL
LDL Cholesterol	196 mg/dL	< 110 mg/dL
Triglycerides	329 mg/dL	< 75 mg/dL
Others		
APTT (plasma)	47.7 sec	24-30 sec
ASO titer (serum)	400 IU/mL	< 200 IU/mL
Serum Albumin	2 g/dL	3.5-5.5 g/dL

Question & Answers Leading to Diagnosis:

Question 1: Based on chief complaints, medical history, physical examination, what initial diagnosis can we suspect?

Question 2: Which findings in the above lab investigations are confirmatory to reach the final diagnosis?

Question 3: What is the main cause of the final diagnosis?

** For answers please check the next chapter.

Medical terminology/Abbreviations:

- Oliguria – Oliguria is defined as passing a reduced urine volume. It is defined as a urine output that is[4]:
  - Less than 1 mL/kg/hour in infants.
  - Less than 0.5 mL/kg/hour in children.
  - Less than 400 mL/day in adults.

- Edema – Oedema is a collection of fluid in the spaces between cells of the body. Fluid leaks out of damaged cells. The fluid cannot be simply drained with a needle and may not improve if you take 'water pills' (diuretics).[5]
- Mantoux test – The Mantoux tuberculin skin test (TST) is one method of determining whether a person is infected with Mycobacterium tuberculosis.[6]

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Further Reading

32.

CASE 1-2020: ANSWERS TO THE QUESTIONS

Answer to Question 1: Based on the chief complaints of low urine output and edema along with heavy proteinuria and hypoalbuminemia, a diagnosis of nephrotic syndrome was made initially.[1] Nephrotic syndrome was suspected due to the presence of the classical triad of edema, proteinuria, and hypoalbuminemia.[2]

Answer to Question 2:

- According to the literature, the diagnosis of nephrotic syndrome includes:
    - Heavy proteinuria (dipstick 3–4+ or urine protein/creatinine ratio >0.2 g/mmol = >200 mg/mmol)
    - Hypoalbuminemia (<25 g/L) .[2]
- In this case study, the presence of heavy proteinuria in the urine dipstick test along with urine protein/creatinine ratio 7.3 g/mmol (Normal range: <0.2 g/mmol) and hypoalbuminemia <2.5 g/L (Normal range: 3.5- 5.5 g/dl) are confirmatory features for diagnosing nephrotic syndrome.[1]

Answer to Question 3:

- While idiopathic, or unknown, diseases are the most common cause of primary childhood nephrotic syndrome, researchers have linked certain diseases and some specific genetic changes that damage the kidneys with primary childhood nephrotic syndrome.[7]
    - The incidence of idiopathic nephrotic syndrome (INS) is 1.15–16.9 per 100 000 children, varying by ethnicity and region.[1]
- The cause of secondary childhood nephrotic syndrome is an underlying disease or infection. Called a primary illness, it's this underlying disease or infection that causes changes in the kidney function that can result in secondary childhood nephrotic syndrome.[7]
- Most children with nephrotic syndrome have "minimal change disease". This means that their kidneys appear normal or nearly normal if a tissue sample is studied under a microscope. But changes to the tissue sample can be seen if it's studied under an extremely powerful electron microscope. The cause of minimal change disease is unknown.[3]

Diagnosis [1]

- Based on these clinical presentations and lab investigations, the nephrotic syndrome was confirmed.

Treatment and Prognosis [1]

- After establishing the diagnosis, optimal supportive treatment including Enalapril p.o., Prednisolone p.o., intravenous albumin, furosemide, low salt intake, high caloric, and protein diet were given along with Ceftriaxone and Ascoril-LS. The urine output and blood pressure were monitored. Successful control of peripheral edema with the administration of albumin and diuresis with furosemide was seen. Peri-orbital edema and leg swelling reduced, and there was a concomitant increase in serum protein levels. The lipid levels also gradually decreased in due course of time without any medication.

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33.

CASE 2-2007: A 60-YEAR-OLD MALE WITH BREATHLESSNESS AND WEIGHT LOSS

Spontaneous regression of metastatic renal cell carcinoma: case report. Journal Of Medical Case Reports,2007, 1(1). doi: 10.1186/1752-1947-1-89

Lekanidi, K., Vlachou, P., Morgan, B., & Vasanthan, S.

Case Summary [1]

A 60-year-old male with a medical history of ***myelofibrosis*** *was presented with increased shortness of breath, lethargy, and weight loss at a routine clinic visit. Clinical examinations for this patient included a chest x-ray and a computed tomography (CT) scan that revealed* ***splenomegaly*** *and multiple pulmonary metastases in both lungs. Further investigations were conducted to determine the diagnosis of this patient.*

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://ecampusontario.pressbooks.pub/clinicalcases/?p=105#audio-105-1

Learning Objectives

- Investigating the clinical history of the patient and selecting appropriate examinations to be conducted for further analysis.
- Interpreting physical symptoms and test results to infer possible diagnosis.
- Familiarizing and defining new medical terminology associated with renal disease.
- Extrapolating key lifestyle factors that have contributed to renal disease and preventative measures that can be put in place, if applicable.

Clinical History [1]

- Age: 60 years old
- Sex: Male

Medical History [1]

- The patient has suffered from myelofibrosis.

Symptoms [1]

- Shortness of breath
- Weight loss
- Lethargy

Examinations (Clinical Assays/Tests/Imaging) [1]

Physical Examination [1]

- Normal

Chest X-Ray (CXR) [1]

- Results showed multiple lung lesions consistent with **metastatic** deposits.

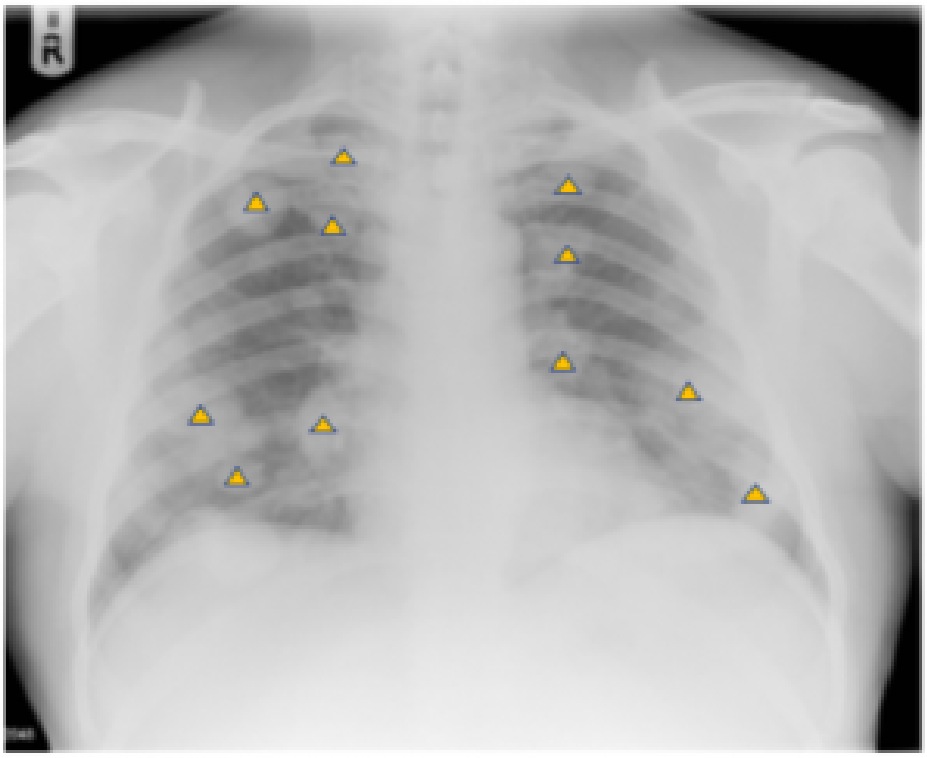

Figure 1: Chest X-Ray shows multiple lung lesions aligned with metastatic deposits (yellow arrows).[1]

Staging Computed Tomography (CT) Scan[1]

- Images showed marked splenomegaly, causing displacement of the left kidney medially.
- The left kidney had a 5 cm soft tissue mass arising from the middle of the kidney.
- Characterized to potentially be renal cancer.
- Multiple pulmonary metastases in both lungs were shown in the staging CT chest.

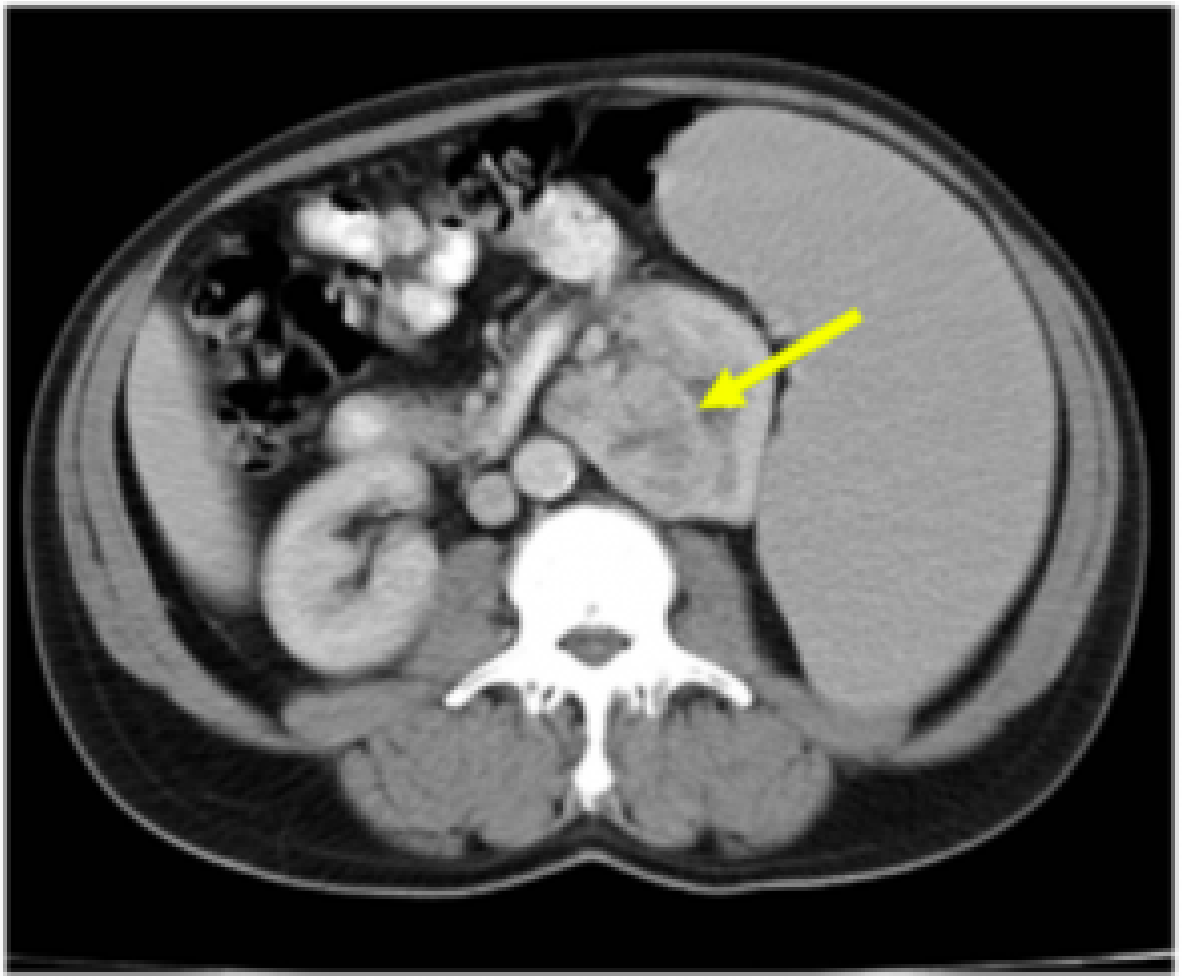

Figure 2: Computed Tomography shows splenomegaly and left renal carcinoma (yellow arrow).[1]

Laparoscopic Cytoreductive Nephrectomy [1]

- No complications and immunotherapy with alpha-interferon.

