


# An intimal sarcoma of pulmonary artery mimicking pulmonary embolism: a case report and literature review

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## Keywords

Intimal sarcoma, pulmonary artery, pulmonary embolism, pulmonary thromboembolism.

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## Introduction

Pulmonary artery intimal sarcoma arises from the intimal layer of the right, left, or main pulmonary arteries [1]. It is extremely rare, clinically unpredictable, and often misdiagnosed as pulmonary thromboembolism (PTE) because of the similar clinical presentation. Although the prognosis is poor, the misdiagnosis of pulmonary artery sarcoma may delay any possible treatment. In this study, we report a patient who was initially diagnosed with PTE but ultimately correctly diagnosed with pulmonary artery intimal sarcoma by pathology after surgical resection.

## Case Report

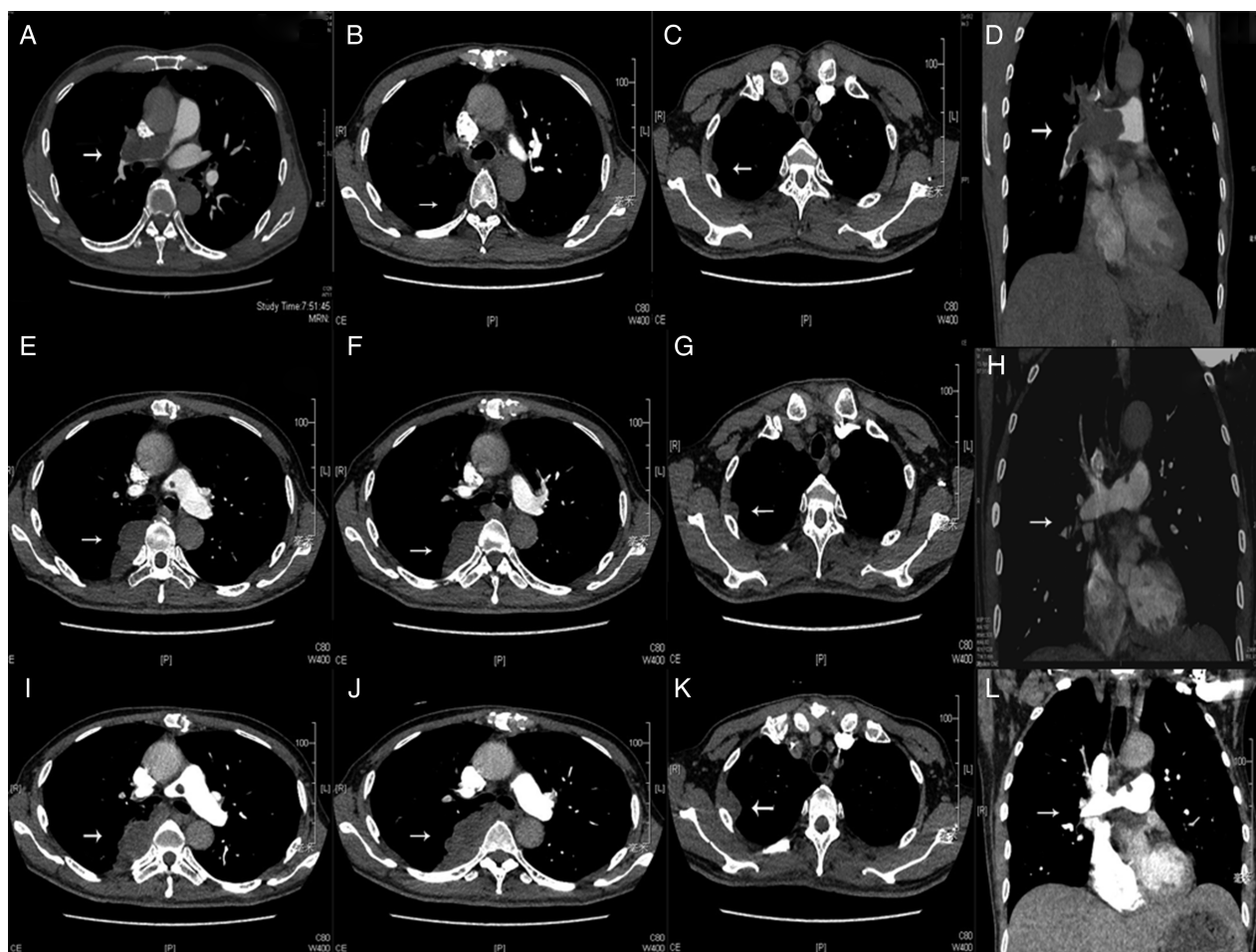
A 63-year-old male presented to the emergency department of Zhongshan Hospital with complaints of right-sided chest pain for the past 2 weeks. The patient reported that the pain had increased gradually. He had mild chest congestion with mild cough and no haemoptysis, breathlessness, or fever. He had no hypoxaemia (partial pressure of oxygen (PaO<sub>2</sub>) 84 mmHg, peripheral capillary oxygen saturation (SpO<sub>2</sub>)

