

A new-onset pulmonary artery stenosis in a young man: case report

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Background

Poorly differentiated and undifferentiated sarcomas are the most common primary tumours of the pulmonary arteries. They usually affect large-calibre vessels and present with predominantly intraluminal growth. Dyspnoea, cough, chest pain, and haemoptysis are the most common presenting symptoms. Clinical and imaging manifestations can mimic pulmonary embolisms and correct diagnosis may require multimodal imaging. The overall prognosis is poor; however, early diagnosis and complete surgical resection seem to improve the prognosis.

Case summary

A 31-year-old male was admitted to our department after a pre-syncopal episode associated with dyspnoea of recent onset. Echocardiography showed a mass with irregular borders attached to the pulmonary artery trunk, almost obliterating its lumen and determining a flow acceleration with a peak velocity and gradient, respectively, of 3.8 m/s and 60 mmHg. At cardiac magnetic resonance imaging and positron emission tomography-computed tomography scan, the mass had inhomogeneous contrast impregnation and an intense 18-fluorodeoxyglucose uptake, both findings are highly suggestive of an angiosarcoma of the pulmonary artery. Biopsy specimens were taken through bronchoscopy but the material was insufficient for diagnosis. The patient decided to continue treatment in another hospital, where he died a few months later.

Discussion

The presence of a unique mass involving the main trunk of the pulmonary artery or proximal branches associated with rapidly progressive dyspnoea in a patient at low risk for pulmonary embolism should raise the suspicion of primary sarcoma of the pulmonary artery. There are no guidelines for the treatment. Surgery and neo/adjunct chemotherapy are reported in literature but burdened by bias and concerning a small number of cases.

Keywords

Pulmonary artery sarcoma • Pulmonary angiosarcoma • Pulmonary embolism • Immunohistochemistry • Case report

Introduction

Pulmonary artery sarcoma is a rare type of malignant vascular tumour characterized by a very aggressive clinical course and an unfavourable

prognosis.^{1,2} Its rarity and the absence of specific symptoms, especially at the onset, make the diagnosis difficult and often delayed, or only post-mortem.^{1,3} The therapeutic options are limited and often sub-optimal, and the median survival without radical resection is about

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Learning points

- The diagnosis of artery sarcoma must be suspected in patients with relevant respiratory symptoms but a low probability of pulmonary embolism (e.g. Wells score ≤ 1).
- The evaluation of an intravascular mass requires a multiparametric approach for better tissue characterization and assessment of its haemodynamic impact.
- No guidelines are currently available. Therapeutic strategy must be individually tailored, combining surgical and medical treatment. Radical resection seems to be the mainstay of therapy.

30–50 days.^{1,3} In this report, we present the case of a young man with an isolated pulmonary artery sarcoma.

Timeline

Data	Events and diagnostic tests
Month 0	Dyspnoea during sport and asthenia
From Month 0 to Month 7	Worsening of dyspnoea, pre-syncope
Month 8	Spirometry test, syncope, and loss of consciousness at work > thoracic high resolution computed tomography (HRCT) and echocardiography
From Day 0 to Day 6 (Month 8)	Hospital admission: echocardiography; thoracic HRCT; venous Doppler; esophago-gastroduodenoscopy/colonoscopy; cardiac magnetic resonance; positron emission tomography scan, oncologic visit
Day 8	Bronchoscopy with biopsy and lack of histologic confirmation
Day 13	Voluntary hospital discharge

Case presentation

A 31-year-old, non-smoking male presented to the hospital complaining of progressive asthenia and exertional dyspnoea for 4 months before. He had an unremarkable past medical history and physical examination.

Before the patient presented at hospital, the spirometry had provided normal results, a high resolution computed tomography (HRCT) pulmonary scan had shown a non-specific inflammatory parenchymal pattern and an enlarged pulmonary artery trunk. In addition, echocardiography showed a marked increase of transpulmonary peak flow velocity and an unspecified mass in the pulmonary arterial trunk. The patient was admitted to the hospital for further investigation. On admission, his vital signs were stable, and peripheral oxygen saturation was normal. Laboratory data showed mildly increased inflammatory markers (D-dimer: 528 $\mu\text{g/L}$, fibrinogen: 609 mg/dL , high-sensitivity C-reactive protein (hs-CRP): 23 mg/L) and

low ferritin, while white blood cell count, haemoglobin, renal function, hepatic and cardiac enzymes were normal. The laboratory investigation for genetic thrombophilia was negative.

Echocardiography (Figure 1) confirmed a mass with irregular borders within the pulmonary trunk, almost obliterating its lumen and determining a flow acceleration with a peak velocity and a gradient of 3.8 m/s and 60 mmHg , respectively. All other Doppler, morphologic and functional findings of the pulmonary valve and right ventricle were normal.

