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A Silent Culprit– Protein S Deficiency In A Morbidly Obese Male As An Overlooked Cause Of Acute Pulmonary Embolism

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Abstract

Pulmonary embolism is a potentially life-threatening cardiopulmonary emergency characterized by a broad and often unpredictable clinical spectrum, ranging from subtle unexplained dyspnoea to severe hypoxemia, and catastrophic hemodynamic collapse. Saddle thrombi represent a unique form of pulmonary embolism, and are generally severe and frequently associated with significant morbidity, mortality and increased duration of hospital and intensive care unit stay.

We hereby describe a case with an unusual presentation of a saddle pulmonary embolus identified by contrast-enhanced computed tomography scan of the thorax in a middle-aged male presenting with acute dyspnoea and chest pain, without prior history of venous thromboembolism or clinically identified risk factors.

Further evaluation identified protein S deficiency as the cause of the underlying prothrombotic state. The patient was managed successfully with systemic thrombolysis followed by anticoagulation. Although more commonly reported in females, protein S deficiency remains an underrecognized cause of pulmonary embolism in males. This case highlights the importance of early clinical suspicion, timely risk stratification, and prompt reperfusion therapy, even in the absence of conventional risk factors, in order to optimize outcomes.

Keywords: NIL

Introduction

Pulmonary embolism (PE) is a major cause of cardiovascular morbidity and mortality worldwide. It occurs when emboli, originating from the deep veins of the lower extremities, traverse into the pulmonary arterial circulation causing vascular obstruction. The clinical presentation of pulmonary embolism is often variable and nonspecific, often mimicking acute coronary syndromes, acute exacerbations of obstructive airway diseases, or acute respiratory distress syndrome, making early diagnosis challenging.

Saddle pulmonary embolism refers to a thrombus located at the bifurcation of the main pulmonary artery extending into both pulmonary arteries. Though saddle thrombi are relatively uncommon, they are associated with larger thrombotic burden leading to right ventricular dysfunction, cardiovascular collapse, and hemodynamic compromise.

Inherited thrombophilias are important contributors to venous thromboembolism, particularly in patients without obvious provoking risk factors. Protein S deficiency, a rare inherited disorder affecting the natural anticoagulant pathway, predisposes individuals to thrombotic events by impeding activated protein C from inactivating factors Va and VIIa. Although more frequently reported in females, it may remain undiagnosed in males until a significant thrombotic event occurs.

We hereby present a case of acute saddle pulmonary embolism in a morbidly obese male in whom further evaluation revealed protein S deficiency as the underlying prothrombotic condition.

Case Report:-

A middle-aged male presented with acute onset breathlessness since three days, associated with chest

pain, dizziness and presyncope on standing upright, and mild bilateral lower limb pedal edema. He was obese with a body mass index (BMI) of 43 kg/m² and diagnosed with concurrent hypothyroidism and type 2 diabetes mellitus, both well controlled on regular oral medications with good compliance.

On arrival his pulse rate was 112 beats per minute, respiratory rate was 22 breaths per minute, saturation on room air was 99%, blood pressure was 140/90 mm of Hg and auscultation revealed normal breath sounds bilaterally. Arterial blood gases revealed mild hypoxia with respiratory alkalosis with a pH of 7.43, PaCo2 of 24 mmHg, PaO2 of 73 mmHg, serum bicarbonate of 15.6 mEq/L and SaO2 of 94.5%

A chest x ray was also done on admission which revealed lower lobe atelectasis with mild pleural effusion on the left side. ECG showed sinus tachycardia and primary cardiac screen showed a BNP 517 pg/ml with troponin I and creatine kinase MB being within the normal range.

There was no history of recent surgery, prolonged immobilization, trauma, or prior venous thromboembolism.

Initial clinical evaluation raised suspicion for pulmonary embolism. The Wells score for pulmonary embolism was calculated to be 4.5, stratifying the patient in the "PE likely" category.

