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Hypercoagulability As A Paraneoplastic Manifestation Of Suspected Primary Lung Malignancy: A Case Report

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ABSTRACT

Background

Trousseau syndrome is a paraneoplastic hypercoagulable state most often associated with mucin-producing adenocarcinomas. Lung adenocarcinoma commonly presents with venous thromboembolism, but multifocal arterial thrombosis as the initial manifestation is rare and diagnostically challenging. Recognition of occult malignancy is essential when unexplained, recurrent, or multi-territorial thrombosis occurs in older adults.

Case Report

A 62-year-old non-smoking woman presented with acute breathlessness, altered sensorium, and severe subacute pain involving the left upper and lower limbs. General examination showed presence of cyanosis of the left-sided nail beds, cold peripheries. In addition, there were absent peripheral pulses and absent Doppler signals on left side. These findings suggested acute limb ischemia. Examination of respiratory system showed reduced right basal air entry with dullness to percussion. Additionally, there was progressive leukocytosis, neutrophilia, hypoalbuminemia, and progressive coagulopathy on serial testing. Hypokalaemia was also present. Pleural fluid was lymphocyte-predominant, exudative, and cytology-negative for malignant cells. CT aortogram demonstrated complete thrombosis of the left axillary and left iliac arteries, splenic thrombosis, bilateral peripheral vascular compromise, and involvement of the abdominal aorta and mesenteric vessels. CT brain showed left temporal ischemic changes suggestive of embolic phenomena. High-resolution CT thorax revealed a heterogeneously enhancing right lower lobe mass with satellite nodules and right-sided pleural effusion, radiologically favouring primary lung adenocarcinoma. A diagnosis of suspected right lung adenocarcinoma with paraneoplastic hypercoagulability causing multifocal arterial thrombosis was made. Histopathological confirmation could not be obtained during the hospital stay. The patient was managed in intensive care with unfractionated heparin followed by subcutaneous heparin, dual antiplatelet therapy, statin therapy, supportive care, and monitoring. Surgical vascular intervention was considered unfeasible because of extensive thrombotic disease.

Conclusion

Multifocal arterial thrombosis may be the first manifestation of occult lung adenocarcinoma. Clinicians should evaluate for malignancy in unexplained arterial thromboembolism, particularly when vascular involvement is extensive and conventional risk factors are insufficient.

Keywords: Adenocarcinoma, Arterial Thrombosis, Lung Neoplasms, Paraneoplastic Syndromes, Trousseau Syndrome

INTRODUCTION

Lung cancer is one of the most common and deadly cancers in the world. Adenocarcinoma is the most commonly occurring type of lung cancer.[1] In addition to directly invading tissues and spreading to distant sites (metastasizing), lung cancer can cause many different types of paraneoplastic syndromes—a variety of systemic effects caused by the tumor, but which are not due to metastasis—by the use of hormonal, immune-mediated, or metabolic means.[2] One of the paraneoplastic syndromes seen in lung cancer patients is hypercoagulability, also known as Trousseau Syndrome, which may be severe enough to cause death.[3]

Armand Trousseau first recognized that cancer could result in a hypercoagulable state in 1865 when he identified migratory thrombophlebitis in patients with visceral carcinomas.[4] Since then our understanding has grown and now includes arterial thromboembolism, deep vein thrombosis, pulmonary embolism, and disseminated intravascular coagulation as manifestations of the complex relationship between malignancy and coagulopathy.[5]

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The pathologic mechanism underlying this relationship involves expression of tissue factor by the tumor, mucin secretion, and activation of pathways involved in platelet aggregation resulting in a prothrombotic shift that favours pathological clot formation over normal haemostasis.[6]

Because of their ability to produce mucins, lung adenocarcinomas have been found to be particularly likely to develop hypercoagulability as a paraneoplastic effect.[7] However, cases where multifocal arterial thrombosis develops as the initial presentation of an unsuspected lung cancer are rare and pose diagnostic challenges. This paper presents a case of a 62-year-old woman who developed acute bilateral lower extremity ischemia and multi-vessel arterial thrombosis and was subsequently found to have a right lower lobe lung mass radiologically suspicious for adenocarcinoma, though histopathological confirmation could not be done during the hospital stay.