Initially, these findings were interpreted as possible venous thromboembolism, and we started anticoagulant therapy with low molecular weight heparin. However, compression ultrasonography ruled out a deep vein thrombosis.

Repeated pulmonary HRCT showed dilatation of the pulmonary trunk with an irregular mass within its lumen with extremely limited enhancement by contrast medium, mistakenly reported as a big thrombus (Figure 2), and isolated areas of ground-glass opacity in the lung parenchyma for which we started large spectrum antibiotic therapy.

Colonoscopy and esophagogastroduodenoscopy were performed to exclude a paraneoplastic thrombosis and were both negative for malignancies.

Follow-up echocardiography performed after 10 days demonstrated a dilated right ventricle with increased systolic pressure.

Due to the atypical clinical manifestations and the unresponsiveness to anticoagulant therapy with Low-molecular-weight heparin (LMWH), we performed a cardiac magnetic resonance (MR) (Figure 3) that confirmed an intravascular mass with a thrombotic component adherent to the right side of the pulmonary trunk and inhomogeneous impregnation by contrast medium, highly suggestive for an angiosarcoma of the pulmonary artery.

Positron emission tomography scan (PET-SCAN) with 18-fluorodeoxyglucose (^{18}F -FDG) (Figure 4) revealed an intense local glucose metabolism at the pulmonary trunk level, without any extrapulmonary lesion, which excluded a metastatic nature of the mass.

Finally, the lesion was biopsied by bronchoscopy transbronchial, but the resulting material was inadequate for a specific diagnosis. The histologic report highlighted the presence of rare and isolated atypic cells, not further typable, interspersed with cylindrical hair cells and globular red cells; it was technically impossible to search for the different types of markers, with the exception of Citokeratyn 5.2 (CAM 5.2), which was positive.

The patient decided to continue the treatment in another hospital, where he was operated 2 weeks after diagnosis. However, he developed a local relapse after 6 months and died within a few weeks.

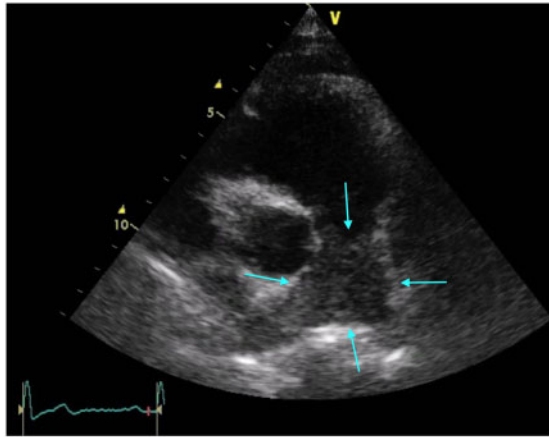


Figure 1 Echocardiographic image of the mass in the pulmonary trunk in parasternal short-axis view (PSAX view).

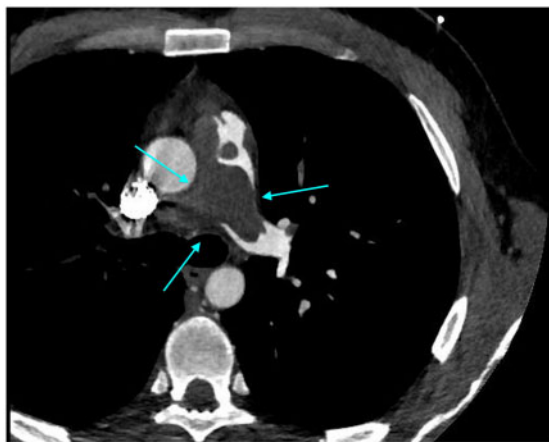


Figure 2 Axial contrast-enhanced computed tomography scan image showing filling defect in the pulmonary trunk. The mass shows extremely limited enhancement by contrast medium and it was originally reported as a big thrombus.

Discussion

Primary pulmonary artery sarcomas are rare malignant tumours whose proliferative cells arise from the mesenchymal cells of the pulmonary artery.⁴ It is the most common primary tumour of the pulmonary arteries, usually affecting large-calibre branches with predominantly intraluminal growth.^{1,3} There are some different histopathologic patterns of primary artery sarcomas (undifferentiated sarcoma, rhabdomyosarcoma, leiomyosarcoma, spindle cells sarcoma, angiosarcoma, and few other rare forms), but the histopathological classification does not seem to have clinical or prognostic usefulness.^{1,5} These tumours may metastasize to the lung, brain, liver, spleen, small bowel, and adrenal glands.⁶