He was admitted to the intensive care unit and evaluated for acute pulmonary embolism. Treatment was commenced with oxygen support at 2L/min and further laboratory investigations were sent which revealed a thyroid stimulating hormone (TSH) of 6.17 mIU/L, consistent with the patient's known hypothyroid state, and an elevated C-reactive protein (CRP) of 8.9 mg/L. Other laboratory parameters including urine analysis were within normal limits.

Transthoracic 2-dimensional echocardiography demonstrated a left ventricular ejection fraction of 55% with mild dilatation of the right atrium and ventricle, moderate tricuspid regurgitation with pulmonary artery systolic pressure (PASP) of 80 mmHg, estimated by tricuspid jet regurgitant velocity, suggestive of severe pulmonary hypertension. Presence of an echogenic structure near the bifurcation of the pulmonary artery raised the suspicion of an intraluminal thrombus.

Given the high index of clinical suspicion, computed tomography pulmonary angiography (CTPA) was performed which revealed acute pulmonary thromboembolism involving the right and left main pulmonary arteries with extension into bilateral lobar, segmental, and subsegmental branches, consistent with a saddle pulmonary thrombus. Additionally, there was dilatation of the main pulmonary trunk and both pulmonary arteries indicating pulmonary arterial hypertension; borderline cardiomegaly with minimal pericardial effusion; and patchy areas of mosaic attenuation within the lung parenchyma. A bilateral lower limb deep vein thrombosis scan was also done to look for the source of the saddle thrombus, however the results showed no evidence of deep vein thrombi in the lower limbs.

The patient was treated with systemic thrombolysis using tissue plasminogen activator tenecteplase in a single IV bolus of 40 mg diluted with 10 ml of normal saline. Following thrombolysis, anticoagulation was started with low molecular weight heparin in a dose of 0.6 cc given subcutaneously twice daily. The patient was closely monitored for bleeding complications and hemodynamic instability. He remained hemodynamically stable throughout hospitalization and no bleeding complications were observed.

Further evaluation for hypercoagulable states revealed a Protein S functional activity level of 16% , which was significantly lower than the lower limit of the normal range (60%), suggesting an inherited thrombophilic predisposition due to deficiency of functional protein S.

The patient showed marked clinical improvement, was successfully weaned off supplemental oxygen, and discharged in stable condition on oral anticoagulation with rivaroxaban 15 mg twice daily for 21 days, which was stepped down to 20 mg once daily thereafter.

During his scheduled follow up appointment one week later, he was clinically and hemodynamically stable, and a repeat CTPA showed moderate resolution in bilateral lobar and subsegmental arteries, with filling defects persisting in right upper lobe, middle lobe and lower lobe arteries causing 40-50% luminal compromise, reduced from 70-80% luminal compromise detected in the previous scan prior to thrombolysis. There was significant resolution seen in left lower lobe arterial occlusion with residual luminal compromise of about 10-20% post thrombolysis,

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compared to 50-60% luminal compromise prior to lysis. Similar results were noted in the left upper lobe artery revealing residual filling defects with 10% luminal compromise, down from 70-80% prior to treatment.

Discussion:-

Pulmonary embolism remains a significant cause of cardiovascular morbidity and mortality, particularly in the intensive care unit and emergency department settings. Early clinical suspicion, risk stratification, diagnosis, and prompt initiation of anticoagulant and thrombolytic are essential to improve prognosis and reduce adverse outcomes. Clinical prediction tools such as the Wells score play an important role in stratifying patients according to the probability of pulmonary embolism and guiding further diagnostic evaluation.

Saddle pulmonary embolism represents a substantial clot burden and may lead to right ventricular strain due to increased pulmonary vascular resistance. Echocardiographic findings of right atrial and right ventricular dilatation along with severe pulmonary hypertension (PASP 80 mmHg) in this case further supported the presence of significant pulmonary vascular obstruction.