CASE REPORT

A 62 years old female non-smoker from Kalaburagi, Karnataka was admitted in HDU of GIMS Gulbarga Institute of medical sciences, Kalaburagi on 20-11-25 with complaints of acute onset breathlessness & subacute onset if severe left upper and lower limb pain. She was non orientated and thus unable to provide history directly; thus, her collateral history was taken from her accompanying relatives.

Her vitals were as follows at the time of admission HR 88/min BP 130 /80mmHg SpO2 99% with supplemental oxygen RR 18/min. Her ABG results were pH 7.518 PO_2 147.4 HCO_3 22.2. General examination demonstrated an elderly lady who was moderately distressed, with cyanosis noted in nail bed of left upper and lower limb. Cardiovascular examination was normal. Limb examination demonstrated cold peripheries on left side, no peripheral pulses and no Doppler signals. Left side was colder then right and there were no peripheral pulses palpable (Figure 1,2).

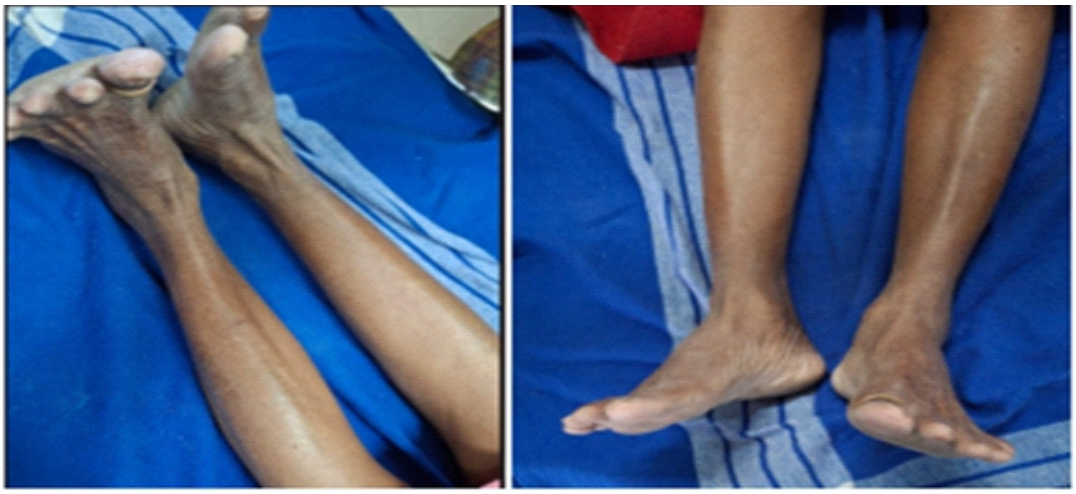

Figure 1: Bilateral lower limb showing dry skin with loss of hair. Left limb cyanosis noted over nail bed of toes.Upper limb examination revealed an intravenous access site with dressings at the right wrist; the forearms showed dry, ichthyotic skin with prominent superficial venous patterns bilaterally.