Histology [1]

- Revealed clear cell renal cell carcinoma.

Post-operation [1]

- The patient attended a routine follow-up at the hematology clinic, six weeks post-operation and prior to beginning immunotherapy.
    - A repeat chest radiography of his lungs showed completely resolved symptoms with evidence of metastatic deposits.

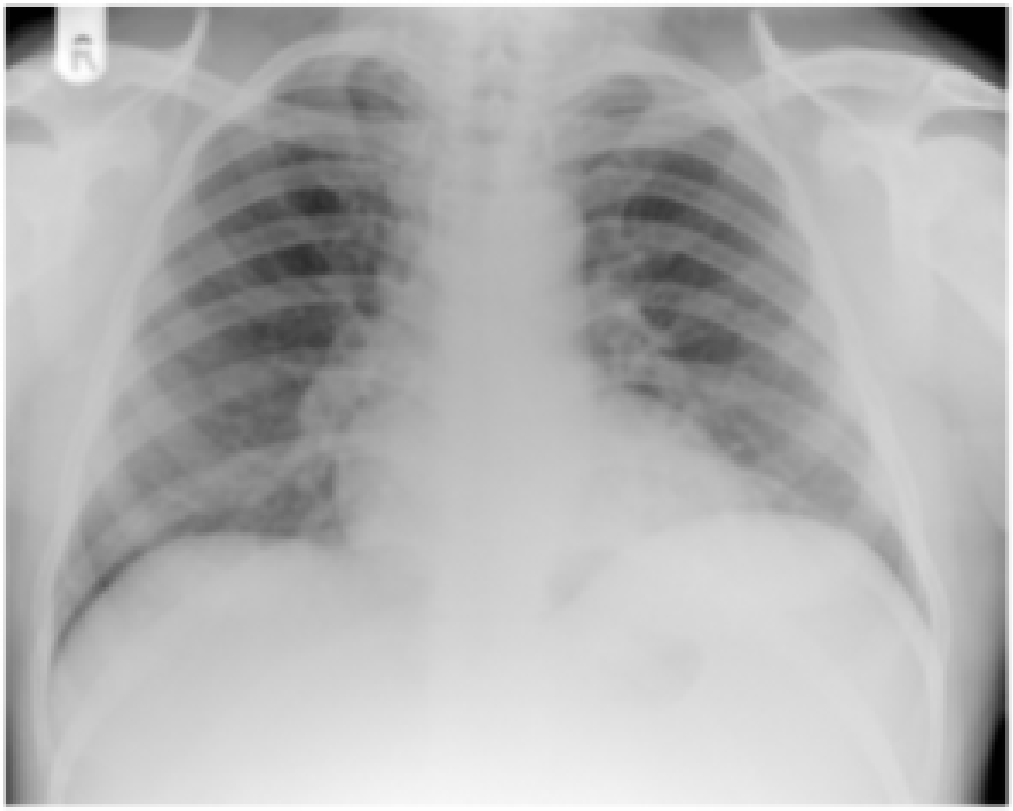

Figure 3: Chest X-Ray from routine follow-up showing no metastases six weeks after the operation.[1]

Question & Answers Leading to Diagnosis:

Question 1: Based on this patients' previous medical history, current symptoms, and imaging tests, what may be the preliminary diagnosis of this patient?

Question 2: After the successful laparoscopic cytoreductive nephrectomy, histology was used to characterize the morphology of this patient's cells, what was the patient's diagnosis? What other methods could have been used to assistin the diagnosis?

Question 3: Post-operation and immunotherapy, what investigations would be appropriate for the follow-up?

** For answers please check the next chapter.

Medical terminology/Abbreviations:

- Hematological – Relating to blood and body tissue. [4]
- Metastatic/Metastasis – Cancer that can spread to different areas of the body. [3]
- Myelofibrosis – A rare blood cancer, a form of chronic leukemia. [2]
- Nephrectomy – Surgical removal of whole or parts of a kidney. [5]
- Splenomegaly – the enlargement of the spleen. [6]

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Further Reading

34.

CASE 2-2007: ANSWERS TO THE QUESTIONS

Answer to Question 1: This patient has had a history of myelofibrosis, a bone marrow cancer that has been known to disrupt the normal productions of red blood cells and has the potential to spread throughout the body due to the copying of faulty genes.[9] Today, this patient is presenting symptoms of lethargy and shortness of breath, which may indicate the spreading of this disease to his lungs – this was confirmed with a chest x-ray (figure 1) revealing multiple lung lesions and consistent with metastatic deposits – spreading of cancer cells to new areas of the body.[1,10]

Answer to Question 2:

- Histology would reveal that the patient was suffering from cell renal cell carcinoma.[1] A staging computed tomography (figure 2) would later reveal an enlarged spleen and a 5 cm soft tissue mass arising from the left kidney from the middle of the kidney.[1] These findings would support metastatic characteristics and potential renal cancer leading physicians to conduct a laparoscopic cytoreductive nephrectomy.[1]
- Other methods that would help assist in this diagnosis would be biomarkers such as, CXCL16, vascular-derived growth factor (VEGF), and carbonic anhydrase IX, as supported in the literature.[13] CXCL16 is among the newest biomarkers used for renal cell carcinoma detection, with specificity for papillary renal cell carcinoma while acting as an "independent prognostic marker for patient survival".13 VEGF is a good biomarker for determining the stage, increased levels, and grade of cancer. Carbonic anhydrase IX has been shown to have "excellent specificity and ability to predict treatment response(s)".[13]

Answer to Question 3: Post-operation and immunotherapy, appropriate investigations for this patient's follow-up should consist of a chest X-ray to monitor the previously revealed metastatic deposits in the lungs, a CT scan or abdominal U/S to investigate the condition of the spleen and surrounding areas, and blood investigations (blood count, serum chemistries and liver function tests).[7]

Diagnosis [1]

- Metastatic renal cell carcinoma.

Treatments [1]

- The patient had undergone a laparoscopic cytoreductive nephrectomy (removal of tissue mass on kidney) with no complications, followed by immunotherapy with alpha-interferon.
- The chest x-ray from the follow-up 6 months later would suggest a successful response to treatment with the clearing of metastatic deposits in the lungs.

PART VIII

RESPIRATORY CASE STUDIES

35.

CASE 1-2010: A 68-YEAR-OLD MALE WITH BREATHLESSNESS

Lower respiratory tract infection and rapid expansion of an abdominal aortic aneurysm: a case report. Journal of Medical Case Reports,2010, 4(1). doi: 10.1186/1752-1947-4-333

Naylor, S., Gamie, Z., Vohra, R., Puppala, S., Kent, P., & Scott, D.

Case Summary [1]

A 68-year-old Caucasian male was admitted with a contaminated ***lower respiratory tract infection*** *(LRTI), increasing back pain and* ***epigastric*** *discomfort. This patient's medical history includes consistent cigarette smoking for 20 years, a* ***coronary artery bypass graft*** *for* ***ischemic heart disease****, and an existing aortic aneurysm. Clinical examinations showed tender epigastrium and left bronchopneumonia. A computed tomography (CT) aortogram, CT thorax, and coronal CT angiogram were used to further investigate this patient's condition and diagnosis.*

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://ecampusontario.pressbooks.pub/clinicalcases/?p=107#audio-107-1

Learning Objectives

- Investigating the clinical history of the patient and selecting appropriate examinations to identify this respiratory infection.
- Correlating the patient's symptoms and the case study clinical examinations to narrow down the possible diagnosis.
- Familiarizing and defining new medical terminology associated with this patient's condition.
- Extrapolating key lifestyle factors that have contributed to the respiratory infection and preventative measures that can be put in place to ensure the future health of the patient.

Clinical History [1]

- Age: 68 years old
- Sex: Male
- Ethnicity: Caucasian

Medical History [1]

- Has been previously diagnosed with infra-renal **AAA** which had been monitored for six-months.
  - Maximum diameter was 4.9 cm, grown to 5.2 cm over one year.
  - Most recent ultrasound scan was conducted two months before admission.
    - Maximal diameter of the **AAA** was 5.4 cm.
- 20 years of cigarette smoking.
- **Ischemic heart disease** thus underwent coronary artery bypass graft in 1987.

Symptoms [1]

- Shortness of breath
- Presumed community acquired LRTI (lower respiratory tract infection)
- Increasing back pain
- Epigastric discomfort
- 48-hours after admission, patient experienced pre-syncope with brief periods of hypertension

Examinations (Clinical Assays/Tests/Imaging) [1]

Physical Examination [1]

- Hemodynamically stable, however pyrexial and **hypoxic**.

Clinical Examinations [1]

- Signs of tender epigastrium.

Blood Investigations [1]

- Leukocytosis with neutrophilia: 15.03 x 10^9/L (Normal range: 2.5-7.5 x 10^9/L)[4]

Computed Tomography (CT) Aortogram [1]

- Confirmed non-leaking 5.6 cm AAA (abdominal aortic aneurysm) (figure 1, yellow arrow).
- Extensive lower lobe consolidation and collapse with hilar lymphadenopathy was observed (figure 2, yellow arrow).

