American Journal of Case Reports

e-ISSN 1941-5923
© Am J Case Rep, 2020; 21: e923554
DOI: 10.12659/AJCR.923554

Received: 2020.02.16
Accepted: 2020.05.15
Available online: 2020.06.04
Published: 2020.07.26

Recurrent Stroke Due to Pulmonary Vein Thrombosis in a Patient with Metastatic Lung Adenocarcinoma

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Male, 64-year-old
Final Diagnosis: Atrial fibrillation • lung cancer • stroke • thrombosis of the vein
Symptoms: Confusion
Medication: —
Clinical Procedure: —
Specialty: Cardiology

Objective: Rare co-existance of disease or pathology

Background: Pulmonary vein thrombosis (PVT) is a rare clinical entity. Etiologies include malignancy, hyper-viscosity syndromes, and other etiologies. Patients may present with dyspnea, cough, or hemoptysis.

Case Report: We present a case of a 64-year-old man with a history of metastatic lung cancer diagnosed with PVT through transesophageal echocardiography (TEE) and complicated by 2 cerebrovascular accidents. The patient had a complicated hospital course and died later due to his malignancy burden and overall condition, despite anticoagulation therapy.

Conclusions: Patients with PVT are often asymptomatic or may have a nonspecific clinical presentation. Anticoagulation should be considered in patients with PVT given the life-threatening complications such as peripheral embolization. More research is needed to address this potentially catastrophic finding.

MeSH Keywords: Embolism and Thrombosis • Lung Neoplasms • Pulmonary Veins

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/923554

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Background

Pulmonary vein thrombosis (PVT) is a rare clinical entity. Etiologies can be classified into surgical-related and non-surgical-related etiologies [1,2]. Surgical-related PVT can occur as a complication following lung transplantation, lobectomy, and radiofrequency catheter ablation for atrial fibrillation [1,2]. Non-surgical etiologies can be due to cardiac-related causes such as atrial myxoma, pulmonary venous narrowing, atrial fibrillation, or non-cardiac-related causes such as primary or secondary lung malignancies, polycythemia, and hemoglobinopathies such as sickle cell disease [1–6]. The pathogenesis of PVT is unclear, but previous studies have speculated that it could be due to turbulent flow or stasis in the pulmonary vein (PV) stump after lobectomy [2]. Malignancy-related etiologies are thought to be due to direct extension of the tumor into the vein, compression of the vein by the tumor, epithelial damage as a result of tumor invasion, or due to a hypercoagulable state [2]. Patients with PVT are usually asymptomatic but may present with nonspecific symptoms such as dyspnea, cough, or hemoptysis [3,6]. The diagnosis of PVT is difficult and requires conventional imaging modalities such as pulmonary angiography, Computed Tomography (CT) angiography, and transesophageal echocardiography (TEE), which can distinguish between tumor and thrombus and has an advantage in post-lobectomy diagnosis of PVT [2]. More recently, magnetic resonance imaging (MRI) is used to distinguish between a bland thrombus and a tumor thrombus in patients with PVT [2]. Although it is a rare and underdiagnosed finding, it may have significant and life-threatening complications such as peripheral embolization [3,6]. There are limited data regarding PVT prognosis comparing malignant to benign etiologies given its rarity as a diagnosis; however, unsuspected pulmonary vein thrombosis discovered during surgery carries a life-threatening prognosis due to the high incidence of embolization [2]. We present a case of PVT with multiple risk factors that led to recurrent strokes and poor outcome.

Case Report

A 64-year-old man with a past medical history significant for a recent diagnosis of adenocarcinoma of the right lung with metastasis to vertebral and mediastinal lymph nodes and coronary artery disease was admitted for back pain. The patient was found to have a T7 pathological compression fracture with lytic bone lesions on thoracic MRI secondary to metastatic disease. He also was found to have new-onset atrial fibrillation with rapid ventricular response, which resolved spontaneously after admission without intervention. The patient had a transthoracic echocardiogram (TTE), which did not reveal intra-cardiac thrombi. Since he had a low CHADS-VASC score, he was discharged on aspirin and β-blockers.