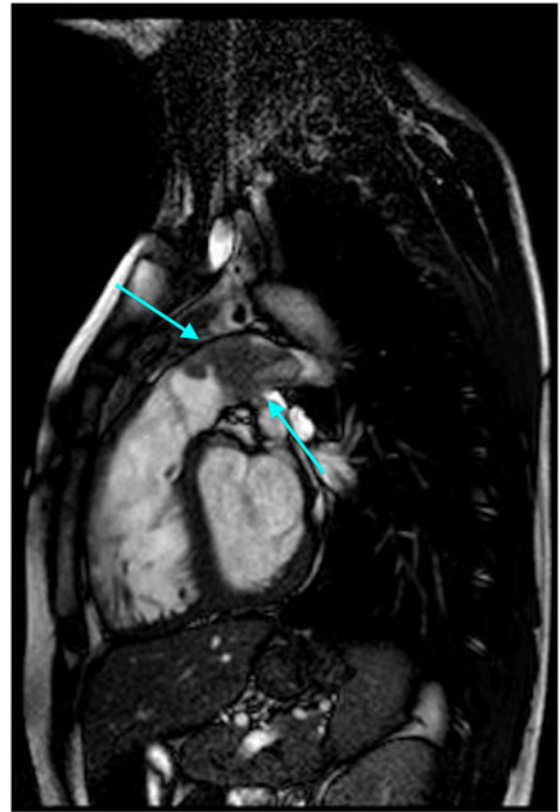


Figure 3 Sagittal cardiac magnetic resonance image showing the pulmonary trunk with inhomogeneous impregnation of the mass by contrast medium.

Bandyopadhyay *et al.*,⁴ in their literature research from 1991 to 2010, reported 391 primary pulmonary artery sarcomas; the first published case was in 1923 from an autopsy by Mandelstam.⁷

Symptoms of pulmonary sarcoma are non-specific: dyspnoea, cough, chest pain, malaise, haemoptysis, pulmonary hypertension, and lipothymic events, due to right ventricular dysfunction or pulmonary valve obstruction, are frequently reported.^{1,2,4} As symptoms are non-specific, the diagnosis is often delayed. Indeed, the tumour may develop silently, and symptoms of pulmonary obstruction may be the first manifestation, usually at an advanced stage.^{1,2,4} The differential diagnosis includes lung cancer, pulmonary embolism, pulmonary hypertension, and congenital pulmonary stenosis when the pulmonary valve is involved.^{1-4,6} Pulmonary embolism is the most frequent misdiagnosis.⁴ Pulmonary artery sarcoma should be suspected whenever there is no clinical improvement with anticoagulant therapy in patients with a low probability of thromboembolic events (Wells clinical prediction score ≤ 1).^{1,3,8} Clinical and laboratory data may help in the differential diagnosis: fever, high hs-CRP, or Erythrocyte Sedimentation Rate (ESR), weight loss, lack of history of deep vein thrombosis, absence of procoagulant mutations, should all orient towards a non-thrombotic cause.¹

Chest radiography and computed tomography (CT)-scans may show different patterns, from solitary lesions to multiple nodular

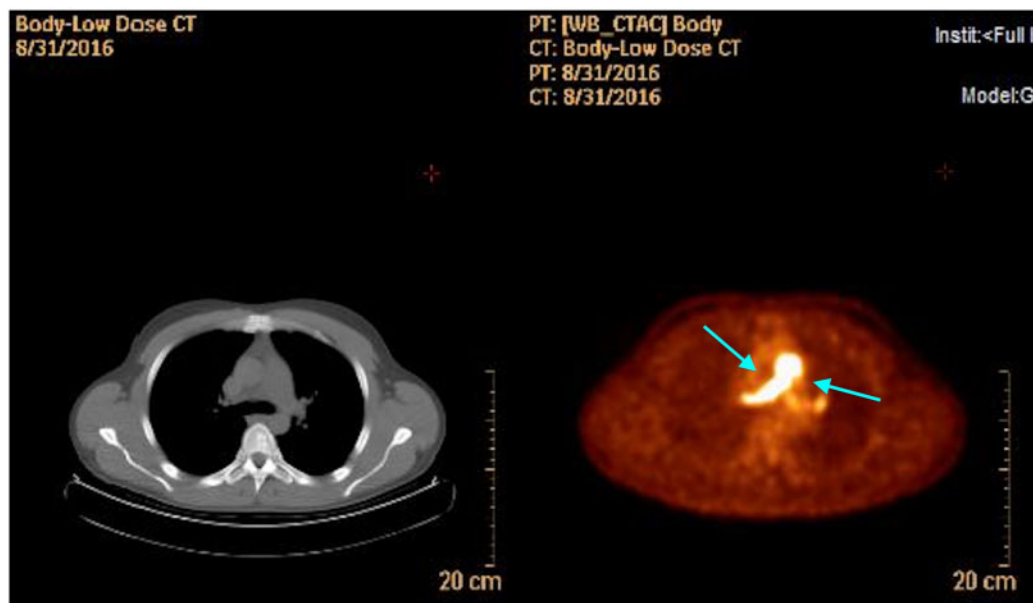


Figure 4 Sagittal image of the thorax with isolated intense 18-fluorodeoxyglucose metabolism of the mass at positron emission tomography scan that confirms the primary origin of the tumour.