Protein S is a vitamin K–dependent glycoprotein that functions as a cofactor for activated protein C in the inactivation of clotting factors Va and VIIIa. Deficiency of functionally active protein S leads to impaired regulation of the coagulation cascade and predisposes individuals to venous thromboembolism. Although inherited protein S deficiency is relatively uncommon, it is an important cause of unprovoked thromboembolic events, particularly in those without obvious risk factors.

In this patient, the absence of common precipitating factors such as recent surgery, immobilization, or malignancy prompted evaluation for inherited thrombophilia, which revealed protein S deficiency. Additionally, his morbid obesity, hypothyroidism and diabetes mellitus also played a role in enhancing his underlying prothrombotic state.

Morbid obesity can contribute to a hypercoagulable state through mechanisms such as chronic inflammation, endothelial dysfunction, and increased levels of procoagulant factors. The coexistence of obesity and inherited thrombophilia may therefore significantly increase the risk of venous thromboembolism.

Systemic thrombolysis remains an important therapeutic option in selected patients with pulmonary embolism, particularly in those with significant thrombotic burden or evidence of right ventricular strain. In the present case, tenecteplase administration resulted in rapid clinical improvement without bleeding complications, highlighting the effectiveness of timely reperfusion therapy when appropriately indicated.

Relatively stable clinical and hemodynamic status at initial presentation, isolated unilateral atelectasis, elevated hemidiaphragm and minimal pleural effusion suggest diagnostic clues to pulmonary embolism when more classical signs such as pulmonary oligemia are absent on the chest radiograph.

Conclusion:-

This case report aims to highlight that a saddle thrombus causing massive acute pulmonary embolism can also present with rather benign clinical symptoms like dizziness and dyspnea without overt hypoxemia, hypotension and cardiovascular collapse. Such an atypical presentation signifies marked clinico-radiological dissociation.

This case aims to reinforce protein S deficiency as an important yet often underrecognized cause of unprovoked pulmonary embolism, particularly in patients lacking identifiable precipitating risk factors such as recent surgery, immobilization, or malignancy. While inherited thrombophilias are traditionally acknowledged as more common in younger patients and females, available literature suggests that protein S deficiency is likely underdiagnosed in males, often remaining clinically silent until a significant thromboembolic event occurs.

The presence of a large thrombotic burden in the form of a saddle pulmonary embolism, along with echocardiographic evidence of right heart strain and severe pulmonary hypertension, underscores the importance of early risk stratification using clinical tools such as the Wells score in conjunction with imaging. Such approaches facilitate timely decision-making regarding advanced therapies and facilitate in reducing morbidity, mortality, duration of hospital/ICU stay and economic burden, as well as improve outcomes and treatment success rates.

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This case also reinforces the role of systemic thrombolysis in selected patients with intermediate-to-high risk pulmonary embolism, especially in the presence of right ventricular dysfunction or saddle thrombus which places the patient at a risk for eventual hemodynamic instability with likely grave outcomes without timely intervention. The favourable outcome observed with systemic thrombolysis followed by systemic anticoagulation and direct oral anticoagulation therapy, in the absence of any contraindications to thrombolysis and close monitoring of the patient to watch for bleeding complications, highlights the importance of appropriate patient selection.

Furthermore, the coexistence of morbid obesity and inherited thrombophilia may act synergistically to amplify thrombotic risk, warranting a lower threshold for comprehensive evaluation in such patients.

In conclusion, clinicians should maintain a high index of suspicion for underlying prothrombotic states in cases of unprovoked pulmonary embolism, irrespective of gender, and adopt a systematic approach to risk stratification and management. Early recognition and individualized therapy remain key to improving clinical outcomes in this potentially life-threatening condition.