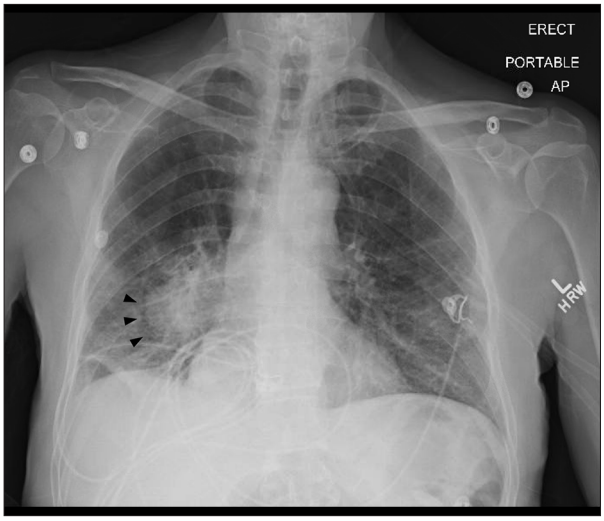

Figure 1. Chest x-ray showing right-sided infrahilar mass with adjacent subsegmental atelectasis (black arrow heads).

The patient came back the following day confused. Further workup for his altered mental status included a brain MRI, which revealed an acute lacunar ischemic infarction in the right centrum semiovale. On admission, he was in atrial fibrillation with rapid ventricular response. His chest x-ray revealed a stable right infrahilar mass with adjacent subsegmental atelectasis (Figure 1). A repeat TTE was negative for any intracardiac thrombus or masses. The acute ischemic stroke was minor, with no hemorrhagic conversion; therefore, he was placed on IV heparin. As part of the stroke protocol, the patient received a brain and neck magnetic resonance angiography (MRA) and transesophageal echocardiogram (TEE). The MRA revealed mild atherosclerotic disease and TEE showed a small echo density noted at the orifice of the right upper pulmonary vein, suspicious for a thrombus, with a low flow velocity across the pulmonary vein 26.6 cm/s (normal 30–80 cm/s) and no other left atrial or left ventricular thrombus formation (Figures 2–4; Videos 1, 2).

The patient had recently had multiple thoracic CT scans to evaluate his lung cancer and thoracic spine for back pain. Prior CT scans did not reveal any PVT due to different contrast timing, which possibly missed the PVT in the right upper pulmonary vein. A decision was made not to repeat a thorax CT scan to confirm the findings of PVT as the patient was already on anticoagulation, which did not alter the management or expose the patient to excessive radiation doses.

The patient improved a few days later, but he again became confused afterward. Subsequently, a repeat brain MRI revealed a new acute non-hemorrhagic stroke in the right thalamus, and the he was switched to a low-molecular-weight heparin given the new finding of probable PVT and history of malignancy.

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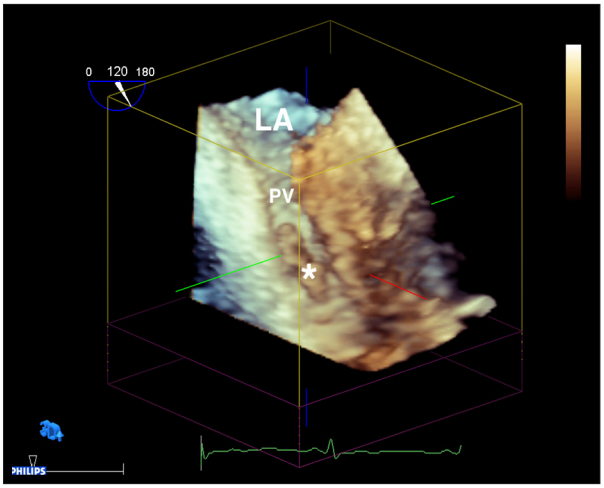

Figure 2. 3D transesophageal echocardiography (TEE) showing left atrium (LA) and pulmonary vein (PV) with thrombus formation (white asterisk).

