

A case report of pulmonary artery intimal sarcoma negative for 18F-FDG mimicking pulmonary thromboembolism

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Background

Pulmonary artery sarcoma is a rare malignant neoplasm arising from intimal mesenchymal cells in the pulmonary artery wall and is often difficult to differentiate from pulmonary embolism, however, 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET) can be useful for a differential diagnosis. Here, we present a rare case of pulmonary sarcoma undetectable by PET.

Case summary

A 77-year-old woman who had worsening dyspnoea on effort for a month and progressive chest discomfort with nocturnal cough for a week presented to our hospital. Contrast-enhanced computed tomography (CT) demonstrated a massive filling defect in the left pulmonary artery (PA). Two major differential diagnoses were considered; pulmonary thromboembolism and tumour-like lesions. Positron emission tomography-computed tomography (PET-CT) revealed that there was no abnormal accumulation of 18F-FDG in the mass. However, even after effective anti-thrombotic treatment for 3 weeks, a follow-up CT showed no reduction at all in the size of the lesion in the pulmonary artery. Therefore, surgery for diagnostic therapeutic purposes was performed.

Discussion

The present case is informative because it supports the idea that being aware of PA angiosarcoma as a potential differential diagnosis of pulmonary thromboembolism is essential, particularly in cases of no evident peripheral venous thrombosis and a negative D-dimer test, even if neither heterogenous contrast enhancement in CT and magnetic resonance imaging nor accumulation of 18-FDG in PET-CT is evident.

Keywords

Pulmonary artery sarcoma • Intimal sarcoma • FDG-negative • Case report

ESC Curriculum

6.8 Cardiac tumours • 7.5 Cardiac surgery • 9.5 Pulmonary thromboembolism

Learning Points

- The diagnosis of pulmonary angiosarcoma could be challenging, particularly when considering the differential diagnosis with pulmonary thromboembolism.
- A negative result for 18F-FDG does not rule out malignancy.

Introduction

Mesenchymal origin pulmonary artery (PA) angiosarcoma is a rare tumour with poor prognosis.¹ To date, fewer than 300 cases of primary PA sarcoma have been described in the literature.^{2,3}

Pulmonary artery angiosarcoma is often difficult to differentiate from pulmonary embolism, however, 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET) is useful for a differential diagnosis. Here, we present a rare case of pulmonary sarcoma undetectable by PET.

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Timeline

Time	Event
1 month prior to presentation	Worsening dyspnoea on effort
1 week prior to presentation	Chest discomfort with nocturnal cough
Admission day (Day 1)	Vital signs were all within-normal ranges. Contrast-enhanced CT demonstrated a massive filling defect in the left PA. Serum D-dimer was undetectable, and all measured serum tumour markers (CEA, CA19-9 and CA125) were negative. Anticoagulant therapy (unfractionated heparin) started.
Day 4	MRI →No contrast enhancement
Day 5	⁶⁷ GA scintigraphy →No pathological radiotracer accumulation
Day 9	Contrast-enhanced CT →Unchanged condition of the mass
Day 14	PET-CT →No abnormal accumulation of 18F-FDG in the mass with max SUV 0.90
Day 15	Replaced heparin with apixaban 20 mg/day
Day 18	Pulmonary perfusion scintigraphy →Almost no RI accumulation in the entire left lung
Day 22	Contrast-enhanced CT →Unchanged condition of the mass
Day 25	Admission to the operating room Rapid intraoperative histological diagnosis showed that mass was a sarcoma.
Day 32	Discharge from the hospital following the surgery

Case presentation

A 77-year-old woman with a history of medically treated diabetes and hypertension who had worsening dyspnoea on effort for a month and progressive chest discomfort with a nocturnal cough for a week presented to our hospital. At presentation, her body mass index (24.5 kg/m²), heart rate (70 b.p.m.), blood pressure (112/78 mmHg), respiratory rate (14 per minute), and oxygen saturation level (96% in room air) were all within-normal ranges, no abnormal heart murmur was heard, and no specific pathological finding, such as right ventricular overload, was found on an electrocardiogram or trans-thoracic echocardiography (maximal flow velocity of tricuspid regurgitation: 2.3 m/s). Nevertheless, contrast-enhanced computed tomography (CT) demonstrated a massive filling defect in the left PA which was located from the left PA trunk to the left lower lobe branches [Figure 1(A)]. Two major differential diagnoses were considered; pulmonary thromboembolism, although contrast-enhanced CT showed no evidence of peripheral venous thrombosis, and serum D-dimer was undetectable, and tumour-like lesions, even though there was no contrast-enhancement in the CT and all serum tumour markers measured to detect occult cancer were negative, including CEA, CA19-9, CA125, and soluble interleukin-2 receptor.