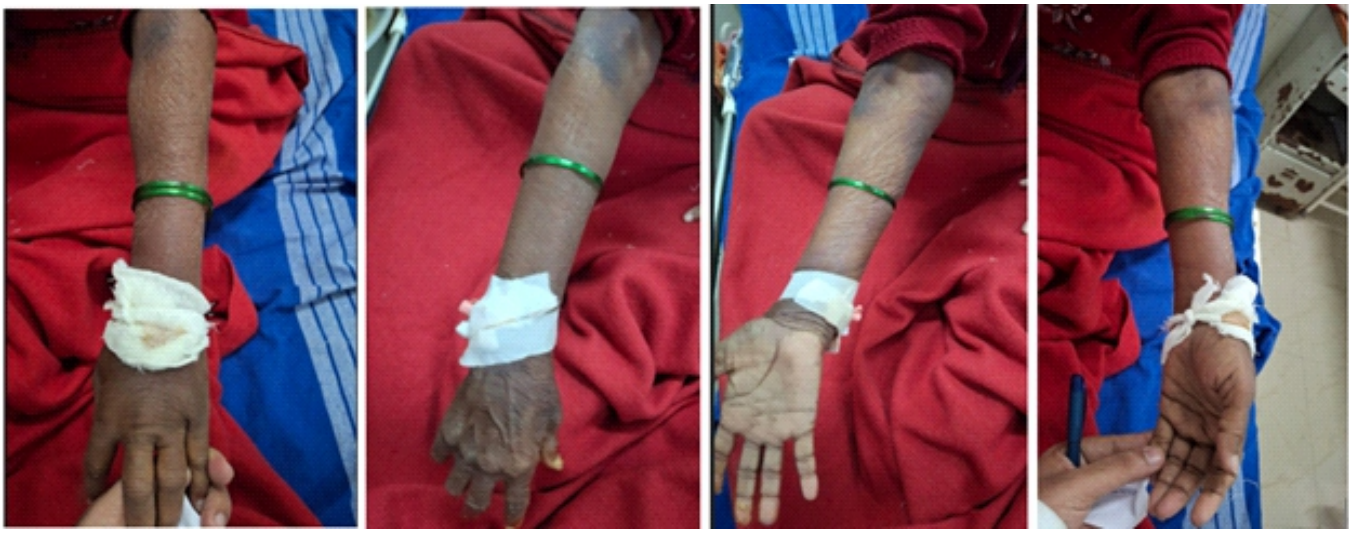

Figure 2: Upper limb with IV access and dry ichthyotic skin and cyanosis evident in nail bed of left upper limb.

Respiratory examination revealed decreased air entry at the right lung base with dullness on percussion, suggesting pleural effusion. Central nervous system examination revealed altered sensorium; the patient was not oriented to time, place, or person. Fundoscopic examination by ophthalmology revealed no papilledema and mild arteriosclerotic retinopathy with mild background changes.

The initial laboratory results are summarized in TABLE 1. The patient's haemoglobin level was 9.7 g/dl. The white cell count (WBC) was of 9900 cells/cu mm. Polymorphonuclear (PMN) white cells made up 93% of the WCC. Lymphocyte percentage was 4%. Platelet count was 486,000/cu mm. The coagulation studies included activated partial thromboplastin time (APTT) of 31.16 seconds, prothrombin time (PT) of

15.09 seconds, and international normalized ratio (INR) of 1.04. The serum electrolyte levels were as follows: Sodium 134.4mEq/litre, Potassium 3.06mEq/litre, Chloride 107.9mEq/litre. Total protein was 5.7g/dl. Albumin levels were 3.1g/dl. The total serum bilirubin was 0.4mg/dl. Serum glutamic oxaloacetic transaminase (SGOT) was 31 units/litre. Serum glutamic pyruvic transaminase (SGPT) was 21 units/litre. Alkaline phosphatase levels were 56units/litre. The renal function studies included blood urea of 24mg/dl and serum creatinine of 1.1mg/dl. Blood grouping was B positive. HBs Ag and HIV were negative. On lipid profile analysis, the patient had total cholesterol of 157mg/dl. Triglyceride levels were 112mg/dl. HDL levels were 46mg/dl (Table 1).

