Pulmonary Embolism owing to Iron Deficiency Anemia: A Case Report

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Abstract

The diagnosis of pulmonary embolism (PE) and venous thromboembolism (VTE) associated with iron deficiency anemia is rare and underappreciated. In this case study, a 29-year-old presented with pleuritic chest pain. She was subsequently diagnosed with PE, due to IDA, which is attributed to heavy menstrual bleeding

Introduction:

Pulmonary embolism (PE) is associated with many etiologies, such as hematological disorders, contraceptive use, tumors, trauma, infection, and dehydration.[1] However, iron deficiency anemia (IDA) is a very rare etiology of PE.[1] IDA leads to relative thrombocytosis, causing hypercoagulation and venous thromboembolism.[2] This is a case study of a 29-year-old female who presented with shortness of breath and left-sided pleuritic chest pain. The diagnosis of a PE most likely due to IDA was established based on CT angiogram (CTA) of the chest and blood findings and ruling out other differential diagnoses related to PE.

Case Presentation:

A 29-year-old female presented to the hospital with left-sided pleuritic chest pain that started in the morning. The patient described the pain as a pressure-like sensation with no radiation, 6/10 in intensity, exacerbated by deep breathing without relief. She reported shortness of breath with deep inspiration only. The patient denied having headaches, dizziness, nausea/vomiting, fever or chills, a cough, or recent travel. She reported heavy menstrual bleeding and severe IDA, requiring iron infusion in the past, the last being in 2021 during her second pregnancy. She had a history of C-sections. The patient had no history of COVID-19 infection. The patient was not taking any oral contraceptive pills.

On the physical examination, the patient was alert, oriented, and in mild distress, had a blood pressure of 120/76, heart rate of 73 beats per minute, respiratory rate of 18 breaths per minute, and oxygen saturation of 99% on room air and had conjunctival pallor and koilonychia. Heart and lung sounds were within normal limits. The abdomen was soft, non-distended, and non-tender. There was no erythema or edema on the bilateral lower extremity examination. Initial laboratory examination showed a decrease in international normalized ratio to 1.0, decrease in PT to 10.5, APTT was within normal limit, D- Dimer Quant was elevated- 2.50 (normal range- 0.00- 0.49 mg/L FEU), Due to active thromboses, protein C and S and mixing investigations were inconclusive. It also showed RBC (red blood cells)- 4.06, hemoglobin 7.7, (normal range-12.0-16.0 g/dl), hematocrit- 27.0 (normal range-37.0-47.0 g/dl), MCV (mean corpuscular volume)- 66.5 (normal range-81.0-99.0 fl), MCH (mean corpuscular hemoglobin)- 19.0 (normal range-27.0-31.0 pg), MCHC (mean corpuscular hemoglobin concentration)- 28.5 (normal range-33.0-37.0 g/dl), RDW (red cell

distribution width)- 19.1 (normal range-0-14.5%),WBC- 13.6 and Platelet- 706,000 (normal range 150,000 -400,000 mL). CMP (comprehensive metabolic panel) and renal function tests were normal. Laboratory results were also significant for nucleated RBC-0.0, slight polychromasia, moderate hypochromasia, moderate microcytosis, and a few teardrop cells (a few schistocytes). Iron profile showed serum iron - 9 ug/dL (normal range- 50-170 ug/dL), serum ferritin - 15 ug/L (normal range- 41-400 ug/L), total iron binding capacity- 480 ug/dL (normal range- 250-450 ug/dL), transferrin saturation - 3% (normal range 15% to 50%). The pregnancy test was negative. In Figure 1, the ECG of the patient showed sinus arrhythmia at a rate of 61, no ST elevation, and no ectopy. The chest x-ray was normal. CTA chest showed subsegmental pulmonary embolism in the left lower lobe with adjacent pulmonary infarct/hemorrhage.