In order to diagnose potential thromboembolism, we initiated the intravenous administration of unfractionated heparin while maintaining the activated partial thromboplastin time at >60 s. In parallel, further evaluations by multiple imaging modalities including contrast-enhanced magnetic resonance imaging (MRI) and total-body ⁶⁷GA scintigraphy

were performed to detect signs of malignant neoplasm and possible metastasis of remote cancers. However, no contrast enhancement in MRI or pathological radiotracer accumulation by scintigraphy was demonstrated. Moreover, positron emission tomography-computed tomography (PET-CT) revealed that there was no abnormal accumulation of 18F-FDG in the mass with maximum standardized uptake value (SUV) 0.90 [Figure 1(B)]. Despite no positive findings with respect to either thromboembolism or the tumour by these imaging modalities, anticoagulation was extended by replacing unfractionated heparin (approximately 800 unit/day) with apixaban 20 mg/day, as we believed that the mass in the PA was more likely to be a thromboembolism, rather than a malignant neoplasm at that time point. However, even after effective anti-thrombotic treatment for 3 weeks, a follow-up CT showed completely no reduction in the size of the lesion in the pulmonary artery. Therefore, integrally assessing the clinical course, such as deteriorating dyspnoea on effort without any efficacy of anticoagulants, and the findings of the imaging modalities, the lesion in the PA was finally diagnosed to be an intravascular tumour rather than thromboembolism.

After careful and intensive discussion among cardiologists, radiologists, and cardiovascular and thoracic surgeons, surgery to remove the tumour-like lesion in the PA was performed. Although the surgery was initially planned to be a left-upper lobectomy, it was expanded to a left pneumonectomy, as the tumour had occupied and almost totally occluded the left main, A1+2, A3 (arteries of apical-posterior and anterior segments), and A6 (superior segmental artery of the lower lobe) of the PA and rapid intraoperative histological diagnosis showed that it was a sarcoma. The tumour was generally jelly-like, partly solid, soft,

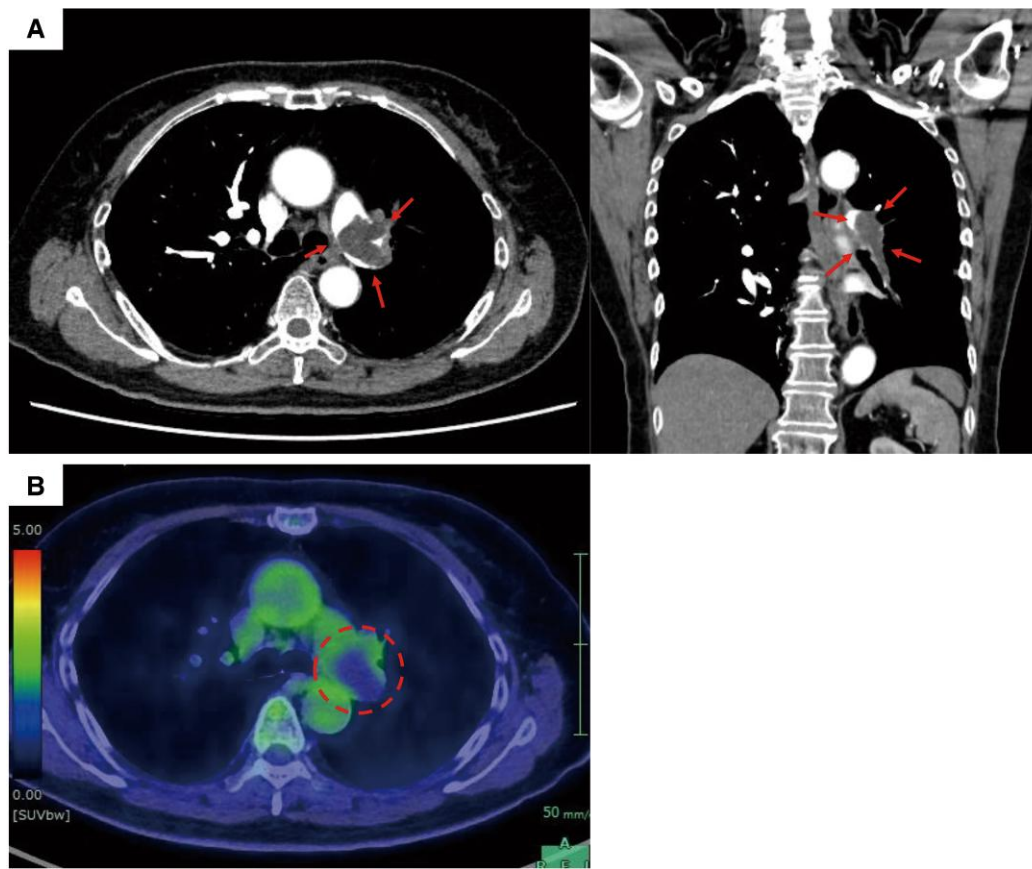


Figure 1 Massive filling defect in the left main pulmonary artery in contrast-enhanced computed tomography, but negative for fluorodeoxyglucose-positron emission tomography. (A) A massive filling defect in the left main pulmonary artery which continued to the left lower lobe branches (red arrows). (B) The filling defect was negative for ^{18}F -fluorodeoxyglucose (max standardized uptake value in the region was 0.90).