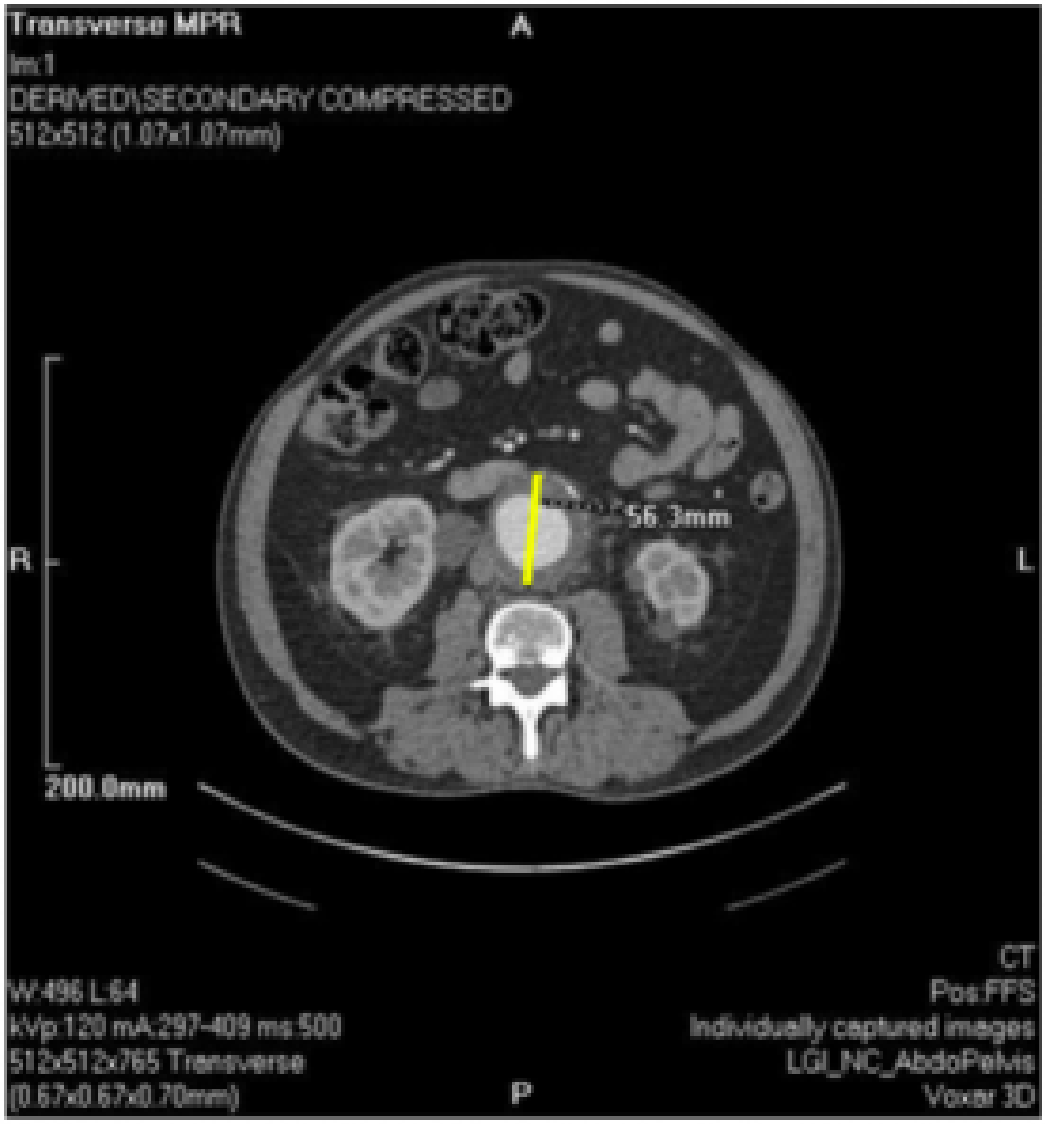

Figure 1: CT aortogram revealing the 5.6 cm (yellow line) anteroposterior diameter AAA.[1]

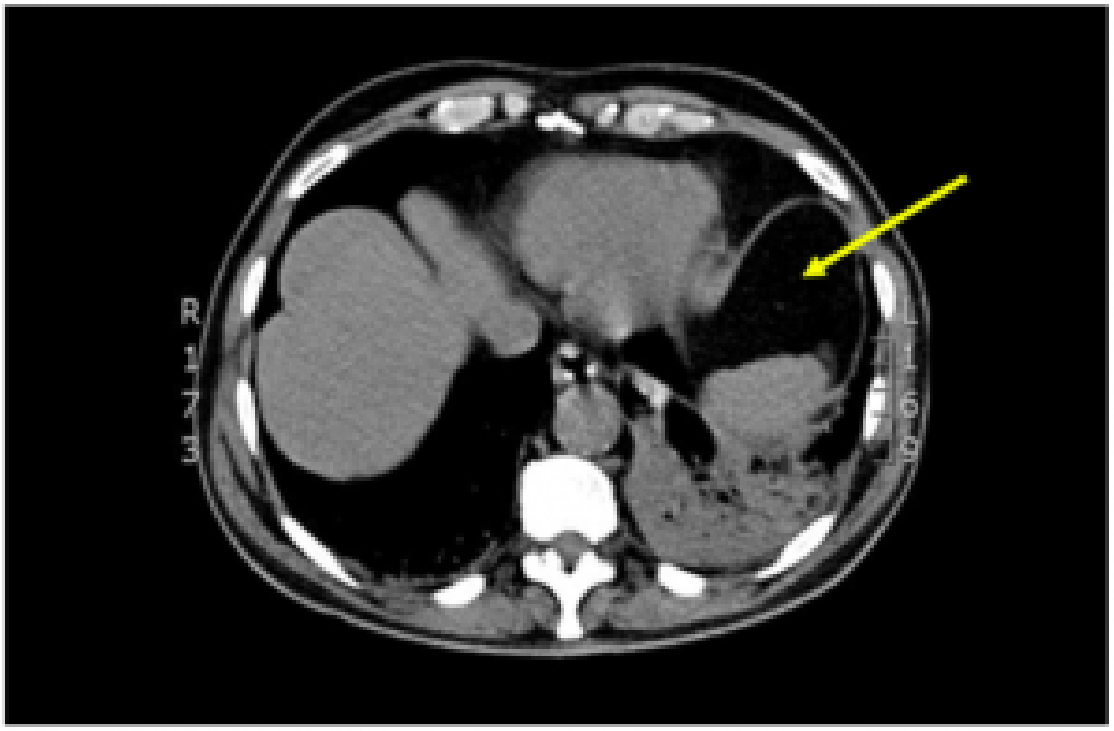

Figure 2: CT thorax shows the lower lobe consolidation and collapse in the left lung (yellow arrow) with extensive hilar lymphadenopathy.[1]

- Due to symptoms of hypotension 48-hours after admission, a repeat CT aortogram was conducted revealing the increased size of the AAA to 7.0 cm (figure 3, yellow line). This would also reveal retroperitoneal fat stranding (figure 4, yellow line).
- No significant angulation (changes in angle formation) was shown in the neck of the aneurysm. The juxta-renal diameter (aneurysms adjacent to renal artery origins) had been 22.1 mm before increasing to 25.4 mm in its infra-renal (below the renal artery origins) segment (figure 4).
    - These repeat CT scans revealed significant **stenosis** (narrowing) of the left common iliac artery.

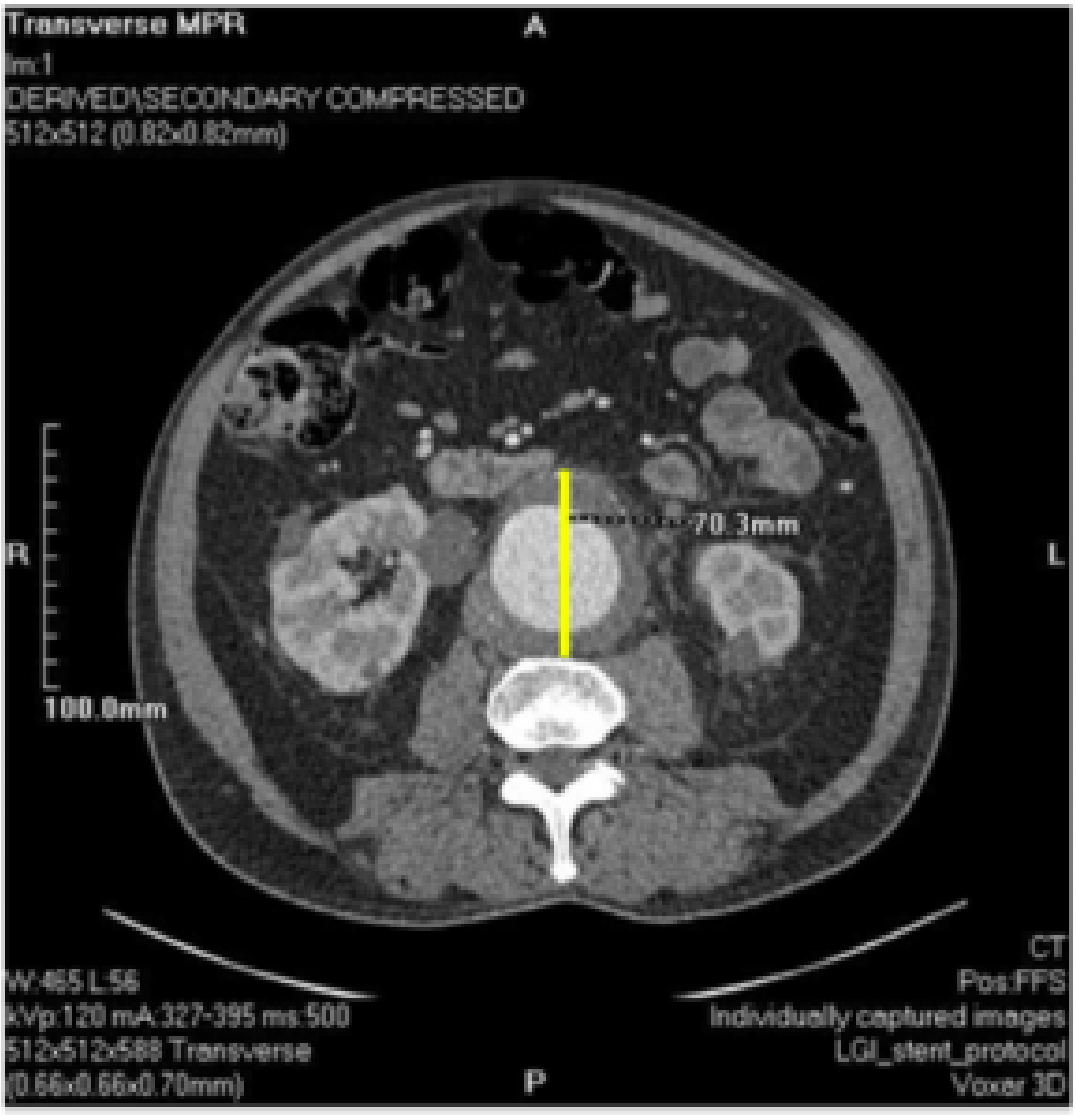

Figure 3: CT aortogram shows a rapid increased 7.0 cm (yellow line) size of the AAA in the anteroposterior diameter. This also shows sign of impending rupture and beak in left lateral aortic thrombus.[1]