## Abstract

Pulmonary artery intimal sarcoma is a highly aggressive disease, and is most often misdiagnosed as pulmonary thromboembolism (PTE) due to the similar clinical symptoms and its rarity, which leads to the use of inappropriate treatments such as prolonged anticoagulant therapy. We reported a case of pulmonary artery intimal sarcoma in a patient who was misdiagnosed as having PTE. Pathology after surgery confirmed malignant disease. We concluded that when a patient presents with mild clinical manifestations yet with strong imaging manifestations, pulmonary artery malignancy should be suspected.

95%). Electrocardiogram (EKG) showed a left anterior fascicular block. Computerized tomography (CT) showed suspicious embolus in the right pulmonary artery. Computerized tomographic pulmonary angiography (CTPA) showed pulmonary embolism (PE) in the right pulmonary artery and upper right pulmonary artery and possible pulmonary infarction focally (Fig. 1A–D). D-dimer was 0.49 mg/L (normal range is 0.02–0.80 mg/L). Complete blood count (CBC), hepatic function, renal function, serum electrolytes, cardiac biomarkers, autoantibodies, and coagulation were normal. There was no internal bleeding. He was diagnosed with PE and was treated with low-molecular weight heparin (LMWH) for 2 weeks.

The patient was then transferred to the respiratory department for further treatment. D-dimer was monitored continuously and remained normal. Autoantibody, tumour markers, mycological examination, and T-spot were all normal. Relative examinations showed no deep vein thrombosis (DVT) on colour Doppler ultrasound and the echocardiography (echo) was normal (left ventricular ejection fraction (LVEF) 66%; all chambers of the heart and



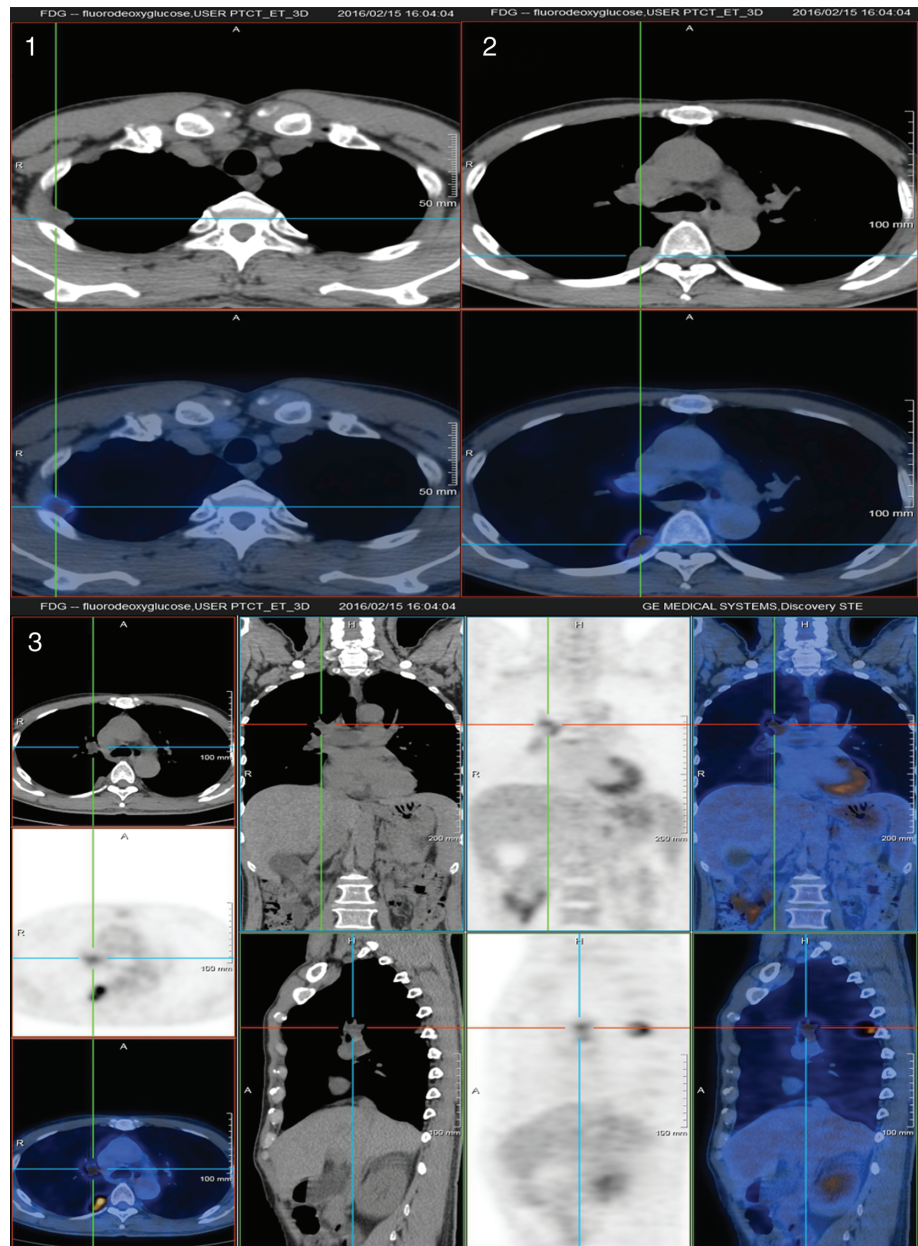
**Figure 1.** Series of images of computerized tomographic pulmonary angiography (CTPA) of the patient. (A–D) Images taken when the patient presented to hospital for the first time without any treatment. (E–H) Images taken 7 weeks after surgery and before chemotherapy. (I–L) Images taken after two cycles of chemotherapy.