and appeared to be yellow (arrows, *Figure 2*). Histological analyses demonstrated that the tumour was an intimal angiosarcoma that had originated from the PA. Histologically, atypical cells with spindle- or circular-shaped nuclei proliferated against the background of a myxoma-like matrix, which arose from the intima of the PA (*Figure 3*). Nucleated cells were positively stained for P53 and smooth muscle cell (SMC) markers, including smooth muscle alpha actin (SMA-actin), vimentin, and desmin, indicating that sarcoma cells differentiated into vascular SMC lineage. As the edges of the resected tumour tissues were positive for atypical sarcoma cells, adjuvant therapy by radiation (60 grey) was added. Serum levels of B natriuretic protein (BNP) before surgery and at hospital discharge were continuously low (38.5 and 36.0 pg/mL, respectively). The patient has been followed without critical event for 3 years since surgery.

Discussion

Mesenchymal origin PA angiosarcoma is a rare tumour with poor prognosis.^{1,3} The literature has described fewer than 300 cases of primary PA sarcoma to date.² Previous studies reported that the incidence

of angiosarcoma amongst all types of soft tissue sarcomas was 2%,¹ and that amongst all pulmonary sarcomas to be 3.6%.^{4,5} Because of the substantial difficulty in diagnosing, most cases of PA angiosarcoma are found at an advanced stage with local invasion or distal metastasis.⁵ Symptoms of PA angiosarcoma are non-specific, such as dyspnoea, chest pain, and cough, and they might be similar to those in patients with pulmonary thromboembolism. Moreover, radiographically, as both PA angiosarcoma and thromboembolism may manifest as large masses as a filling defect in PA, it may be difficult to distinguish these two diseases only by radiography. In contrast, the median survival period could be extended to 36.5 months by the early induction of multimodality treatment, including radical surgical resection.⁶

In the present case, the initial symptoms were non-specific, dyspnoea on effort, chest discomfort, and cough. Images of contrast-enhanced CT showed a homogenous mass located at the left main PA and extended to A3 and A6 with no enhancement effect of the contrast. However, previous case series indicated that PA angiosarcoma was positively enhanced in CT, reflecting its tissue heterogeneity, such as intra-tumour hemorrhage, necrosis, and cysts.⁷ Consistent with CT, the tumour in this case had no contrast enhancement by MRI.