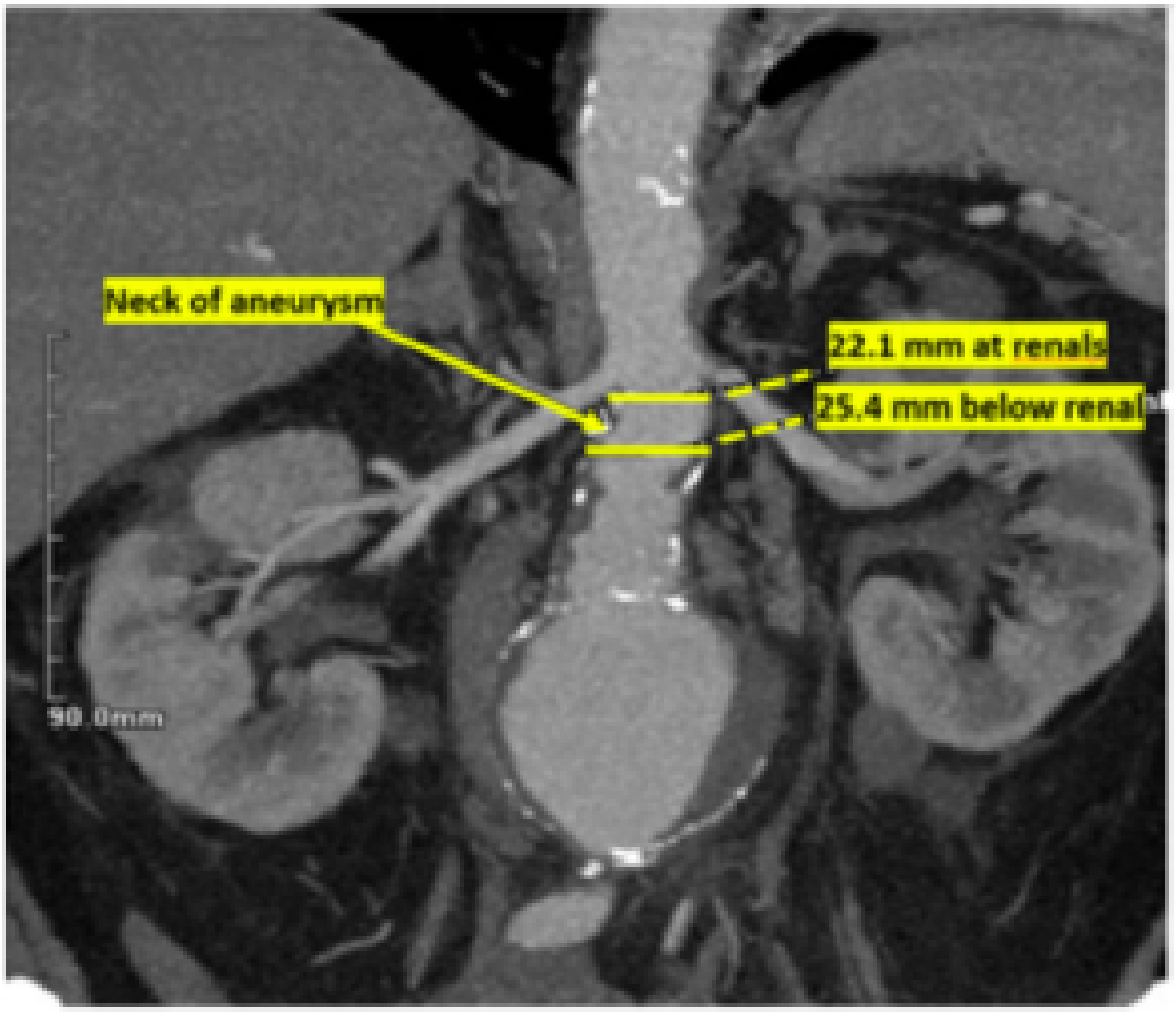

Figure 4: Coronal CT angiogram image shows 7.0 cm aneurysm. The diameter of the neck of aneurysm at the renal arteries were 22.1 mm and the renal arteries below were 25.4 mm.[1]

Question & Answers Leading to Diagnosis:

Question 1: Considering the patient's previous medical history and current symptoms, what diagnosis could we expect?

Question 2: From the patient's respiratory symptoms, lab investigations and CT scans, what is the confirmatory diagnosis?

Question 3: The CT scans have shown AAA expansion and lower lobe consolidation, what biomarkers could be used to support this diagnosis? How can both diagnoses be correlated?

** For answers please check the next chapter.

Medical terminology/Abbreviations:

- Abdominal aortic aneurysm (AAA) – The enlargement of the lower area of the major vessel which supplies blood to the body.[10]
- Chemokines – A family of chemoattractant cytokines which are secreted by cells in response to the body's immune system.[11]
- Computed tomography (CT) aortogram – A technique using CT scanning and an injection of contrast material into the blood vessels to examine and diagnose cardiovascular diseases. [12]
- Computed tomography (CT) thorax – An imaging test to examine organs and chest using X-ray and computer technology. [13]
- Coronal computed tomography (CT) angiogram – A technique using CT scanning and an injection of contrast material into the blood vessels to evaluate structure and patency of arteries suppling lower limbs and abdomen with blood. [14]
- Coronary artery bypass graft – Surgery redirecting blood around a blocked artery of the heart. [15]
- Cytokines – Group of glycoproteins, peptides and proteins secreted by cells in response to the immune system, they regulate and mediate immunity. [16]
- Epigastric – Upper central region of the abdomen. [17]
- Growth factor – Substance required for growth stimulation in living cells. [18]
- Hypoxic – Condition where the areas of the body or the body does not have an adequate oxygen supply at the tissue level. [19]
- Ischemic heart disease (or coronary heart/artery disease) – Disease with the heart is getting an inadequate supply of blood and oxygen due to narrowing of arteries. [20]

- Lower respiratory tract infection (LRTI) or pneumonia – Infection that involves the lungs abscess and acute bronchitis. [21]
- Pro-inflammatory biomarkers – Regulatory proteins that can be used to detect inflammation. [22]
- Sepsis – Condition where the body's response to an existing infection begins to damage it's own tissues, this can be a potentially life-threatening. [23]
- Stenosis – Narrowing of the diameter of bodily passages. [24]

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dictionary/stenosis

Further Reading

CASE 1-2010: ANSWERS TO THE QUESTIONS

Answer to Question 1: This patient has had a history of infra-renal AAA, ischemic heart disease, however, his presenting symptoms of back pain and shortness of breath are common indicators of a worsening abdominal aortic aneurysm.[2] A differential diagnosis could be made as well, this patient's drug history of 20 years of cigarette smoking puts him at a higher risk of pneumonia. Correlating symptoms of shortness of breath could be early signs of this condition.[3]

Answer to Question 2: In this case study, lab investigations revealed high levels of neutrophils confirming increased levels of inflammation in the body. CT scans would not only reveal the expansion of the abdominal aortic aneurysm from previous reports of 5.2 cm to now, 7.0 cm (figure 4, yellow line), but a CT thorax would show lower lobe consolidation (lung collapsing, figure 2, yellow arrow). This would lead to the confirmatory diagnosis of AAA expansion and lobar pneumonia, all supported with the patient's presenting symptoms.[1]

Answer to Question 3: Biomarkers that could support this diagnosis would be pro-inflammatory IL-1b, IL-6, IL-10, and TNF.[5,6] These biomarkers have been previously shown to positively correlate with aneurysm growth, as they can be present within the wall of an AAA.[5,6] Not only would these biomarkers be great indicators of AAA expansion, but the literature reports these chemokines, cytokines, and growth

factors levels increase during septic events of lower respiratory tract infections due to close proximity.[7] The literature also documents an association between AAA and pulmonary sepsis.[8,9] This patient's lobar pneumonia can be upregulating the previously mentioned inflammatory mediators within the AAA wall, weakening the aortic wall and leading to expansion.[1]

Diagnosis [1]

- The patient was diagnosed with lobar pneumonia and abdominal aortic aneurysm expansion.

LABORATORY TESTS REFERENCE RANGES

Complete Blood Count [1]

RBC Tests [1]	**Conventional units**	**SI units**
RBC	Men: 4.5-5.9 x 10^6/mcl Women: 4.1-5.1 x 10^6/mcl	Men: 4.5-5.9 x 10^{12}/L Women: 4.1-5.1 x 10^{12}/L
Hb	Men: 14-17.5 g/dL Women: 12.3-15.3 g/dL	Men: 140-175 g/L Women: 123-153 g/L
Hematocrit	Men: 41.5-50.4% Women: 35.9-44.6%	Men: 0.415-0.504 volume f Women: 0.359-0.446 volun
MCV	80-96 micrometer	80-96 fL
MCH	27.5-33.2 pg	27.5-33.2 pg
MCHC	33.4-35.5 g/dL	334-355 g/L
RBC Distribution Width (RDW, RDW-SD, RDW-CV) Not always reported	This indicates that RBC are uniform in size.	
Reticulocyte count (Not always done)	0.5-1.5% or 25-125 x 10^3/mcl	0.005-0.015 number fracti 25-125 x 10^9/L

WBC Tests [1]	Conventional units	SI units
WBC counts	4,500-11,000 white blood cells per microliter (mcL)	4.5-11.0 x 109 per liter (L)
Absolute neutrophil count, % neutrophils (Neu, PMN, polys)	Percent (mean): 56% Absolute count: 1800-7800 cells per microliter (mcL)	Mean number fraction: 0.56 Absolute count: 1.8-7.8 x 109 per liter
Absolute lymphocyte count, % lymphocytes (Lymph)	Percent (mean) 34% Absolute count: 1000-4800 cells per microliter (mcL)	-Mean number fraction: 0.34 -Absolute count: 1.0-4.8 x 109 per liter
Absolute monocyte count, % monocytes (Mono)	Percent (mean) 4% Absolute count: 0-800 cells per microliter (mcL)	Mean number fraction 0.04 Absolute count: 0-0.80 x 109 per liter
Absolute eosinophil count, % eosinophils (Eos)	Percent (mean) 2.7% Absolute count: 0-450 cells per microliter (mcL)	Mean number fraction 0.027 Absolute count: 0-0.45 x 109 per liter
Absolute basophil count, % basophils (Baso)	Percent (mean) 0.3% Absolute count: 0-200 cells per microliter (mcL)	Mean number fraction 0.030 Absolute count: 0-0.20 x 109 per liter

Platelet tests [1]	Conventional units	SI units
Platelet Count (Plt)	150-450 x 103/microliter	150-450 x 109/L
MPV (Mean Platelet Volume) Not always reported	This indicates the average size of platelets is small; older platelets are generally smaller than young ones and a low MPV may mean that a condition is affecting the production of platelets by the bone marrow.	
PDW (Platelet Distribution Width) Not always reported	Indicates uniformity in size of platelets.	