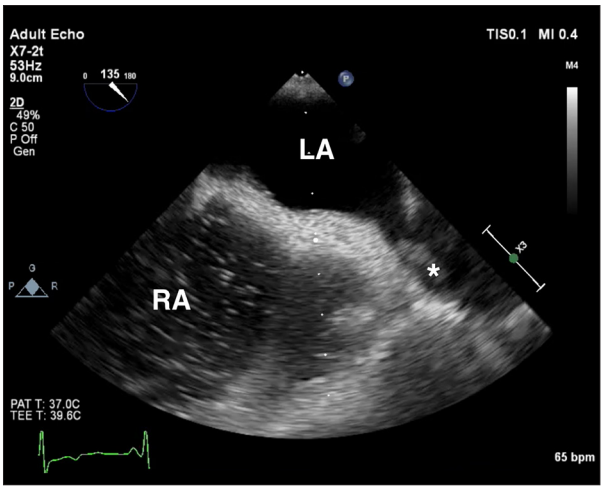

Figure 3. Mid-esophageal view 2D transesophageal echocardiography (TEE) showing the left atrium (LA) and right atrium (RA) as well as thrombus inside the pulmonary vein (white asterisk).

Due to low suspicion, no further diagnostic testing was performed to rule-out other sites of peripheral embolization.

Unfortunately, the patient's mental status continued to worsen due to his malignant burden, multiple metabolic derangements including hypercalcemia secondary to bone metastasis, recurrent ischemic strokes, and other co-morbidities. A discussion was held with his family regarding goals of care and they decided to proceed with comfort care and no resuscitation. The patient died a few days later.

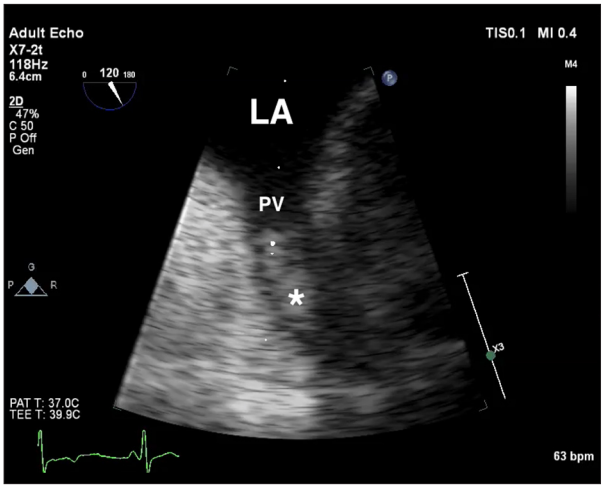

Figure 4. Magnified mid-esophageal view of the 2D transesophageal echocardiography (TEE) showing left atrium (LA), pulmonary vein (PV), and thrombus (white asterisk).

Discussion

Risk factors for PVT include lobectomy, lung transplant, and lung malignancy, as in our case. The pathophysiology in malignancy is unclear, but some theories suggest endothelial injury or hypercoagulable state secondary to malignancy as the possible cause of thrombus formation [6]. Direct extension of the tumor into the vein is another differential diagnosis, but is considered extremely rare, especially with non-sarcoma malignancies, and very few cases have been reported around the world [8].

Most of the PVT cases are asymptomatic, but some patients experience dyspnea, cough, or hemoptysis [3,6]. Various imaging modalities have been used to detect PVT, including TEE, cardiac CT scan, cardiac MRI, and angiography. The choice of imaging method depends on the clinical context; for example, cardiac CT scan and cardiac MRI are less invasive than TEE, which requires sedation. However, TEE can be done at bedside and thus is preferred in critically ill patients. TEE can show the extent of vein obstruction by the thrombus, while cardiac MRI and cardiac CT scan require less skill [6]. In our case, the finding of PVT was not confirmed by thoracic CT scan due to different contrast timings needed to visualize the pulmonary veins. A decision was made not pursue further imaging using cardiac CT scan due to high risk of radiation since the patient had received multiple thoracic CT scans in a short period given his lung adenocarcinoma diagnosis and the risk of contrast-induced nephropathy. The patient was placed on anticoagulation to treat the atrial fibrillation and PVT.