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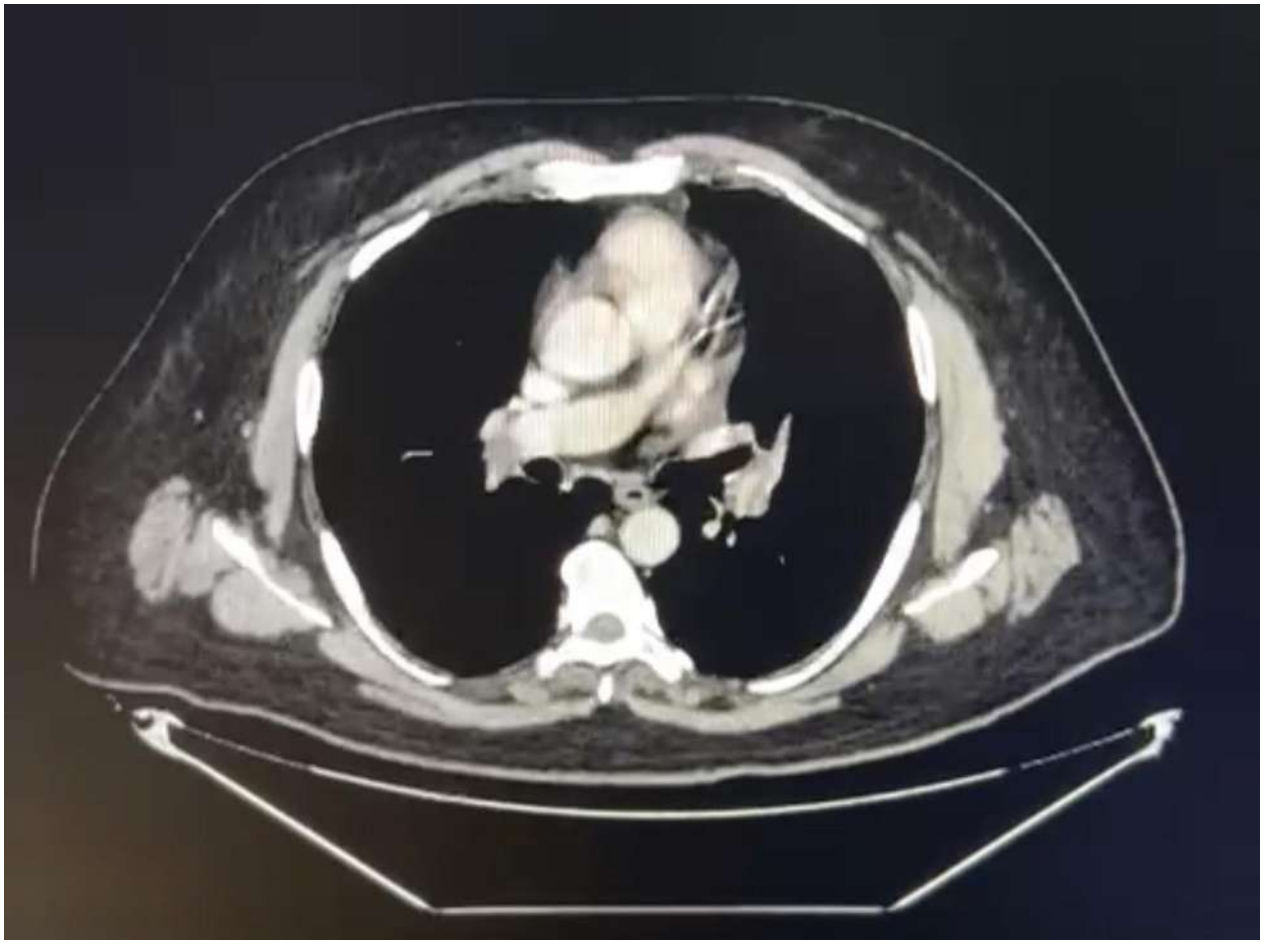
Initial CTPA showing thrombus at the bifurcation of the main pulmonary trunk