Coagulation (Hemostasis) profile [2]

Clinical laboratory test [2]	Normal value in adults
Bleeding time (Ivy method), blood	1–9 min
International normalized ratio (INR), nonanticoagulated, blood	0.9–1.2
Activated partial thromboplastin time (APTT), nonanticoagulated, blood	22–30 s
Prothrombin time (PT), blood	10–14 s

Lipid panel [3,4,5,6,7]

Test	Optimal or Desirable	Near/Above Optimal	Borderline High	High	Very High
LDL Cholesterol[4]	Less than 100 mg/dL; with CVD or diabetes: less than 70 mg/dL	100-129 mg/dL	130-159 mg/dL	160-189 mg/dL	Greater than 190 mg/dL
Total Cholesterol[5]	Less than 200 mg/dL		200-239 mg/dL	240 mg/dL or higher	
Fasting Triglycerides[3]	Less than 150 mg/dL		150-199 mg/dL	200-499 mg/dL	Greater than 500 mg/dL
Non-HDL Cholesterol[6]	Less than 130 mg/dL	130-159 mg/dL	160-189 mg/dL	190-219 mg/dL	Greater than 220 mg/dL

HDL Cholesterol[7]	Low Level, Increased Risk	Average Level, Average Risk	High Level, Less than Average Risk
Women	Less than 50 mg/dL (1.3 mmol/L)	50-59 mg/dl (1.3-1.5 mmol/L)	60 mg/dL (1.55 mmol/L) or higher
Men	Less than 40 mg/dL (1.0 mmol/L)	40-50 mg/dL (1.0-1.3 mmol/L)	60 mg/dL (1.55 mmol/L) or higher

Liver function tests[8]

Alanine transaminase (ALT)	7 to 55 units per liter (U/L)
Aspartate transaminase (AST)	8 to 48 U/L
Alkaline phosphatase (ALP)	40 to 129 U/L
Albumin	3.5 to 5.0 grams per deciliter (g/dL)
Total protein	6.3 to 7.9 g/dL
Bilirubin	0.1 to 1.2 milligrams per deciliter (mg/dL)
Gamma-glutamyl transferase (GGT)	8 to 61 U/L
L-lactate dehydrogenase (LD)	122 to 222 U/L
Prothrombin time (PT)	9.4 to 12.5 seconds

Iron panel[9,10,11]

Iron Panel Tests	**Adult Male**	***Adult* Female**
Iron(µg/dL)[9]	35-165	35-165
Ferritin(µg/L)[11]	24-336	11-307
Transferrin(mg/dL)[10]	215-365	250-380
TIBC(µg/dL)[9]	252-479	252-479
Iron Saturation(%)[9]	20-50	15-50

Arterial Blood Gas[11]

Clinical laboratory test[11]	**Normal value in adults**
pH, arterial blood	7.38–7.46
Pco2, arterial blood	32–45 mm Hg
Po2, arterial blood	83–116 mm Hg
Bicarbonate (HCO3), arterial blood	22–27 mmol/L
Base excess, arterial blood	–2.5 to 2.5 mmol/L

Thyroid profile[11]

Clinical laboratory test[11]	Normal value in adults
Thyroid peroxidase antibody, blood	< 35 IU/mL
Thyrotropin (thyroid-stimulating hormone), blood	0.34–5.60 mIU/L
Thyroxine, free (FT4), blood	7.0–17.0 pmol/L
Triiodothyronine, free (FT3), blood	3.3–6.0 pmol/L

Chemical constituents in blood[11]

Clinical laboratory test[11]	Normal value in adults
Adrenocorticotropic hormone (ACTH), blood	At 8 AM: 2.2–13.3 pmol/L At 4 PM: < 4.5 pmol/L
Albumin, blood	34–50 g/L
Aldosterone, blood	61–978 pmol/L
Alkaline phosphatase, blood	50–136 IU/L
Transaminase	
Alanine aminotransferase (ALT), blood	17–63 IU/L
Aspartate aminotransferase (AST), blood	15–37 IU/L
γ-Glutamyltransferase (GGT), blood	5.0–55.0 IU/L (Female) 15.0–85.0 IU/L (Male)
Ammonia, blood	≤ 35 μmol/L
Amylase, blood	25–115 IU/L
Anion gap, blood	5–12 mmol/L
Bicarbonate (HCO3), blood	21–32 mmol/L
Bilirubin, blood	
Direct (conjugated)	2–9 μmol/L
Total	3–17 μmol/L
Brain-type natriuretic peptide (BNP)	
BNP, blood	≤ 50 pg/mL
◈-terminal pro–brain-type natriuretic peptide (NT-proBNP), blood	≤ 125 pg/mL
CD4 T-cell count, blood	500–2000 cells/μL
C-reactive protein, blood	≤ 10 mg/L
Calcium (Ca), blood	
Total	2.12–2.52 mmol/L
Ionized	1.14–1.28 mmol/L
Cancer antigen (CA) 125, blood	< 35 kIU/L
Cancer antigen (CA) 19-9, blood	< 35 kIU/L
Carbamazepine, blood	17–51 μmol/L
Carcinoembryonic antigen (CEA), blood	< 3.0 μg/L
Chloride (Cl), blood	98–107 mmol/L

Cortisol, blood	Morning (AM): 185–624 nmol/L Evening (PM): ≤ 276 nmol/L
Creatine kinase (CK), blood	30–190 IU/L (Female) 30–250 IU/L (Male)
Creatinine, blood	22–75 μmol/L (Female) 49–93 μmol/L (Male)
D-dimer, blood	< 600 μg/L
Estimated glomerular filtration rate (eGFR), blood	≥ 60 mL/min/1.73 m2
α1-Fetoprotein, blood	≤ 9.0 μg/L
Folate (folic acid), blood	≥ 10.0 nmol/L
Glucose, blood	4.0–6.0 mmol/L (Fasting) 4.0–11.0 mmol/L (Random)
Hemoglobin A1c (HbA1c), blood	4.8%–6.0%
Hepatitis B surface antibodies, blood	≥ 10 mIU/mL (Positive) < 10 mIU/mL (Negative)
Lactate, blood	0.5–2.5 mmol/L
Lactate dehydrogenase (LDH), blood	100–205 IU/L
Lipase, blood	73–393 IU/L
Lithium (Li), blood	0.6–1.2 mmol/L (Age 18–65 y) 0.4–0.8 mmol/L (Age > 65 y)
Magnesium (Mg), blood	0.74–1.03 mmol/L
Osmolality, blood	275–295 mmol/kg
Parathyroid hormone (PTH), blood	1.6–9.3 pmol/L
Phosphate (PO4), blood	0.81–1.58 mmol/L
Potassium (K), blood	3.5–5.1 mmol/L
Prostate-specific antigen (PSA), blood	< 3.1 μg/L
Protein, total, blood	65–83 g/L (Age 18–<30 y) 65–78 g/L (Age ≥30 y)
Rheumatoid factor (RF), blood	≤ 20 kIU/L
Troponin I, blood	≤ 45 ng/L

Troponin T (TnT), blood	≤ 0.1 μg/L
Uric acid, blood	155–400 μmol/L (Female) 208–400 μmol/L (Male)
Urea, blood	2.1–8.0 mmol/L
Valproic acid, blood	350–700 μmol/L
Vitamin B12, blood	133–675 pmol/L
Vitamin D (25-hydroxyvitamin D), blood	75–250 nmol/L

Urinalysis11

Clinical laboratory test11	**Normal value in adults**
Specific gravity, urine	1.005–1.030
pH, urine	5.0–8.5
Urobilinogen, urine	≤ 16.0 μmol/L
Albumin to creatinine ratio, urine	≤ 2.0 g/mol Cr
Osmolality, urine	38–1400 mOsm/kg H2O

24-hour specimen[11]

Clinical laboratory test[11]	Normal value in adults
Urine calcium (Ca), unrestricted diet, 24-h specimen	2.5–7.5 mmol/24 h
Urine chloride (Cl), 24-h specimen	110.0–250.0 mmol/24 h
Urine creatinine, weight-based, 24-h specimen	5.3–15.9 mmol/24 h (Female) 7.1–17.7 mmol/24 h (Male)
Urine metanephrine, 24-h specimen	0.2–1.3 μmol/24 h (Female) 0.3–2.0 μmol/24 h (Male)
Urine protein, 24-h specimen	< 0.2 g/24 h
Urine potassium (K), 24-h specimen	25.0–125.0 mmol/24 h
Urinary free cortisol, 24-h specimen	58.0–306.0 μg/24 h
Urine sodium (Na), 24-h specimen	40.0–220.0 mmol/24 h

Reproductive hormones[11]

Clinical laboratory test[11]	Normal value in adult female	Normal value in adult male
Dehydroepiandrosterone sulfate (DHEA-S), blood	1.4–8.7 µmol/L (18–20 y) 0.5–10.6 µmol/L (21–29 y) 0.6–7.2 µmol/L (30–39 y) 0.5–6.3 µmol/L (40–49 y) 0.2–5.1 µmol/L (50–59 y) 0.3–3.6 µmol/L (60–69 y) 0.2–4.8 µmol/L (70–118 y)	0.7–14.6 µmol/L (18–20 y) 2.3–18.7 µmol/L (21–29 y) 2.9–12.6 µmol/L (30–39 y) 1.9–13.4 µmol/L (40–49 y) 1.0–8.5 µmol/L (50–59 y) 0.7–6.6 µmol/L (60–69 y) 0.1–6.9 µmol/L (70–118 y)
Estrogens, total, blood	60–400 ng/L (Female) 50–100 pmol/L (Follicular phase)	
Estradiol (E2) [report the phase of the menstrual cycle], blood	50–200 pmol/L (Midcycle peak) 70–150 pmol/L (Luteal phase) 3.9–8.8 IU/L (Midfollicular phase)	37–110 pmol/L
Follicle-stimulating hormone (FSH) [report the phase of the menstrual cycle], blood	4.5–22.5 IU/L (Midcycle peak) 1.8–5.1 IU/L (Midluteal phase) 16.7–113.6 IU/L (Postmenopausal)	1.0–19.0 IU/L
Human chorionic gonadotropin (β-hCG), nonpregnant, blood	< 5 IU/L (Female) 2.1–10.8 IU/L (Midfollicular phase)	
Luteinizing hormone (LH) [report the phase of the menstrual cycle], blood	19.2–103.0 IU/L (Midcycle peak) 1.2–12.9 IU/L (Midluteal phase) 10.9–58.6 IU/L (Postmenopausal)	1.0–9.0 IU/L
Progesterone [report the phase of the menstrual cycle], blood	1.0–4.8 nmol/L (Midfollicular phase) 16.4–59.0 nmol/L (Midluteal phase)	0.5–6.6 nmol/L

Prolactin, blood	3–27 µg/L (Premenopausal) 3–20 µg/L (Postmenopausal)	3–13 µg/L
Testosterone, blood	≤ 2.6 nmol/L	6.1–27.1 nmol/L

Semen analysis[11]

Clinical laboratory test	Normal value in adults
Ejaculate volume, semen	≥ 1.5 mL
pH, semen	≥ 7.2
Sperm concentration, semen	≥ 15 × 106 spermatozoa/mL
Total sperm number, semen	≥ 39 × 106 spermatozoa/ejaculate
Motility, semen	≥ 40%
Forward progression, semen	≥ 32%
Normal morphology, semen	≥ 4% normal
Sperm agglutination, semen	Absent
Viscosity, semen	≤ 2-cm thread after liquefaction

Stool[11]

Clinical laboratory test	Normal value in adults
Fecal fat	< 5 g/day in patients on a 100-g fat diet

Tests and analyses that do not require a normal value[11]

Urine (not dipstick)	· Eosinophils, urine · Sodium (Na), urine · Glucose, urine · Bilirubin, urine · Ketone, urine · Blood, urine · Protein, urine · Nitrite, urine · Leukocytes, urine
Urinalysis, dipstick testing	· Bilirubin, urine · Blood, urine · Glucose, urine · Ketones, urine · Leukocyte esterase, urine · Nitrite, urine · Protein, urine
Chemical Constituents	· Ethanol (ethyl alcohol) · Hepatitis A IgM antibody · Hepatitis A IgG antibody · Hepatitis C antibody · HIV viral load
Stool	· Stool culture

Analyses	· Pleural fluid · Cerebrospinal fluid · Synovial fluid · Ascitic fluid

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MEDICAL TERMINOLOGY

A

Abdominal aortic aneurysm (AAA) – The enlargement of the lower area of the major vessel which supplies blood to the body.[1]

Acquired Hemophilia A – Acquired Hemophilia A (AHA) is a rare bleeding disorder related to the formation of autoantibodies to Factor VIII.[2]