Unfortunately, there are no specific guidelines for the treatment of PVT, but anticoagulation and anti-tumor therapy are

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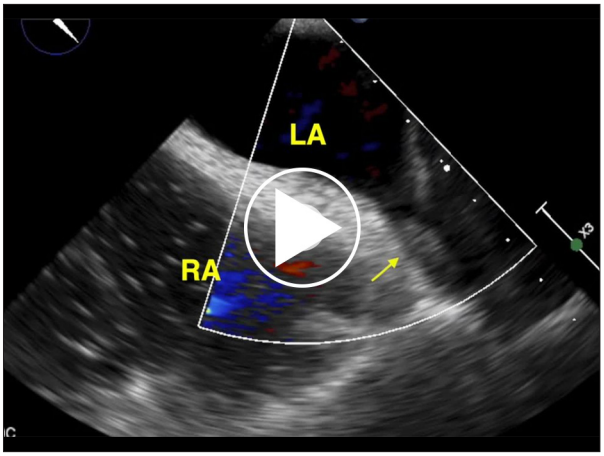
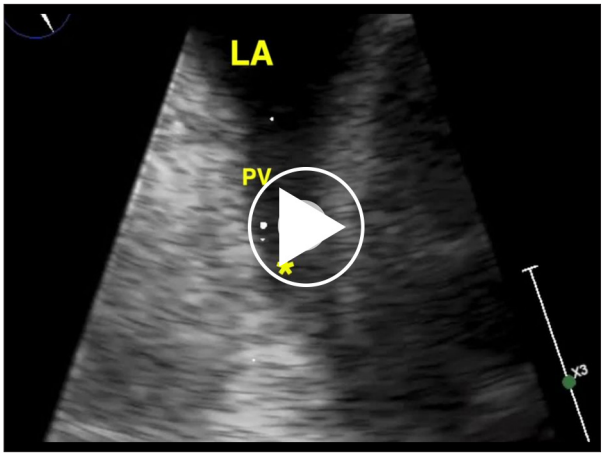


Video 1. Color Doppler mid-esophageal view of transesophageal echocardiography (TEE) corresponding to Figure 2, showing left atrium (LA), right atrium (RA), and mobile pulmonary vein thrombus (yellow arrow).



Video 2. Magnified video of mid-transesophageal echocardiography (TEE) corresponding to image 3, showing left atrium (LA), pulmonary vein (PV), and thrombus (yellow asterisk).

used in non-resectable tumors [5,6]. Other forms of treatment include thrombectomy, which is considered if medical therapy fails and also has been tried successfully for PVT after lobectomy and lung transplant; however, limited data are available in malignancy-induced PVT [2]. Lobectomy is considered when PVT is complicated with massive hemoptysis or pulmonary necrosis [2]. Complications include cerebrovascular accident, renal infarction, and other rare complications such as massive hemoptysis and peripheral embolization [3,6,7]. There are published cases of PVT causing a cerebrovascular accident, although a previous report by Grau et al. did not support the theory of PVT as a cause of cryptogenic stroke, but the study was limited by inadequate visualization of the pulmonary veins [8].

We hypothesize that our patient had a stroke secondary to PVT predisposed by multiple risk factors, including atrial fibrillation, with a rapid ventricular response and hypercoagulable state due to malignancy. A cardiac origin of the thrombus is the likely etiology since the brain/neck MRA revealed mild atherosclerosis, which makes plaque rupture less likely to be the cause of his stroke. Definitive diagnosis in our case was challenging due to the lack of histopathological evidence of thrombus and possible direct extension of the tumor. Previous reports found that direct extension of the tumor via pulmonary veins is uncommon and reported cases were associated with sarcoma rather than direct extension of bronchogenic carcinoma [2].

The finding of recurrent strokes also supports the diagnosis of PVT, as a direct extension of the tumors has rarely been reported to be associated with recurrent strokes [2]. Finally, the response to anticoagulation could not be assessed, as the patient died shortly after starting anticoagulation therapy.

Conclusions

PVT is a rare finding and may have an asymptomatic presentation. Establishing the diagnosis is crucial given the serious adverse outcomes, including peripheral embolization. Aggressive management with anticoagulation in addition to treating the underlying condition such as malignancy, atrial fibrillation, and others must be considered to prevent life-threatening complications.

Conflict of interest

None.

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