Parameter	Result	Reference Range
Haemoglobin (g/dL)	9.7 → 9.0 → 11.3	12–15
WBC (cells/cu mm)	9900 → 11500 → 16400	4000–11000
Platelets (×10⁹/L)	486 → 330 → 407	150–450
APTT (seconds)	31.16 → 34.25 → 38.2	25–35
PT (seconds)	15.09 → 17.24 → 23.0	11–13.5
INR	1.04 → 1.35 → 1.88	0.8–1.1
Sodium (mEq/L)	138.2 → 134.4	136–145
Potassium (mEq/L)	3.06	3.5–5.1
Albumin (g/dL)	3.0 → 3.1	3.5–5.2
Blood Urea (mg/dL)	23 → 24	15–40
Serum Creatinine (mg/dL)	1.2 → 1.1	0.4–1.3
Total Cholesterol (mg/dL)	157	130–231

Table 1: Summary of Laboratory Investigations

Pleural fluid analysis indicated that the fluid appeared to be cloudy; had a total white blood cell count of 2,000 cells per cubic millimetre (90 percent lymphocytes and 10 percent neutrophils); red blood cells were present in large numbers (+++) and there were no malignant cells found when the pleural fluid was examined using cytological techniques. The protein level in the pleural fluid was 3.0 grams per decilitre and the glucose level was 116 milligrams per decilitre, which, when compared to the serum total protein of 5.7 g/dL, yields a pleural fluid-to-serum protein ratio of 0.53, meeting the protein criterion of Light's criteria for an exudative pleural effusion (ratio >0.5). LDH-based criteria were not assessed. Pleural fluid ADA (adenosine deaminase) activity was 13.3 units per litre.

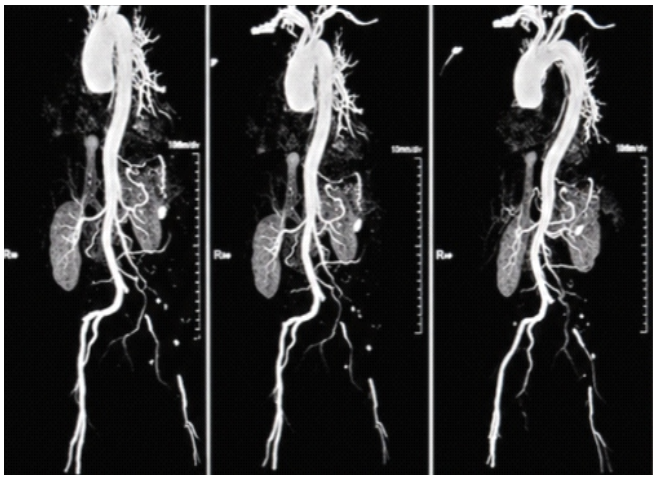

Figure 3: CT aortogram showing multifocal arterial thrombosis involving the abdominal aorta and iliac arterial system, with complete left iliac artery thrombosis and reduced distal peripheral vascular opacification, suggestive of a hypercoagulable thromboembolic state.

CT Aortogram demonstrated ascending aorta mildly ectatic with left axillary artery thrombosis; descending aorta with wall thickening; abdominal aorta, SMA, and IMA involvement; common iliac, internal iliac, and external iliac arteries showing thrombus in the left iliac artery. The spleen showed two hypodense calcified vessels with post-contrast peripheral enhancement; a complete thrombosis of the left iliac artery was identified with peripheral vascular compromise bilaterally, along with splenic and internal iliac artery thrombosis. The report concluded: complete thrombosis of the left axillary artery and left iliac artery, splenic thrombosis, and bilateral peripheral vascular compromise suggesting a hypercoagulable state; thromboembolism versus Leriche syndrome was considered.

Chest HRCT revealed a heterogeneously enhancing mass lesion in the right lower lobe measuring approximately 19 × 18 mm, involving the right lower lobe bronchus, with a few adjacent satellite nodules. Few calcified nodules were also noted in the right lower lobe. Mild right-sided pleural effusion was present, with an associated pleural-based nodular/mass-like lesion measuring approximately 13 × 18 mm. Overall imaging findings were suspicious for a neoplastic lesion of the right lower lobe, radiologically favouring primary bronchogenic carcinoma, likely adenocarcinoma, with associated satellite lesions and right-sided pleural effusion. Vascular abnormalities were also noted on imaging, supporting the possibility of an associated hypercoagulable state.