pulmonary artery pressure were normal; no thrombus echo was observed in the main pulmonary artery and the right and left branches of pulmonary artery). Considering all the atypical clinical manifestations, we suggested that the patient undergo a (18)F-positron emission tomography (PET)/CT, which revealed PE in the right pulmonary artery. The PET/CT also showed a mass originating from the endothelial cells in the right pulmonary artery (maximum standard uptake value (SUV) was 3.5). Meanwhile, there were multiple abnormal foci with high SUV in the right lung (maximum SUV was 7.9 and maximum diameter was 28.8 mm) (Fig. 2).

After a cardiac surgery consultation, the tumour was resected. The patient received right pulmonary artery tumorectomy and pulmonary endarterectomy. During the surgery, we could see the right pulmonary artery was occupied by the tumour. Two arterial-wall-like tissues were sent for pathologic analysis. One mass, in which there was

4.5 × 2.5 × 2 cm large grey transparent sticky colloidal tissue, was 6.5 × 3.5 × 3 cm large and the wall was 0.3 cm thick. The other mass, with sticky colloidal tissue focally, was 3 × 2 × 1.5 cm large and the wall was 0.3 cm thick too. It was diagnosed as a spindle cell tumour that can be seen under an optical microscope. The immunological histological chemistry (IHC) results were S-100 (small amount +), α-smooth muscle actin (SMA; partial +), Desmin (Des) (–), CD34 (vascular +), CD31 (vascular +), Ki-67 (30% positive), F8 (vascular +), epithelial membrane antigen (EMA) (–), CK<sub>pan</sub>: a kind of immunohistochemical mark (CKPAN) (–), vimentin (VIM; +) (Fig. 3). Both the gross investigation and the IHC suggested intimal sarcoma. Then we examined the relevant gene mutation. Next-generation sequencing (NGS) showed gene mutations of CDK4, MDM2, FBXW7, FAT3, and FANCM.

The patient was followed-up closely after the surgery. Seven weeks after the surgery, the patient underwent



