

Pleural Adenocarcinoma Presenting with Deep Venous Thrombosis: An Unusual Incidental Finding

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Abstract

Summary: Deep venous thrombosis (DVT) is a common vascular condition with recognized risk factors such as immobility, trauma, and hypercoagulable states. However, in patients without identifiable causes, the possibility of an underlying malignancy should be strongly considered. We report the case of a 50-year-old non-smoker male who presented with lower limb swelling secondary to extensive DVT and was incidentally diagnosed with pleural adenocarcinoma following evaluation of a right-sided pleural effusion. This case highlights the importance of maintaining a high index of suspicion for occult malignancy in patients with unprovoked DVT to enable early diagnosis and timely management.

Keywords: Adenocarcinoma, Pleural Neoplasms, Venous Thrombosis.

Introduction

Venous thromboembolism (VTE) is strongly associated with cancer, with a relative risk increase of 5–20 times.¹⁻³ Approximately 7–12% of patients with idiopathic DVT are later diagnosed with occult malignancy.³ Pleural adenocarcinoma, a rare malignancy (<5% of pleural cancers), can manifest with pleural effusion, chest pain, or respiratory symptoms.^{10,11} DVT may complicate the disease course in up to 10% of cases.¹² This case highlights pleural adenocarcinoma initially presenting with unprovoked DVT, which is an unusual clinical scenario.

Case Presentation

A 50-year-old non-smoker male, a security guard by occupation, presented with a history of left leg pain for 18 days, which was gradual in onset, sharp, more around the ankle, described as 7/10 on the Visual Analog scale (VAS), persistent, and aggravated by walking, relieved partially by oral or IM analgesics. It was associated with swelling that had progressed to the mid-thigh at the time of presentation. Other risk factors, such as prolonged immobilization, trauma, insect bite, prolonged travel, or drugs contributing to such symptoms, weren't reported. On systemic inquiry, he reported having a dry cough and dull right-sided chest pain on inspiration with MRC grade II dyspnea. Past medical and surgical history was unremarkable. The patient was a *Naswar* addict for 30 years, but had no history of smoking, alcoholism, or IV drug abuse. Upon admission, the patient was calm and comfortable, vitally stable, maintaining saturation on room air with a notable left leg swelling extending from ankle to mid-thigh with 2cm of girth difference on comparison with the right leg, with overlying skin being shiny and erythematous, warm, and tender to touch with grade II pitting edema and positive Homan's sign. Peripheral pulses were palpable with no lymphadenopathy.

Contributions:

ZU SS FM SM - Conception, Design
ZU SS FM SM - Acquisition, Analysis, Interpretation
ZU SS FM SM - Drafting
ZU SS FM SM - Critical Review

All authors approved the final version to be published & agreed to be accountable for all aspects of the work.

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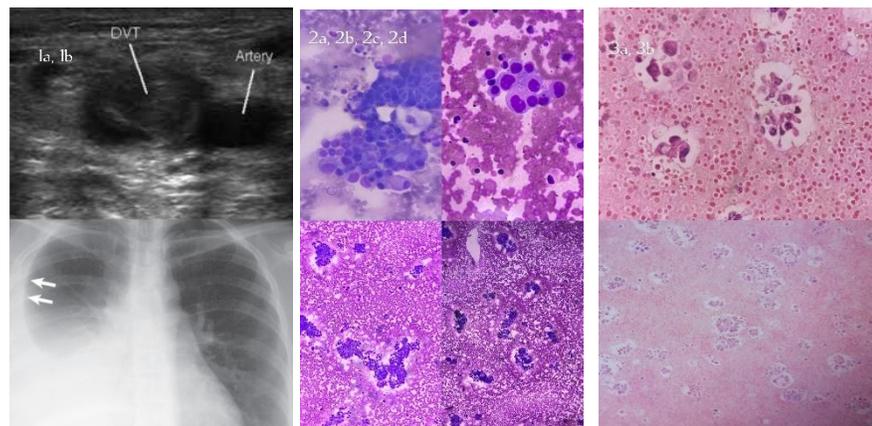


Figure 1: Leg Doppler and Chest X-Ray

Figure 2 & 3: Pleural fluid cytology

Systemic examination, unmasked presence, reduced chest movements, reduced focal fremitus, stony dull percussion note, and reduced breath sounds in the right middle and lower chest.

Investigations

Preliminary laboratory workup revealed normocytic normochromic anemia with normal liver and kidney functions. Inflammatory markers were raised along with D-dimer levels (2000ng/mL). The coagulation profile was normal. Doppler Ultrasound (Leg) revealed acute DVT extending to the left common, internal, and external iliac, superficial femoral, and great saphenous veins (Figure 1a). Chest X-ray (Figure 1b) showed right-sided costo-phrenic angle blunting and opacifications consistent with right-sided pleural effusion, thus prompting the need to get USG chest for quantification as well as to perform radiologically guided diagnostic pleurocentesis. Pleural fluid was exudative lymphocytic on microscopy with negative Gram and ZN staining, thus ruling out tuberculous effusion, which is quite common in our setup. Pleural fluid cytology revealed atypical cell clusters with pleomorphic, eccentrically placed nuclei, a high nuclear to cytoplasmic ratio, and abundant cytoplasmic mucin, consistent with metastatic adenocarcinoma. (Figure 2a, 2b, 2c, 2d) (Figure 3a, 3b). Immunohistochemistry was positive for TTF-1, CK7, AE1/AE3, and Napsin-A, which are markers associated with adenocarcinoma.⁷⁻⁹ Molecular genetics studies were negative for EGFR mutation. CECT chest (pre- and post-contrast) showed massive right pleural effusion with compressive collapse, pleural thickening, and an enlarged pre-tracheal lymph node (Figure 4a, 4b, 4c). Coronal images revealed diaphragmatic and mediastinal pleural thickening with right lung collapse and mediastinal shift (Figure 5). CT abdomen and pelvis showed a central filling defect extending from the left common iliac to the femoral vein, consistent with extensive DVT (Figure 6a, 6b, 6c). The bone scan showed no evidence of metastasis. Bronchoscopy was normal.