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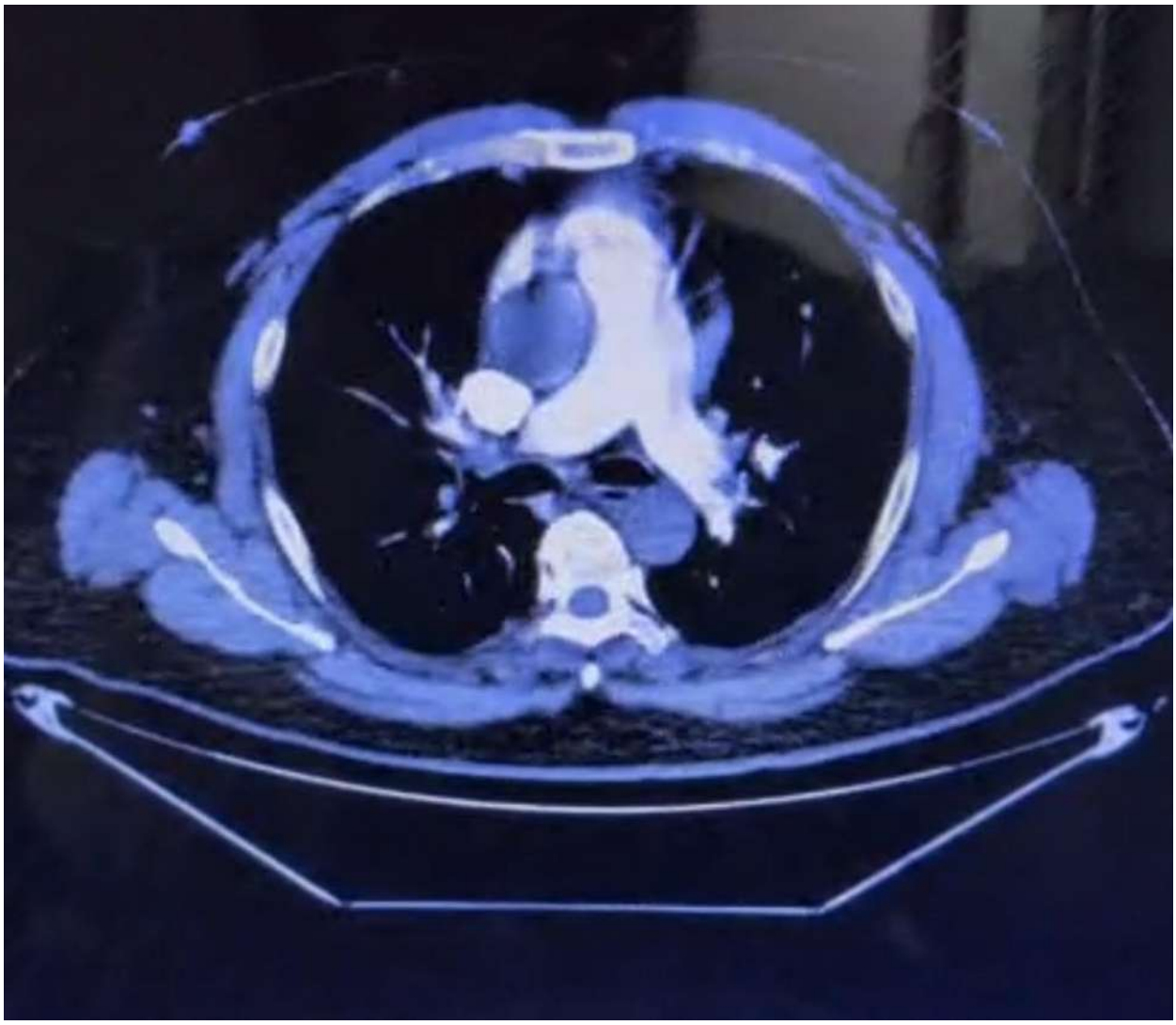
Follow up CTPA showing restoration of blood flow in the pulmonary trunk post thrombolysis and anticoagulation therapy



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