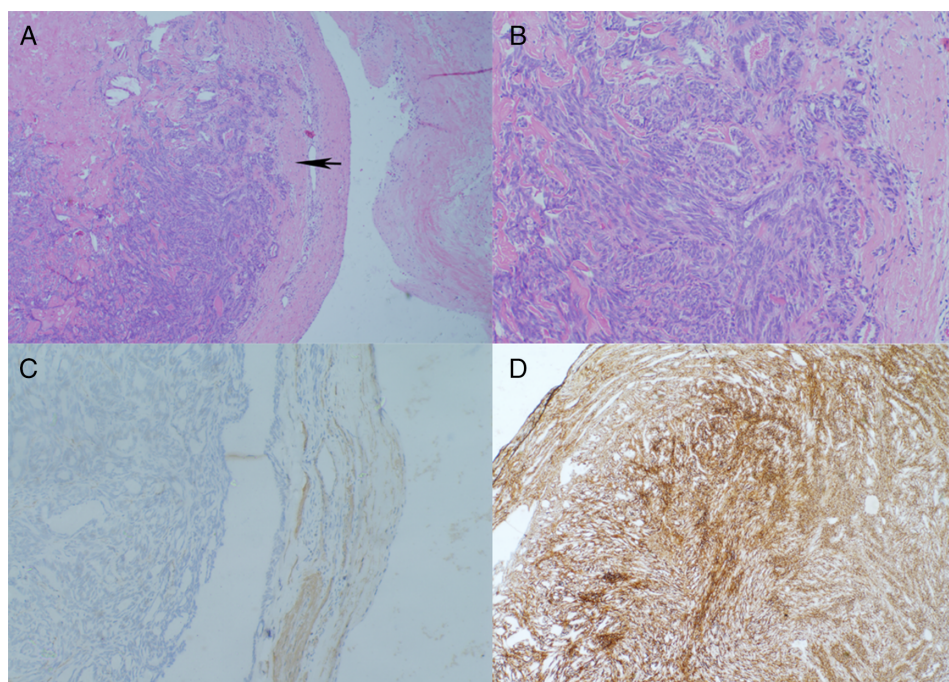
**Figure 2.** Images of  $(^{18}\text{F})$ -positron emission tomography (PET)/computerized tomography (CT) of the patient.

CTPA examination again before he was started on chemotherapy. The second CTPA showed recurrence in the right pulmonary artery and the right upper pulmonary artery with nodular filling defect. Maximum metastasis seen was 6.3 cm in the right lung (Fig. 1E–H). The patient then agreed to receive chemotherapy the next day at our oncology department. The chemotherapy drug administered was epirubicin ( $90 \text{ mg/m}^2$ ), for every 3 weeks. After two cycles of the chemotherapy, he underwent a third CTPA, which showed progress in the right pulmonary artery and the metastasis in the right lung (maximum diameter 9.7 cm)

together with new lesions in the right lung and the right pleura (Fig. 1I–L). Afterwards, he was lost to follow-up.

### Discussion

Intimal sarcoma is a totipotent-intimal-cell originated tumour. Pulmonary artery intimal sarcoma arises from the intimal layer of the right, left, or main pulmonary arteries, where pulmonary metastases are common [2]. In extremely rare cases, it may extend in a retrograde manner to the pulmonary valve and right ventricle [1]. Most cases



**Figure 3.** Pathology of the tumour. (A) Haematoxylin and eosin (HE) stain of the tumour shows that the tumour arose from the intimal of pulmonary artery (50 $\times$ ). The black arrow indicates the neoplasm from the artery wall. (B) Microscopically, the tumour was composed of pleomorphic spindle cells (HE stain, 200 $\times$ ). (C) Tumour cells were immunohistochemically positive for  $\alpha$ -smooth muscle actin (SMA). (D) Immunostaining for vimentin (VIM) highlights numerous neoplasm cells derived from mesenchymal tissue.

of this disease are diagnosed on autopsy or with surgical specimens; therefore, the true incidence of intimal sarcoma of the pulmonary artery is unknown.

The clinical presentation is often non-specific and related to tumour emboli. The most common symptoms are dyspnoea, tachypnoea, followed by chest or back pain, cough, haemoptysis, and malaise, which is quite similar to PTE. With such non-specific clinical features, the disease may mimic other diseases such as lung cancer, mediastinal masses, and especially acute or chronic PE [3,4]. Diagnosis in this patient was particularly difficult because of its long asymptomatic course and gradual development of symptoms of pulmonary hypertension and right heart failure [5]. As for PTE, if the pulmonary trunk is occluded by a blood clot, the patient often presents rapid-onset dyspnoea and chest tightness with right ventricular dysfunction such as pulmonary artery dilation or pulmonary hypertension [6]. However, the patient's chest pain developed gradually and no obvious shortness of breath was observed. The echo showed relatively normal heart function as well. D-dimer elevation is a sensitive indicator for thromboembolism either in lower limbs deep vein or pulmonary artery. D-dimer was normal for this patient from onset of the disease and during follow-up [7,8].

From the viewpoint of imaging, pulmonary artery intimal sarcoma and PTE are difficult to distinguish in the

differential diagnosis. The presence of extraluminal tumour extension as well as distant metastases are reliable signs in the differential diagnosis, but these are manifestations of advanced cancer of intimal sarcoma [9]. The CTPA demonstrates a filling defect, raising the suspicion of thromboembolism. Although both show enhancement on the CTPA, intimal sarcoma tends to present as a unilateral, central, lobulated, pulmonary artery filling defect with an increase in the diameter of the pulmonary arteries [3,9–12] and acute angles with the vessel wall, in contrast to the PTE [13]. And intimal sarcoma shows heterogeneous densities due to areas of necrosis, haemorrhage, and ossification within the mass [13]. The PET/CT was used to confirm the suspicion of pulmonary artery intimal sarcoma and to distinguish with PTE on the basis of the increased radiopharmaceutical uptake of tumours [14,15]. The echo in these cases may reveal dilation of the right ventricle, with or without signs of obstruction of the right ventricular outflow tract or of the pulmonary trunk whereas PTE usually has right ventricular dysfunction such as right ventricular dilation, hypokinesis, or pressure overload [16,17]. The diagnosis of intimal sarcoma is usually made post-operatively or at autopsy, but PET/CT can be of great help.