CT Brain showed ill-defined hypodense areas involving the left temporal region (−18 to +20 HU), small vessels with ischaemic changes in the left temporal region, and age-related cortical atrophy; these findings were attributed to possible embolic phenomenon. Ultrasonography of the abdomen showed normal liver, grossly normal spleen (note: CT aortogram subsequently demonstrated splenic thrombosis with hypodense lesions and peripheral enhancement suggestive of splenic infarcts, which may not be detectable on ultrasound without contrast), kidneys, urinary bladder, and uterus with no focal lesions.

ECG recorded on 27 November 2025 showed sinus rhythm with frequent premature ventricular contractions (PVCs), classified as abnormal ECG.

On the basis of the above clinical, laboratory, and radiological findings, a presumptive diagnosis of primary lung malignancy, radiologically favouring adenocarcinoma, with hypercoagulability as a probable paraneoplastic manifestation was made, leading to multifocal arterial thrombosis involving the aorta, bilateral iliac vessels, splenic artery, and cerebral vasculature. Histopathological confirmation was not obtained during the index admission; tissue biopsy was planned via oncology referral.

The patient was treated in the Medical Intensive Care Unit (MICU). As an anticoagulant, IV heparin was started. Following this, subcutaneous heparin was given as well. In addition to subcutaneous heparin, antiplatelets were added (aspirin 75 mg and clopidogrel 75 mg). Statins were also used (Atorvastatin 40 mg per day) that had been prescribed prior to admission. Nebulizers using Ipratropium and Levo-salbutamol were provided. Antibiotics (Augmentin – amoxicillin/clavulanate) were also prescribed to treat potential infection. Albumin (1.25 g/kg/day) was infused to help manage hypoalbuminemia. Laboratory tests (CBC, LFT, RFT, and blood clotting studies) were regularly monitored. Due to the multi-faceted nature of the thrombotic disease, surgical vascular intervention was determined to be unfeasible. Plans were made for an oncology consult to evaluate possible tissue biopsy and staging.

DISCUSSION

This case is an illustration of clinically suspected Trousseau syndrome. Hypercoagulability can be the first sign of cancer. It was first identified by Trousseau in 1865. Trousseau syndrome refers to a variety of thrombotic conditions that are caused by hidden cancers. These include thrombophlebitis (blood clots in veins), migratory thrombophlebitis (multiple blood clots in different veins) and arterial thromboembolism (blood clots in arteries). Blood clots in people with cancer occur at a rate of 4 – 7 times higher than in the rest of the population. Arterial thrombosis occurs at a much smaller rate but when it happens it can cause serious injury or death.[8]

The reasons behind why cancers develop hypercoagulable states involve many factors. One reason is that some types of cancer produce more tissue factor than normal. Tissue factor causes the initiation of the outside part of the clotting process. Another reason is because cancer produces a "cancer procoagulant". Cancer procoagulant is a type of enzyme that helps to start the clotting process by activating Factor X.[9] This enzyme works independently of the other enzymes involved in the clotting process. Also, there are small particles produced by tumors called micro-particles.[10] Micro-particles contain tissue factor and phosphatidylserine. They help to amplify the amount of thrombin generated during the clotting process. Some tumors also produce mucin. Mucin can activate platelets and promote selectin mediated pathways. Both of these actions help to enhance the formation of clots. Our patient developed a complex series of arterial thromboses that included the aorta, iliac arteries, spleen and cerebral arteries. This is typical of what happens in a diffuse procoagulant state.

Lung adenocarcinoma has been determined to be one of the most likely of all cancers to lead to thrombosis. There are two main reasons for this. Lung adenocarcinoma tends to be mucin producing and therefore tends to express a large amount of tissue factor.[11] Studies have shown that K-ras mutant and EGFR mutant lung adenocarcinomas tend to have the highest levels of tissue factor and are therefore more prone to developing both venous and arterial thromboembolic events.[12] Since our patient did not undergo tissue biopsy or molecular profiling to identify their specific mutation, the fact that they had a mass in the right lower lobe of the lung with satellite nodules, central necrosis and pleural effusion suggested that they probably had primary lung adenocarcinoma, although this remains a radiological impression without histopathological confirmation.