Adenocarcinoma – Adenocarcinoma is a type of cancer that starts in mucus-producing glandular cells of the body.[3]

Adenomyoma – A benign mass-forming lesion composed of smooth and glandular muscle.[4]

Antibiotic prophylaxis – Antibiotic usage before surgery or procedure in order to prevent bacterial infection.[5]

Anti-thyroid peroxisomal antibodies – Antibodies that are associated with a thyroid disease due to an autoimmune disorder.[6]

Anti-thyroid receptor antibodies – Antibodies responsible for blocking, neutralizing, and activating thyroid receptors, associated with autoimmune thyrotoxicosis.[7,8]

AP (Acute pancreatitis) – Acute pancreatitis means inflammation of the pancreas that develops quickly.[9]

APGAR score (Appearance, Pulse, Grimace, Activity, and Respiration)[10] – The Apgar score is a scoring system that assesses newborn babies' well-being using five different factors: heart rate, breathing, muscle tone, reflexes, and skin color. APGAR is a quick test performed on a baby at 1 and 5 minutes after birth. The 1-minute score determines how well the baby tolerated the birthing process. The 5-minute score tells the health care provider how well the baby is doing outside the mother's womb. The score is based on a total score of 1 to 10. The higher the score, the better the baby is doing after birth.[11]

APTT or PTT – The partial thromboplastin time (PTT; also known as activated partial thromboplastin time (aPTT)) is a screening test that helps evaluate a person's ability to appropriately form blood clots.[12]

ARDS – Acute respiratory distress syndrome.[13]

B

Bleeding diathesis – In medicine (hematology), bleeding diathesis is an unusual susceptibility to bleed (hemorrhage) mostly due to hypocoagulability (a condition of irregular and slow blood clotting), in turn, caused by a coagulopathy (a defect in the system of coagulation).[14]

Brain MRI in Wilson disease- MR imaging is a sensitive method to evaluate the brains of patients with neurologic WD. Whereas abnormalities in the putamen are the most common feature of neurologic WD, brain shrinkage is also frequently observed.[15]

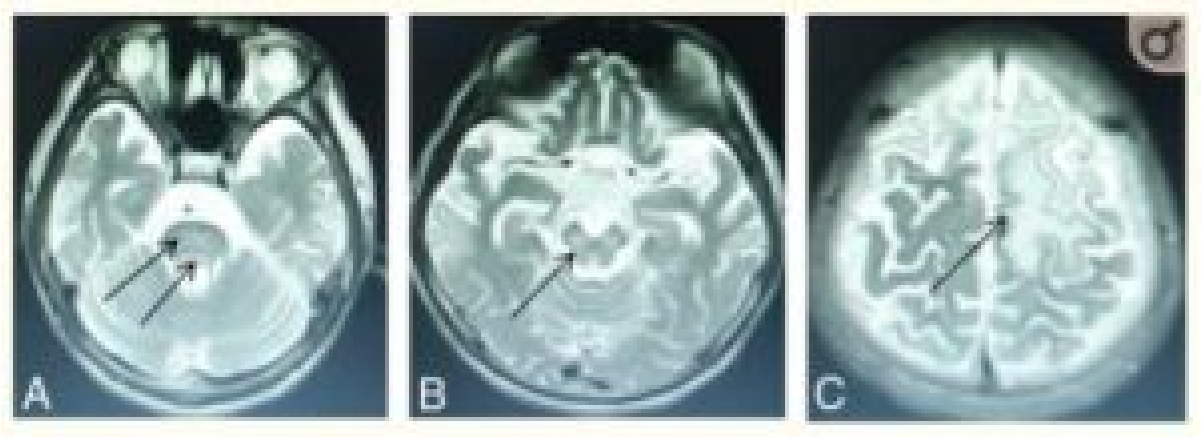

Figure 1: High signal intensity lesions on T2WI. Wilson disease in a 14-year-old girl with dystonia, with a diagnosis lag time 5 years (participant group >3 years) and abnormal signal in the pons (D), midbrain (E), and frontal and parietal lobes (F) (arrows).[15]

Brain natriuretic peptide (BNP) – It is a peptide hormone that is released in response to volume expansion and the increased wall stress of cardiac myocytes.[16]

Bronchoscopy – Bronchoscopy is a procedure that looks inside the lung airways. It can detect tumors, signs of infection, excess mucus in the airways, bleeding, or blockages in the lungs.[17]

Brudzinski's sign – Brudzinski's sign is one of the physically demonstrable symptoms of meningitis. Severe neck stiffness causes a patient's hips and knees to flex when the neck is flexed. (Figure 3) It is used to diagnose meningitis.[18]

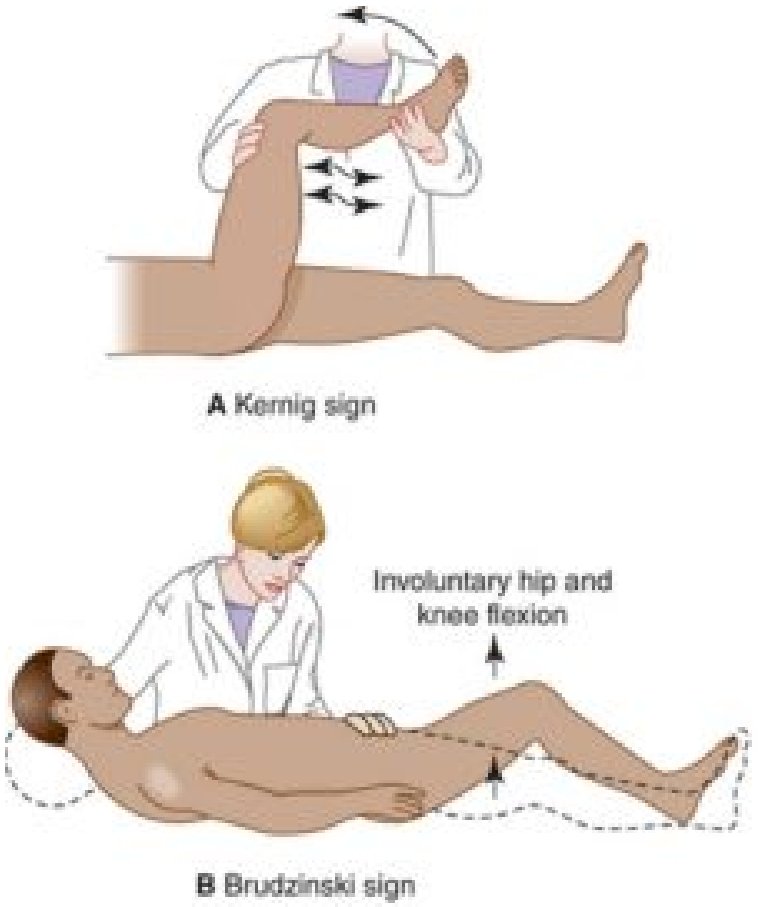

Figure 2: Kernig sign and Brudzinski sign[19]

Kernig's sign – Kernig's sign is one of the physically demonstrable symptoms of meningitis. Severe stiffness of the hamstrings causes an inability to straighten the leg when the hip is flexed to 90 degrees. (Figure 3) It is used to diagnose meningitis.[19]

Bypass graft surgery – Procedure to treat coronary artery disease due to a buildup of fat in the walls of the arteries.[20]

C

Cardiothoracic surgery – A field of medicine involving surgical treatment of organs within the thoracic cavity.[21]

Carious dentition – Dental caries or cavities, more commonly known as tooth decay, are caused by a breakdown of the tooth enamel. This breakdown is the result of bacteria on teeth that break down foods and produce acid that destroys tooth enamel and results in tooth decay. [22]

CEA – A carcinoembryonic antigen (CEA) test is a blood test used to help diagnose and manage certain types of cancers.[23]

Ceruloplasmin test– Ceruloplasmin is a copper-containing enzyme that plays a role in the body's

iron metabolism. This test measures the amount of ceruloplasmin in the blood. The liver binds copper to a protein to produce ceruloplasmin and then releases it into the bloodstream. About 95% of the copper in the blood is bound to ceruloplasmin. Because of this, the ceruloplasmin test can be used along with one or more copper tests to help diagnose Wilson disease, an inherited disorder that can lead to excess storage of copper in the eyes, liver, brain, and other organs. [24]

CfDNA – In addition to the classic biomarkers, cfDNA was first described in 1948, has the potential to be a useful marker in septic shock. CfDNA is released into the circulation through cell lysis, necrosis, apoptosis and active DNA release, resulting in higher concentrations of cfDNA in patients with microbial infections, trauma, cancer and other clinical conditions. Although elevated levels of cfDNA are not specific to a single disease, elevated cfDNA has been shown to be an extremely sensitive and promising prognostic marker in septic shock. This observation may be associated with the shorter half-life of cfDNA than that of PCT and CRP. According to Ahmed, cfDNA is a good prognostic predictor for patients in the ICU and, to a lesser extent, is a good marker of septic shock. However, the inevitable loss of cfDNA during extraction has become a considerable detriment, hindering its clinical applications. We previously developed a duplex real-time PCR assay with an internal control as a novel method for the accurate quantification of plasma cfDNA, which can eliminate preanalytical errors and increase precision and accuracy. Our previous studies showed the clinical value of plasma cfDNA levels, as measured by this novel method, in several conditions. CfDNA levels can be useful not only in evaluating chemotherapy effects and guiding treatment in advanced lung cancer patients but also in assessing liver injury in hepatitis B patients. In this case, cfDNA remained high until the patient died, suggesting that cfDNA could be used to monitor disease progression more effectively than PCT.[25]

Chemokines – A family of chemoattractant cytokines that are secreted by cells in response to the body's immune system.[26]

Cholecystectomy – Cholecystectomy is a surgical procedure to remove the gallbladder. [27]

Cine CMR – It consists of the acquisition of the same slice position at different phases of the cardiac cycle. [28]

Circumcision – Circumcision is the surgical removal of the skin covering the tip of the penis.[29]

Circumflex marginal branches (obtuse marginal branches) – These are the arteries that curve to the left of the heart that branch from the circumflex arteries to supply the left ventricle.[30]

Class II NYHA dyspnea – Mild symptoms of shortness of breath. [31]

CMR imaging – Cardiovascular Magnetic Resonance Imaging.[28]

Computed tomography (CT) aortogram – A technique using CT scanning and an injection of contrast material into the blood vessels to examine and diagnose cardiovascular diseases.[32]

Computed tomography (CT) thorax – An imaging test to examine organs and chest using X-ray and computer technology.[33]

Congestive heart failure – A condition where the heart muscles don't pump blood as efficiently as they should.[34]

Coronal computed tomography (CT) angiogram – A technique using CT scanning and an injection of

contrast material into the blood vessels to evaluate structure and patency of arteries supplying lower limbs and abdomen with blood.[35]

Coronary Angiography – Coronary angiography is a procedure that uses a special dye (contrast material) and x-rays to see how blood flows through the arteries in the heart.[36]

Coronary artery bypass grafting (CABG) – A procedure to treat coronary heart disease from the narrowing of arteries.[37]

Coronary artery disease (CAD) – Narrowing of coronary arteries due to plaque build-up.[37]

Coronary computed tomography angiography (CCTA) – An imaging test used to determine plaque buildup in coronary arteries.[38]