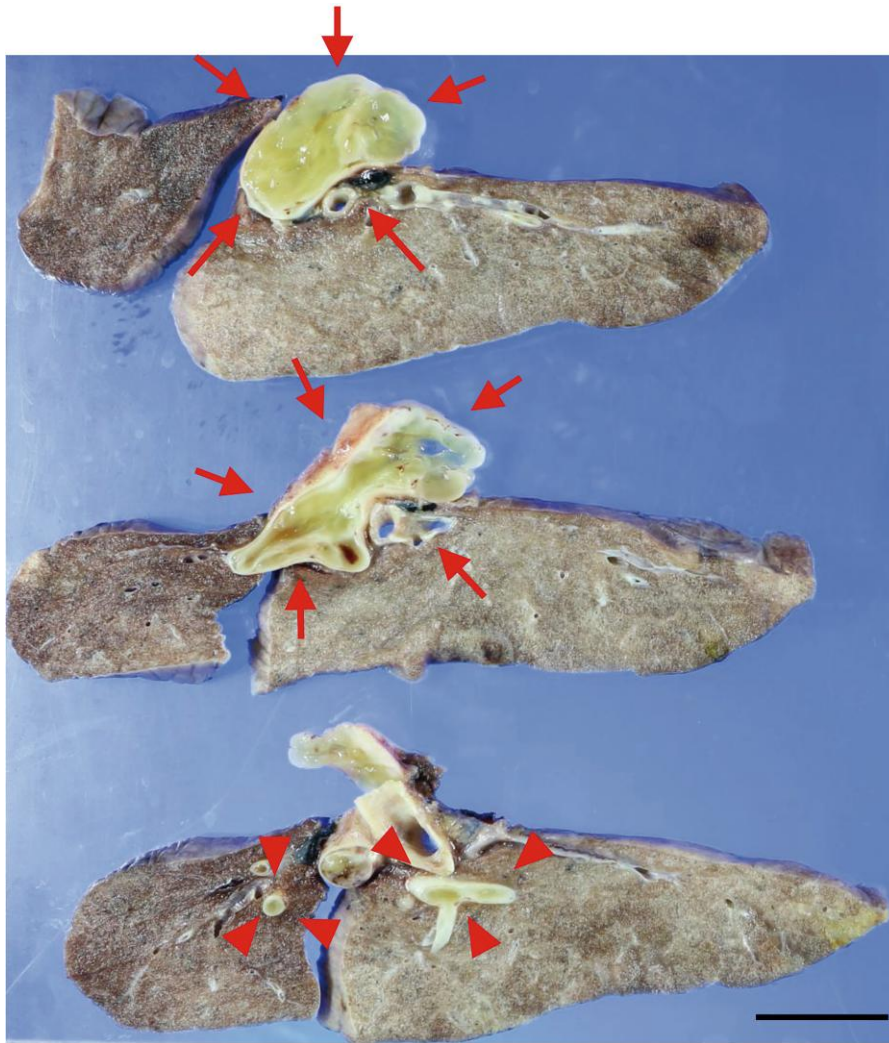


Figure 2 Macroscopic appearance of tumour following left pneumonectomy. Arrows indicate tumour. Arrow heads indicate pulmonary arteries filled by the tumour. Scale bar equals 3 cm.

However, the ability of enhanced MRI to detect subtle tissue heterogeneity in the tumour has been considered to be superior compared to CT.⁸ Moreover, in PET-CT, while a potentially promising modality in distinguishing thromboembolism (FDG-negative) from PA angiosarcoma (usually metabolically active, FDG positive), the max SUV of the present tumour was nearly 0, which was consistent with histological analysis revealing atypical cell proliferation in a myxomatous background. Because we considered that the possibility of thromboembolism was higher in this case, we initially decided to observe the effects of anticoagulant therapy for 3 weeks to reduce the mass size in PA. However, as there was no change in the size of the mass by unfractionated heparin, the surgery aimed at complete removal of the tumour when done. The interval between the mass detection in PA and the final histological diagnosis in the present case might be shorter than that in a

previous study involving 13 patients with primary sarcomas of great vessels (median: 11 weeks).⁹ However, it could be more suppressed if an endovascular catheter biopsy was possibly conducted.¹⁰ We did not perform that because we considered that the risk of pulmonary embolism by the procedure might be high in this case.

Conclusions

The present case is informative because it indicates that being aware of PA angiosarcoma as a potential differential diagnosis of pulmonary thromboembolism is essential, particularly in cases without peripheral venous thrombosis and a negative *D*-dimer test, even in case where neither heterogenous contrast enhancement in CT and MRI nor accumulation of 18-FDG in PET-CT was evident.

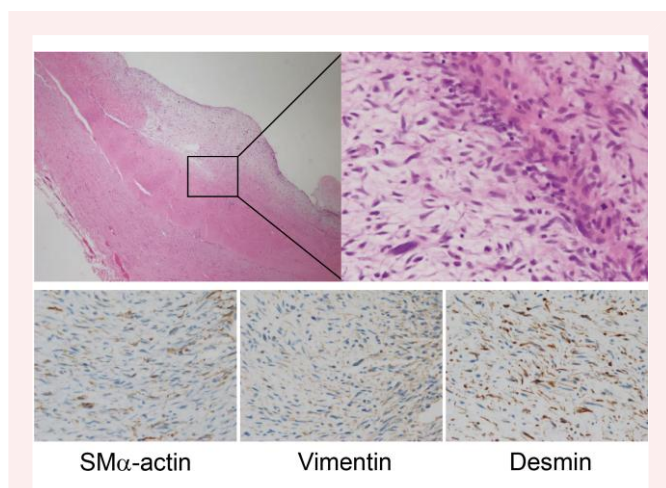


Figure 3 Microscopic and immunohistochemical findings of smooth muscle cell (SMC) markers of the tumour. Upper panels: hematoxylin and eosin (HE) staining showed that atypical cells with spindle- or circular-shaped nuclei arose from the intima of the pulmonary artery (arrow heads). Left panel: 40 \times and right panel: 400 \times , respectively. Lower panels: immunohistochemical staining showed that the tumour cells were positive for SMC markers, SM α -actin (left), vimentin (center), and desmin (right), respectively.

Lead author biography



Takuma Koike received the MD degree from Juntendo University, Kanagawa, Japan in 2016 and subsequently underwent his specialty training in Internal Medicine and Cardiology at Juntendo University, Tokyo, Japan.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports*.

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Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

Consent: The authors confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

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Data availability

The data underlying this article are available in the article and in its online supplementary material.

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