The reason that the case is rare is because it presents with multifocal arterial thrombosis. Venous thromboembolism has been well documented in lung cancer; however, arterial thromboembolism has been rarely reported. When it does happen, it usually represents a more aggressive form of the disease. A systematic review by Mulder et al. noted that arterial thromboembolism occurs in about 2-3 percent of patients with lung cancer. Most of the time arterial thromboembolism presents as acute limb ischemia or as a cerebrovascular event.[13] Our patient presented with both peripheral arterial ischemia and cerebral ischemic changes indicating concurrent multi-territory arterial occlusion, which is similar to non-bacterial thrombotic endocarditis (NBTE) or migratory arterial thrombosis described in association with Trousseau Syndrome.

We want to bring special attention to the pleural fluid findings in this case. The pleural fluid was an exudate containing lymphocytes and mild elevation in ADA (13.3 U/L) needed to be differentiated from tuberculous pleuritis, which is endemic in this geographic area. However, the CT evidence of a right lower lobe mass with satellite nodules and the lack of microbiologic evidence to support a diagnosis of tuberculosis shifted the diagnostic probability toward a diagnosis of malignant effusion. Despite the fact that no malignant cells were found in the pleural fluid cytology, the presence of tumor in the pleura cannot be ruled out since the sensitivity of pleural fluid cytology for lung adenocarcinoma varies widely (40-87%) and is dependent upon the histologic type of tumor and whether adequate sampling was obtained.[14]

Treatment for Trousseau syndrome associated with advanced malignancy is primarily supportive/palliative. Anticoagulation is the treatment of choice. The CLOT trial demonstrated that low molecular weight heparin (LMWH) is superior to warfarin in preventing recurrence of thromboembolism in cancer patients.[15] Therefore, LMWH should be used instead of warfarin. In this case, unfractionated heparin was administered initially due to the acute vascular compromise and plans were made to convert to LMWH. Due to the extensive nature of the arterial thrombi, surgical intervention was not possible. This highlights the role of medical management in this scenario.

The challenging aspect of this case is that the primary presenting complaint was vascular and not respiratory. The lack of obvious pulmonary complaints in combination with acute limb ischemia led us to initially focus on a vascular explanation. We were able to ultimately identify the radiologically suspected underlying lung malignancy after completing a comprehensive investigation that included a chest HRCT, pleural fluid analysis and CT aortogram. This experience emphasizes the necessity for physicians to consider occult malignancies in any patient who develops unexplained, recurrent or multifocal thrombosis, especially in the middle aged and older population.

The principal limitation of this case report is the absence of histopathological confirmation of the suspected lung malignancy. The diagnosis of primary lung adenocarcinoma was based on radiological findings (heterogeneously enhancing right lower lobe mass with satellite nodules, pleural-based lesion, and associated pleural effusion) without tissue biopsy. While the imaging features are highly suggestive of bronchogenic carcinoma, other differential diagnoses—including organising pneumonia, pulmonary tuberculoma with secondary infection, or a benign neoplasm—cannot be definitively excluded. Future follow-up with histopathological and molecular characterisation would strengthen the diagnostic conclusions of this report.

CONCLUSION

This is a case study that shows that hypercoagulable states manifesting as multifocal arterial thromboembolic disease can be the first and most significant symptom of a patient who has a radiologically suspected lung adenocarcinoma. Physicians treating patients who develop unexplained thrombotic events must maintain an elevated level of suspicion for the presence of a malignancy. The physician should include systemic radiologic studies (chest) to evaluate for possible malignancies when conventional cardiovascular risk factors do not account for the extent of thrombotic disease. Detection of the underlying malignancy early on will allow the physician to initiate appropriate treatment to address the malignancy and appropriately manage the coagulopathy, thereby potentially improve the prognosis.

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Author Contribution :
SR and SP - contributed to patient management, data collection, and manuscript drafting; **VD and NR** - participated in data compilation, interpretation, and literature review; **DR** - supervised the study and approved the final manuscript.

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