CRS – Cytokine Release Syndrome. CRS is a systemic inflammatory response due to massive T cell stimulation that can be triggered by a variety of factors such as infections, and certain drugs.39The COVID-19 virus binds to alveolar epithelial cells, activating the innate and adaptive immune systems resulting in the release of pro-inflammatory cytokines. This can lead to the CRS which is characterized by a hyperinflammatory state with raised inflammatory cytokines and biomarkers such as interleukin (IL)-2, IL-6, IL-7, granulocyte-colony stimulating factor, macrophage inflammatory protein 1-α, tumor necrosis factor-α, CRP, ferritin, Pro-BNP and D-dimer.[40]

CT scan – Computerized Tomography scan. (CT) scan combines a series of X-ray images taken from different angles around your body and uses computer processing to create cross-sectional images (slices) of the bones, blood vessels and soft tissues inside your body. [41]

Cytokines – Group of glycoproteins, peptides and proteins secreted by cells in response to the immune system, they regulate and mediate immunity. [42]

D

D-dimers – It is a small protein fragment present in the blood after the degradation of a blood clot. D-dimer concentration help to diagnose thrombosis and intravascular coagulation.[43]

Diagonal 1 – Branches of the left anterior descending coronary artery that supply the left ventricle.[44]

Dysarthria – Dysarthria is a motor speech disorder in which the muscles that are used to produce speech are damaged, paralyzed, or weakened. The person with dysarthria cannot control their tongue or voice box and may slur words.[45]

Dysphagia – Difficulty in swallowing.[46]

Dyspnea – Dyspnea means difficulty in breathing, breathlessness, or a feeling of suffocation.[47]

E

Ecchymosis – Medical term for common bruise caused by the impact of an injury.[48]

ECG – An electrocardiogram or ECG is a test to record the electrical signals in the heart.[49]

Echocardiogram – An echocardiogram (echo) is a graphic outline of the heart's movement done by ultrasound.[50]

Electrocardiogram (ECG) stress test – A method used to record heart's blood pressure, electrical activity, and rate under physical exercise conditions.[51]

Endoscopic ultrasonography (EUS) – Invasive procedure that aids in assessing digestive and lung disease.[52]

Endoscopy – An endoscopy is a procedure in which your doctor uses specialized instruments to view and operate on the internal organs and vessels of your body.[53]

Epigastric/ Epigastric region – Upper central region of the abdomen.[54,55]

Esophagogastroduodenoscopy (EGD)- Esophagogastroduodenoscopy (EGD) is a test to examine the lining of the esophagus, stomach, and first part of the small intestine (the duodenum).[56]

F

Factor IX – Essential clotting factor deficient in Hemophilia B.[57]

Factor VIII – Essential clotting factor deficient in Hemophilia A.[57]

Fibrinogen level – Fibrinogen is a plasma glycoprotein synthesized by the liver and is the major structural component of a clot.[58]

Flow-limiting stenosis (and values) – "Lesion with a diameter narrowing exceeding 50%"[59]

Fractional flow reserve computed tomography (FFR-CT) – Ratio of maximum flow between a stenotic artery to a maximum blood flow of a normal artery of the same type.[60]

Frenulum- Elastic band of tissue under the glans penis.[61]

FST2WI – Fat Suppressed T2-Weighted Imaging.[4] FST2WI fusion technology improves signal differences with surrounding structures and facilitates the better evaluation of disease.[62]

G

Gastric body – Synonymous for the stomach.[63]

Gastroesophageal reflux disease (GERD) – The backflow of stomach acid between the stomach and the mouth through the esophagus.[64]

Gastroesophageal varices- Gastroesophageal varices or esophageal varices are abnormal, enlarged veins in the tube that connects the throat and stomach (esophagus). This condition occurs most often in people with serious liver diseases.[65]

Ground-glass opacities – According to Dr. Cortopassi, Ground glass opacities are a pattern that can be seen when the lungs are sick, while normal lung CT scans appear black, an abnormal chest CT with GGOs will show lighter-colored or gray patches. Those lighter patches don't completely obscure the other structures in the lungs. There is haziness seen overlying an area of the lung, but the underlying structures of the lung (airways, blood vessels, lung tissue) can still be identified. It resembles ground glass or glass that is still transparent but has a matte finish.[66]

GGOs aren't specific to COVID-19 and can be seen in so many different settings. GGOs in chest CT scans can also indicate congestive heart failure, inflammatory interstitial lung diseases, and diffuse alveolar

hemorrhage (bleeding into the airspaces of the lungs), among other issues. But one of the most common diagnoses for GGOs is viral pneumonia, most often caused by respiratory syncytial virus (RSV), cytomegalovirus, herpes simplex virus, and coronavirus.[66]

In terms of COVID-19, Dr. Cortopassi explains GGOs on a CT scan are indicative of COVID-19-related pneumonia, or lung inflammation caused by the viral infection.[66]

A study published in the journal Radiology found that, among 51 Chinese patients with confirmed COVID-19 pneumonia, GGOs showed up in the chest CT scans of 77% of patients. And original research from scientists in China, also published in Radiology, found that CT scans were able to find 97% of COVID-19 infections overall, while blood tests were only able to correctly identify 59% of cases.[66]

Growth factor – Substance required for growth stimulation in living cells.[67]

H

Haptoglobin – Haptoglobin is a protein produced by the liver that the body uses to clear free hemoglobin (found outside of red blood cells) from circulation. This test measures the amount of haptoglobin in the blood.[68]

HDL (high-density lipoprotein) – "Good" cholesterol is responsible for carrying absorbed cholesterol to the liver in order to remove it from the body.[69]

Hematemesis- Hematemesis is a serious condition in which blood is expelled from the mouth. The blood can be bright red, black or dark brown. Blood that is vomited usually comes from what is referred to as the upper GI, or gastrointestinal tract. Pancreatic problems can also be the source of blood vomiting.[70]

Hematocrit – The hematocrit is the proportion, by volume, of the blood that consists of red blood cells. For example, a hematocrit of 25% means that there are 25 milliliters of red blood cells in 100 milliliters of blood.[71]

Hematological – Relating to blood and body tissue.[72]

Hemoglobin electrophoresis – Hemoglobin electrophoresis is a test that measures the different types of hemoglobin in the blood. It also looks for abnormal types of hemoglobin. Normal types of hemoglobin include:

Hemoglobin (Hgb) A, the most common type of hemoglobin in healthy adults

Hemoglobin (Hgb) F, fetal hemoglobin. This type of hemoglobin is found in unborn babies and newborns. HgbF is replaced by HgbA shortly after birth.[73]

High-sensitive cardiac troponin T – Cardiac troponin is the preferred biomarker for the diagnosis of acute myocardial infarction and high-sensitive cardiac troponin T (hs-cTnT) assay permits detection of very low levels of cTnT.[74]

Hypertension – Condition where blood vessels persistently have raised pressure.[75]

Hyperthyroidism – An overactive thyroid, occurring when the thyroid gland produces an excess amount of hormone thyroxine.[76]

Hypochromic RBC – Hypochromia means that the red blood cells have less color than normal when

examined under a microscope. This usually occurs when there is not enough of the pigment that carries oxygen (hemoglobin) in the red blood cells.[77]

Hypoxemia – Hypoxemia refers to a decrease in the partial pressure of oxygen (PaO2) or oxygen saturation in the blood.[78]

Hypoxia – A condition where the body or an area of the body is deprived of adequate oxygen in the tissues.[79]

Hypoxic – A condition where the areas of the body or the body do not have an adequate oxygen supply at the tissue level.[80]

I

IgG – Immunoglobulin G-antibody. IgG is synthesized mostly in the secondary immune response to pathogens.[81]

IgM – Immunoglobulin M-antibody.[81]

Immunophenotyping – A method used to couple specific antibodies to a fluorescent probe which provides a signal to measure a specific expression of a protein.[82]

Infective endocarditis – Inflammation of the heart that is caused by a fungal or bacterial infection of the heart valves or the inner lining of the heart.[83]

Interstitial change in lung – When these interstitial changes occur, your physician may see "increased interstitial markings" on your chest x-ray or CT scan because the inflammation, swelling or scarring of the interstitium makes the tissue denser so that it is now visible as white "interstitial markings" on the x ray or scan.[84]

Ischemic heart disease (or coronary heart/artery disease) – Disease with the heart is getting an inadequate supply of blood and oxygen due to narrowing of arteries.[85]

K

Kayser-Fleischer (KF) ring – Kayser–Fleischer (KF) rings are a common ophthalmologic finding in patients with Wilson disease. Initially thought to be due to the accumulation of silver, they were first demonstrated to contain copper in 1934. KF rings are seen in most of the patients with neurologic involvement from Wilson disease. These rings are caused by the deposition of excess copper on the inner surface of the cornea in the Descemet membrane. A slit lamp examination is mandatory to make a diagnosis of KF rings particularly in the early stages unless the rings are visible to the naked eye in conditions of severe copper overload. Kayser–Fleischer rings do not cause any impairment of vision but disappear with treatment and reappear with disease progression. KF rings are not specific to Wilson disease alone, they are also seen in other chronic cholestatic disorders such as primary biliary cholangitis and children with neonatal cholestasis.[86]

Ki-67 – A protein associated with cellular proliferation and used in immunohistochemistry.[87]

L

Late gadolinium enhancement – Gadolinium is a chemical agent used as a contrast, administered intravenously to achieve optimum contrast between normal and infarcted myocardium.[88]

LDL (low-density lipoprotein) – "Bad" cholesterol as an accumulation of this cholesterol leads to plaque buildup in arteries.[89]

Leads V2, V3 and V4 – Electrodes that are used to monitor the heart during an electrocardiogram, V2 represents the right ventricle, V3 and V4 represent the septum.[90]

Left anterior descending artery (LAD) – Artery which runs anterior to the interventricular septum and is the largest coronary artery.[91]

Left circumflex – Branch off the left coronary artery.[92]

Lesion – Any damage or abnormal change in the tissue of an organism.[93]

Leukopenia – A low white blood cell count.[94]

Lower respiratory tract infection (LRTI) or pneumonia – An infection that involves the lungs abscess and acute bronchitis.[95]

Luminal diameter stenosis – Diameter of permissible blood flow.[96]

Lymphopenia – Reduced leukocytes count.[97]

M

Macroglossia – Macroglossia is the abnormal enlargement of the tongue in proportion to other structures in the mouth. It usually occurs secondary to an underlying disorder that may be present from birth (congenital) or acquired.[98]

Mantoux test – The Mantoux tuberculin skin test (TST) is one method of determining whether a person is infected with Mycobacterium tuberculosis99. A standard dose of five tuberculin units (TU) (0.1ml) is injected intradermally (into the skin) and read 48 to 72 h later. A person who has been exposed to the bacteria is expected to mount an immune response in the skin containing the bacterial proteins.[100]

MCH – MCH stands for "mean corpuscular hemoglobin." An MCH value refers to the average quantity of hemoglobin present in a single red blood cell.[101]

MCV – MCV stands for mean corpuscular volume. There are three main types of corpuscles (blood cells) in our blood–red blood cells, white blood cells, and platelets. An MCV blood test measures the average size of your *red blood cells*, also known as erythrocytes. Red blood cells move oxygen from lungs to every cell in our body. Our cells need oxygen to grow, reproduce and stay healthy. If our red blood cells are too small or too large, it could be a sign of a blood disorder such as anemia, a vitamin deficiency, or other medical condition.[102]