densities, with or without pleural effusion. Multiple infiltration or consolidation and metastatic localization suggest an unfavourable prognosis short term. Thanks to gadolinium-enhancement, magnetic resonance imaging increases the diagnostic sensitivity, while intense ^{18}F -FDG uptake at PET helps to differentiate sarcoma from thrombi (Table 1).^{1,6,9} The different histologic types of sarcomas are frequently indistinguishable at radiologic analysis, but morphological features, location, and clinical presentation may guide in the diagnosis.³

However, definitive diagnosis needs histopathological examination with immunohistochemical markers including desmin, cytokeratin, vimentin, and actin. CD 31, CD34, and factor VIII-related antigen are more specific for angiosarcoma.⁶

Also because of its rarity, guidelines for the management of pulmonary sarcoma are not consolidated. Surgical resection, combined with chemo-radiotherapy and immunotherapy, seems to offer the best survival rates^{1,2,4,6}; nevertheless, the tumour is very aggressive, and the prognosis remains poor, particularly if a complete resection is not feasible, as it happens when the tumour is not locally confined.⁶

Some anti-tumoural agents like anthracycline (doxorubicin, epirubicin) with or without an alkilant (dacarbazine, ifosfamide) have been tested. Other agents are vincristine, paclitaxel, gemcitabine, etoposide, interleukin-2, vincristine, mitomycin, methotrexate, and sunitinib.² Radiotherapy may be used post-surgery to avoid local relapse.¹

Bandyopadhyay et al.⁴ in their retrospective observational analysis, comprehensive of their hospital cases and cases from the literature, showed that adjunctive therapy (chemo/radiotherapy) improves survival and reduces development of distant metastasis but not local recurrence. The improvement of survival with multimodality therapy was also confirmed by Blackmon et al.⁶

Neoadjuvant chemotherapy has been described in stable patients and when the patients were not candidate for a curative resection;

Table 1 Multimodal differential diagnosis of pulmonary sarcoma

Method	Differential diagnosis
Echocardiography	Valvular obstruction (peak velocity at Doppler study), pulmonary hypertension (Vd/Ad increased)
CT-SCAN	Lung cancer (especially if multifocal), pulmonary thromboembolism (pulmonary arterial filling defects)
Contrast magnetic resonance imaging	Pulmonary thromboembolism (increases the sensitivity and specificity thanks to gadolinium-enhancement)
PET-SCAN	Pulmonary metastasis by other tumours (^{18}F -FDG avid masses)

^{18}F -FDG, 18-fluorodeoxyglucose; CT, computed tomography; PET-SCAN, positron emission tomography scan.

Linden et al. reported a case whereby tumour downstaging with neoadjuvant chemotherapy allowed a radical surgery to be performed.^{6,10}

Furthermore, the review conducted by Blackmon et al.⁶ on the treatment of pulmonary artery sarcomas combined between literature cases and theirs shows that a curative resection attempt improves the median and 5 years of survival compared with debulking or palliative surgery.

The possibility of a radical resection remains the most important prognostic factor, which is more likely with an early diagnosis, and with a high definition by multimodal imaging.^{1,2,6} Therefore, radical

surgery with neoadjuvant chemotherapy remains the therapy of choice when the patient is haemodynamically stable; whereas adjuvant therapy is advisable when the patient cannot wait for the resection.⁶

In conclusion: pulmonary artery sarcoma is a highly aggressive malignant vascular tumour with a very poor prognosis. Due to non-specific symptoms, the diagnosis is often delayed, and hence the potential for radical surgery—preceded or followed by chemotherapy and radiotherapy—reduced. Therefore, early diagnosis through a multimodal approach based on combined echocardiography, cardiac MR, CT scan, PET (Table 1), is of crucial clinical relevance to warrant the best possible therapeutic strategy. Because of the small number of cases due to its rarity, no guidelines recommend a univocal therapeutic strategy, and the reported therapeutic strategies present significant limitations, as there is a bias in data collection by different authors between case reports and small case series.

Lead author biography



Francesco Vanni is a Cardiology Resident in Florence and he has special interest in interventional cardiology and in cardiology intensive care. He likes travelling and sporting activities, soccer, and mountain bike in particular.

Supplementary material

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

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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 patient reported in this case is deceased. Despite the best efforts of the authors, they have been unable to contact the patient's next-of-kin to obtain consent for publication. Every effort has been made to anonymize the case. This situation has been discussed with the editors.

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