In our case, the patient had a subacute onset. His chief complaint was chest pain. The CTPA demonstrated an intraluminal filling defect occupying the entire lumen. The

symptom and CTPA outcome indicated a type of vascular occlusion, such as PTE. But considering the mild clinical manifestation including the normal D-dimer and echo results, and the following PET/CT examination, prompted a diagnosis of pulmonary artery malignancy. It was manifested by pathology after surgery. Finally, we diagnosed pulmonary artery intimal sarcoma that originated from the right pulmonary artery with metastasis in the right lung.

Knowledge about the molecular genetics and pathogenesis of intimal sarcoma is limited due to its rarity [18,19]. Intimal sarcomas are usually malignant mesenchymal tumours, which are poorly differentiated with fibroblastic or myofibroblastic differentiation [9]. Pathologic diagnosis can be difficult because the intimal sarcoma does not express specific markers for immunohistochemistry [20].

There are no specific guidelines for the management of patients with pulmonary artery intimal sarcoma [21]. The rarity of this diagnosis made it difficult to standardize the therapy. Surgery is the mainstay of pulmonary artery intimal sarcoma. Reported curative surgical procedures for treating the tumour include tumour endarterectomy, graft reconstruction of the pulmonary artery, and pneumonectomy. Aggressively repeated surgical interventions of the primary tumour, local recurrence, and metastatic lesions were helpful to increase patient survival.

The impact of chemotherapy and radiotherapy remains unclear, although some studies have demonstrated their effectiveness [2]. The use of radiation therapy and chemotherapy after surgical treatment has been found to prolong survival time compared with surgery alone [3,22,23]. Relative studies have shown that doxorubicin, and ifosfamide may be effective [24–27]. Clinical trials to better understand the role of surgery, chemotherapy, and radiation therapy are difficult to carry out due to the rarity of the disease.

The prognosis is also poor. In approximately 50% of the cases, pulmonary artery intimal sarcoma extends directly through the vessel wall to the adjacent lung, bronchial wall, lymph node, or heart. Distant metastases occur in 16–25% of the cases [28]. It can metastasize to the brain, pancreas, adrenal glands, and lungs [21]. The mean survival is 12–18 months [1,29]. Average survival at 5 years is less than 6% [30]. Surgical resection has been reported to decrease clinical symptoms and lengthen survival [31–36]. The prognosis seems to depend on the location and vascular extension [24]. Death is usually due to right heart failure because of obstruction of the pulmonary arteries [30].

In our case, the patient had mild chest pain with subacute onset, together with imaging that strongly suggested tumour involvement. His right pulmonary artery was totally blocked without any signs of heart failure or severe hypoxaemia and dyspnoea. Also, the D-dimer tests were always normal. Furthermore, the patient had metastasis in

his right lung. And finally, he had no risk factors for PTE. All of the above observations were quite different from PTE as we know. Therefore we opted for PET/CT and the following treatment. To summarize, attention should be paid when the patient presents with mild clinical manifestations and severe imaging manifestations. Especially when the D-dimer is within the normal range and the presence of a low-density lobulated filling defect with uneven distribution and contrast enhancement in the entire luminal diameter on CTPA, pulmonary artery malignancy should be strongly suspected. The high uptake on PET/CT scan can prompt suspicion of the disease.

In conclusion, untimely diagnosis leading to late stage presentations contributes to the poor prognosis of this disease. So early and proper diagnosis is necessary to establish appropriate therapy. Due to the high lethality of this tumour and the therapeutic and prognostic implications, it is of paramount importance for clinicians to be aware of the key features that differentiate this pathology from PTE. The PET/CT can be a proper way to help recognize intimal sarcomas when clinical manifestations are atypical. Given the dismal outcome and high risk of recurrence or metastatic spread of intimal sarcomas, the multimodal treatment, including a combinational treatment, appears justified. Difficulties in diagnosis and poor prognosis result in the lack of high volume studies and data registration, which means that further studies are necessary.

## Disclosure Statement

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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