MDB- Mallory bodies (MB), also known as Mallory-Denk bodies (MDB), are cytoplasmic hyaline inclusions of hepatocytes, once thought to be specific for alcoholic hepatitis now occur in other liver diseases which include nonalcoholic steatohepatitis (NASH), cholestatic liver diseases, primary biliary cirrhosis (PBC) and hepatocellular carcinoma (HCC).[103]

Metastatic/Metastasis – Spread of cancer calls from a localized area to another area in the body.[104,105]

METs – Metabolic equivalents – oxygen consumed while at rest.[106]

MINOCA – Myocardial infarction with nonobstructive coronary arteries (MINOCA) is clinically defined

by the presence of the universal acute myocardial infarction (AMI) criteria, absence of obstructive coronary artery disease (≥50% stenosis), and no overt cause for the clinical presentation at the time of angiography.[107]

Murphy's sign – *Murphy's* sign is elicited in patients with acute cholecystitis by asking the patient to take in and hold a deep breath while palpating the right subcostal area. If pain occurs on inspiration, when the inflamed gallbladder meets the examiner's hand, Murphy's sign is positive.[108]

Myalgia – Myalgia describes muscle aches and pain, which can involve ligaments, tendons and fascia, the soft tissues that connect muscles, bones and organs.[109]

Myelofibrosis – A rare blood cancer, a form of chronic leukemia.[110]

N

NASH- Nonalcoholic steatohepatitis (NASH) is liver inflammation and damage caused by a buildup of fat in the liver. It is part of a group of conditions called nonalcoholic fatty liver disease.[111]

Nephrectomy – Surgical removal of whole or parts of a kidney.[112]

Noncalcified plaque – Refers to plaque buildup that may be reversible in the arteries and risk of myocardial infractions.[113]

O

Obtuse marginal 1 – On or close to the left obtuse margin of the heart.[114]

Odynophagia – Painful swallowing.[115]

Oedema – Oedema is a collection of fluid in the spaces between cells of the body. Fluid leaks out of damaged cells. The fluid cannot be simply drained with a needle and may not improve if you take 'water pills' (diuretics).[116]

Oliguria – Oliguria is defined as passing a reduced urine volume. It is defined as a urine output that is[117]:

Less than 1 mL/kg/hour in infants.

Less than 0.5 mL/kg/hour in children.

Less than 400 mL/day in adults.

P

Partial perfusion (TIMI grade 2 flow) – Slow or delayed complete filling of distal coronary bed.[118]

Partial thromboplastin time – Partial thromboplastin time (PTT) is a blood test that measures the time it takes blood to clot.[119]

PCT (procalcitonin) – A peptide precursor of the hormone calcitonin. serum PCT concentrations remain normal in uncomplicated cases of COVID-19 and inflated values may indicate bacterial co-infection in severe cases.[120]

Periorbital edema – Swelling around the eye.[121]

Platelet function testing with screening epinephrine – The PFA is a screening test for platelet dysfunction. The cartridge membrane is coated with collagen, and with one of two platelet agonists

(epinephrine or ADP). The platelets adhere to the collagen and aggregate in response to the collagen and epinephrine (or ADP).[122]

Portal hypertension- Portal hypertension is an increase in the pressure within the portal vein, which carries blood from the digestive organs to the liver. The most common cause is cirrhosis of the liver, but thrombosis (clotting) might also be the cause.[123]

Pressure dressing – It is a pressure bandage that's designed to apply pressure to a particular area of the body to prevent bleeding.[124]

Pretibial myxedema – It describes localized lesions of the skin due to the deposition of hyaluronic acid, a rare thyroid disease.[125]

Pro-BNP – Pro-B-type natriuretic peptide is a hormone produced by the heart.[126]

Procalcitonin – Procalcitonin is a substance produced by many types of cells in the body, often in response to bacterial infections but also in response to tissue injury. The level of procalcitonin in the blood can increase significantly in systemic bacterial infections and sepsis. This test measures the level of procalcitonin in the blood.[127]

Prognathism – Prognathism is an extension or bulging out (protrusion) of the lower jaw (mandible). It occurs when the teeth are not properly aligned due to the shape of the facial bones.[128]

Pro-inflammatory biomarkers – Regulatory proteins that can be used to detect inflammation.[129]

PT – Prothrombin time, a test to evaluate blood clotting.[130]

Pulmonary stenosis/outflow – Associated with structurally abnormal or immunocompromised states of the heart.[131]

R

Ramus intermedius – Variant of the coronary artery.[132]

RDW – The red cell distribution width (RDW) blood test measures the amount of red blood cell variation in volume and size. Normal red blood cells maintain a standard size of 6 to 8 micrometers (μm) in diameter.[133]

Rhinorrhea – Rhinorrhea refers to a thin, mostly clear nasal discharge.[134]

Right coronary artery – One of the two main coronary blood vessels supplying blood to the right atrium, right ventricle, and sinoatrial and atrioventricular nodes – responsible for the heart's natural rhythm.[135]

S

Sepsis – A condition where the body's response to an existing infection begins to damage its own tissues, this can be a potentially life-threatening.[136]

Serial troponin enzyme – Enzymes used to measure the potential evidence of a myocardial infraction.[137]

Slit-lamp examination – A slit lamp is a microscope with a bright light used during an eye exam. It gives your ophthalmologist a closer look at the different structures at the front of the eye and inside the eye. It's a key tool in determining the health of your eyes and detecting eye disease.[138]

Splenomegaly – The enlargement of the spleen.[160]

Stenosis – It represents the narrowing of blood flow and passage diameter.[139]

Sub pulmonary stenosis – A condition when there is blockage below the pulmonary valve due to too much muscle (muscular bundles).[140]

Subepithelial – Underneath the epithelium.[141]

Systolic ejection murmur – It is turbulent blood flow by the obstruction across semilunar valves, arteries and outflow tracts.[142]

T

T wave – Ventricular repolarization during the electrocardiogram stress test.[143]

T1 mapping- It is a cardiac magnetic resonance (CMR) imaging technique, which shows early clinical promise particularly in the setting of diffuse fibrosis. 144

Tachycardia – A condition where a pulse exceeds 100 beats per minute.[145]

Thyroid acropachy – Rare autoimmune thyroid disease.[146]

Thyroid dermopathy – Thickening of the skin usually in the pretibial area, a symptom of hyperthyroidism.[147]

Thyroid-stimulating hormone – Hormone made in the pituitary gland to regulate your weight, body temperature, muscle strength and mood.[148]

Thyrotoxicosis – Excess thyroid hormone in the body.[149]

TIMI grade flow – Method used for assessing coronary artery flow in acute coronary syndromes.[150]

TnI – Troponin I- cardiac bio marker. Cardiac troponin T (cTnT) and troponin I (cTnI) are cardiac regulatory proteins that control the calcium-mediated interaction between actin and myosin.[151]

Tocilizumab – Interleukin-6 antagonist used for CRS treatment. Tocilizumab binds specifically to both soluble and membrane-bound IL-6 receptors.[152]

TOF – Tetralogy of Fallot, a form of cyanotic congenital heart disease.[153]

Toxic granulations – Toxic granulations are purple or dark-blue staining azurophilic granules in the cytoplasm of neutrophils, bands and metamyelocytes resulting from an abnormality in the maturation of the primary granules with consequent retention of their azurophilic property,[79] while toxic vacuolizations are vacuoles representing phagocytosis and depletion of toxic granules.[154]

Transesophageal echocardiography – Specific type of echocardiogram to look more closely at the heart to examine potential blood clots.[155]

Triglycerides – A type of fat found within the blood.[156]

V

Ventricular septal defect (VSD) – A hole in the wall (septum) that separates the lower chambers (ventricles) of the heart, this is a birth defect of the heart.[157]

Von Willebrand factor – Von Willebrand factor is a glycoprotein that plays a key role in blood clotting. The deficiency of this factor leads to Von Willebrand disease.[158]

X

X-linked recessive – X-linked recessive inheritance refers to genetic conditions associated with mutations in genes on the X chromosome. A male carrying such a mutation will be affected because he carries only one X chromosome. A female carrying a mutation in one gene, with a normal gene on the other X chromosome, is generally unaffected.[159]

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Links for Further Reading

I-Case 1-2013: A 72-year-old female with Tetralogy of Fallot and increasing dyspnea

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- https://www.mayoclinic.org/diseases-conditions/heart-murmurs/symptoms-causes/syc-20373171
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- https://www.heart.org/en/health-topics/heart-valve-problems-and-disease/heart-valve-problems-and-causes/heart-valves-and-infective-endocarditis

I-Case 2-2021: A 54-year-old male with chest pain

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I-Case 3-2020: A 42-year-old man with cough and chest pain

youtu.be/feqFLc9SxfA

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://ecampusontario.pressbooks.pub/clinicalcases/?p=6#oembed-1

I-Case 4-2020: A 65-year-old woman chest tightness, nausea, vomiting during bronchoscopy

- https://www.youtube.com/watch?v=xIZQRjkwV9Q

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II-Case 1-2020: A 53-year-old male fever, sore throat and dyspnea with contact history

- https://youtu.be/3oKE3–RKXE

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- https://youtu.be/5DGwOJXSxqg

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II-Case 2-2020: A 32-year-old male with fever, rhinorrhea and myalgia

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II-Case 3-2021: A 53-year-old male with headache and bizarre behavior

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- https://www.youtube.com/watch?v=Evx48zcKFDA

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II-Case 4-2019: A 33-year-old pregnant woman with pneumonia

- How does COVID-19 affect pregnant women and their babies?

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://ecampusontario.pressbooks.pub/clinicalcases/?p=6#oembed-12

- Mayo Clinic Insights: Should pregnant women be vaccinated for COVID-19?

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- Understanding the Virus that Causes COVID-19, Animation

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III-Case 1-2020: A 29-year-old male with high grade fever

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IV-Case 1-2015A 35-year-old female with weight gain, excessive sweating, widening of hands and feet

IV-Case 2-2012: A 38-year-old female with weigh loss, leg edema and hand tremor

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IV-Case 3-2017: A 40-year-old female with epigastric pain, nausea and vomiting

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V-Case 1-2017: A newborn boy with post-circumcisional bleeding

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V-Case 2-2018: A 78-year-old female with anemia and purple blotches in oral cavity

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V-Case 3-2014: A 2.5-year-old boy with anemia and recurrent diarrhea

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- https://www.youtube.com/watch?v=oH6SMG3Ykjg

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VI-Case 1-2016: A 12-year-old boy with fever and recurrent abdominal pain

- https://www.youtube.com/watch?v=O7Vr-r9ef6g

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VII-Case 1-2020: A 2-year-old boy with fever, edema and oliguria

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VII-Case 2-2007: A 60-year-old male with breathlessness and weight loss

- https://www.youtube.com/watch?v=Qs3HQGj5Mp8

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VIII-Case 1-2020: A 68-year-old male with breathlessness

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- https://www.mayoclinic.org/diseases-conditions/abdominal-aortic-aneurysm/symptoms-causes/syc-20350688
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