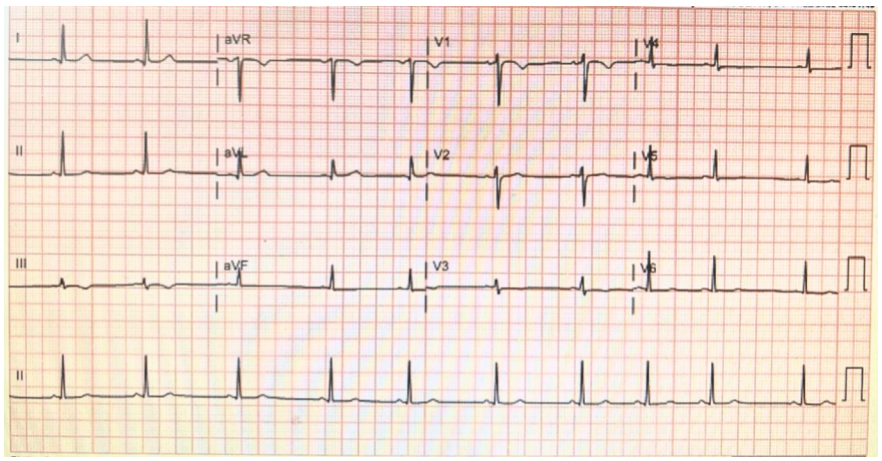

Figure 1: Electrocardiogram (ECG) showing sinus arrhythmia, borderline T abnormalities, diffuse leads, no ST elevations, and ectopy

Hematology services were consulted. According to them, the patient had a clotting tendency with acute pulmonary embolism, most likely related to severe IDA due to heavy menstrual bleeding. Antiphospholipid syndrome was considered a differential diagnosis. Rheumatoid factor, ANA (antinuclear antibody) screen, double-strand DNA antibody, and anti-cardiolipin IgG antibody were within the normal range, which excluded antiphospholipid syndrome. As per the cardiology team, chest pain was likely from acute PE. A transthoracic echocardiogram (TTE) was ordered, which showed an ejection fraction of 55%, mild mitral regurgitation, and moderate to severe tricuspid regurgitation.

The patient was given a heparin drip, intravenous (IV) hydromorphone HCl, PO hydrocodone, intravenous (IV) ferric sodium gluconate complex, and intravenous (IV) methylprednisolone throughout the hospital course. The patient was discharged on the 3rd day with PO rivaroxaban, as-needed pain medication, and was advised to follow up with hematology.

Discussion:

An underrated thromboembolic risk factor is IDA. Moreover, secondary thrombocytosis associated with IDA is typically regarded as benign. However, mounting data suggests that raised platelet counts, particularly in an iron shortage, can increase the risk of thromboembolism in both venous and arterial systems.[3]Moreover, numerous VTE occurrences linked to IDA have been documented in several investigations. An incidence of severe IDA with substantial thrombocytosis was reported in one inquiry and was exacerbated by central retinal vein occlusion.[4] Following the administration of ferrous fumarate, the platelet count was found to have immediately fallen, combined with an improvement in central venous occlusion. This is the only therapy technique that supports the theory that IDA caused the VTE incidence.[4] This process might explain the connection between IDA, reversible localized impairments and strokes identified by specific authors.[5]

The causes of thrombocytosis in IDA and the subsequent VTE are not fully understood. Several theories have attempted to explain this link. First, thrombopoiesis is significantly regulated by iron.[6]Therefore, adequate iron levels are essential to avoid thrombocytosis by suppressing thrombopoiesis. As a result, IDA is linked to a lack of thrombocytosis inhibition, which increases the risk of thrombosis.[7]

Additionally, distinct pathogenic pathways have been hypothesized since not all occurrences of iron-related thrombotic events occur in individuals with simultaneously high platelet counts. One such hypothesized mechanism, for instance, concentrates on the antioxidant effect of iron. Consequently, in addition to the increased thrombotic risk of thrombocytosis, some writers have argued that IDA's impaired antioxidant protection may also increase oxidative stress, which might subsequently contribute to a predisposition for platelet aggregation.[8] An alternative explanation is the disrupted blood circulation pattern found in iron deficiency. Due to the decreased deformability and high viscosity of microcytic red blood cells produced by iron deficiency, blood flow patterns within the arteries may be disrupted, leading to a hypercoagulable condition.[9]

Patients who experience recurrent VTEs undergo a thorough workup that excludes essential, undetectable risk factors like IDA. This is especially true when thrombocytosis is present. Therefore, we recommend that individuals with unexplained, unprovoked VTEs undergo routine screening for IDA.

Conclusion:

Pulmonary embolism (PE) is associated with many etiologies, such as hematological disorders. Iron deficiency anemia (IDA) is a very rare etiology of PE. IDA may lead to relative thrombocytosis, causing hypercoagulation and venous thromboembolism. The patient was admitted to the hospital with chest pain, likely due to an acute pulmonary embolism (PE). A transthoracic echocardiogram showed an ejection fraction of 55%, mild mitral regurgitation, and moderate to severe tricuspid regurgitation. The patient was discharged on rivaroxaban and pain medication, with hematological monitoring. VTE has a well-established link to polycythemia and hyperviscosity. There are surprisingly few incidences of thromboembolism attributed to IDA. Given the possibility of anemic symptoms coexisting with PE signs such as difficulty breathing, there should be a considerable amount of worry for VTE.

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