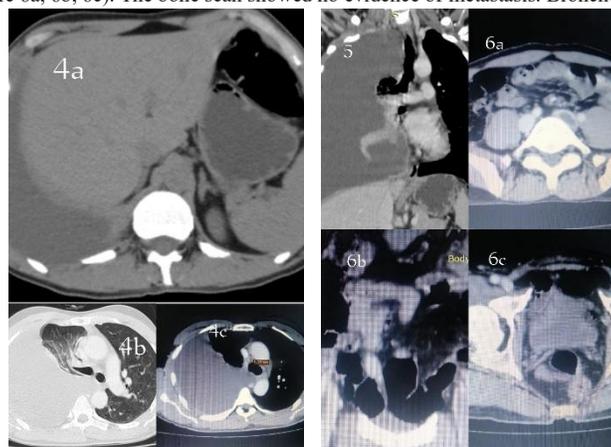


Figure 4: CECT chest

Figure 5 & 6: CT Abdomen & Pelvis

Treatment

As per TNM staging,¹³⁻¹⁵ our patient had stage IV adenocarcinoma with the VTE phenomenon. With good functional status, he underwent chest tube insertion and talc pleurodesis.^{10,11} In a poorer status, an indwelling pleural catheter is preferred. DVT was managed with LMWH 80 mg twice daily. The family was counseled about prognosis and palliative options. The patient received four cycles of platinum-based chemotherapy (cisplatin + pemetrexed). EGFR mutation was negative, precluding targeted therapy.⁴⁻⁶

Outcome And Follow-Up

The patient tolerated chemotherapy and pleurodesis. Symptomatic improvement was noted in breathlessness and limb swelling. Despite the challenges, coordinated care between both facilities (pulmonology and oncology) ensured optimal management, highlighting the value of specialized centers and collaborative medical practice.^{10,11}

Discussion

This case demonstrates the importance of a thorough workup in patients presenting with apparently idiopathic DVT⁽¹⁻³⁾. Malignancy is a major risk factor of DVT with a relative risk of 5-20 times. Occult malignancy is present in 7–12% of idiopathic DVT. In diagnosed malignancies, the 12-month incidence is 4.2% to 4.7%. Approx. 10% case of Pleural Adenocarcinoma develop DVT during the whole disease course. Pleural adenocarcinoma is rare,^{7-9,12} and most often presents with pleural effusion, dyspnea, or chest pain. Diagnosis is usually delayed as symptoms are nonspecific and mimic other benign pleural diseases. In our case, the patient presented with left leg DVT and right-sided malignant pleural effusion, an unusual initial combination. While thromboembolic events are well-documented in association with malignancy, reports describing pleural adenocarcinoma presenting with DVT are scarce.

Venous thromboembolism (VTE) in the context of cancer is associated with poor prognosis and worse long-term survival.^{5,6,12} Therefore, timely diagnosis and treatment are crucial. Current evidence favors LMWH over warfarin and DOACs for both treatment and prophylaxis of malignancy-related VTE, given its superior efficacy and safety profile.⁴⁻⁶

The diagnosis of pleural adenocarcinoma is established primarily through pleural fluid cytology and confirmed with immunohistochemistry. Markers such as TTF-1, CK7, and Napsin A are typically positive and help differentiate pleural adenocarcinoma from malignant mesothelioma and pleural metastases of non-pulmonary origin (e.g., breast or gastrointestinal cancers). Molecular profiling, including EGFR mutation testing, can further refine diagnosis and guide targeted therapy.⁷⁻⁹

Treatment of pleural adenocarcinoma is stage-dependent. Early stages (I–II), though rare, may be managed surgically with adjuvant platinum-based chemotherapy or radiotherapy. Stage III, with mediastinal nodal involvement, is usually unresectable and treated with systemic

chemotherapy such as cisplatin/carboplatin plus pemetrexed, often combined with immunotherapy (e.g., pembrolizumab). Stage IV, defined by malignant effusion or distant metastasis, is treated palliatively with chemotherapy, targeted therapy (EGFR/ALK/ROS1 inhibitors if mutations present), and immunotherapy (PD-1/PD-L1 inhibitors). Malignant effusions are managed with pleurodesis (e.g., talc) or indwelling pleural catheters in poor functional status for symptom relief.

The prognosis of pleural adenocarcinoma remains poor, with median survival ranging between 6 and 12 months depending on stage and treatment response. However, early recognition and multidisciplinary care may improve outcomes.

Learning Points

This case highlights left leg DVT as a rare initial sign of pleural adenocarcinoma with malignant effusion in a patient without typical risk factors. It underscores the need to investigate unexplained DVT for occult malignancy. Early recognition of the cancer–thrombosis link and multidisciplinary management, including pleural drainage and systemic therapy, are key to improving outcomes.

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