



Case Report

Pulmonary Artery Intimal Sarcoma: A Deadly Diagnosis in Disguise

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ABSTRACT

Pulmonary artery intimal sarcoma (PAIS) is a very rare tumour. The prevalence of PAIS is estimated to be between 0.001% and 0.003%, but this may be an underestimation because of potential misdiagnosis due to its similar presentation to that of pulmonary thromboembolism. The prognosis is very poor, with median overall survival between 11 and 18 months. We report a case of a 36-year-old man who presented to our cardiac surgery clinic reporting nonspecific symptoms and was found to have PAIS requiring surgical resection and adjuvant chemotherapy. We outline the radiologic features, pathologic characteristics, surgical approach, and chemotherapy treatment utilized.

RÉSUMÉ

Le sarcome intimal de l'artère pulmonaire est une tumeur très rare. On estime que sa prévalence se situe entre 0,001 % et 0,003 %. Elle pourrait cependant être plus élevée, étant donné que sa présentation est comparable à celle des thromboembolies pulmonaires et que les erreurs diagnostiques sont possibles. Le pronostic du sarcome intimal de l'artère pulmonaire est très sombre, la survie globale médiane variant de 11 à 18 mois. Nous décrivons le cas d'un homme de 36 ans qui s'est présenté à notre clinique de chirurgie cardiaque en décrivant des symptômes non distinctifs et qui a reçu un diagnostic de sarcome intimal de l'artère pulmonaire nécessitant une résection chirurgicale ainsi qu'une chimiothérapie adjuvante. Nous soulignons les caractéristiques radiologiques et pathologiques du patient, l'approche chirurgicale adoptée et la chimiothérapie sélectionnée.

A 36-year-old man was referred to our cardiac surgery clinic reporting a 2-week history of atypical chest pain and mild shortness of breath on exertion. His past medical history is remarkable for type 2 diabetes mellitus that is well controlled with oral hypoglycemic medications. A transesophageal echocardiogram revealed a large mobile mass of 20 × 21 mm in the main pulmonary artery above the pulmonic valve, and a second large fixed mass of 17 × 14 mm in the distal main pulmonary artery (Fig. 1A; Video 1 , view video online). The left ventricle was normal in size, with a normal ejection fraction of 65%-70%. The right ventricle was normal in size and function. There was no pulmonary stenosis or regurgitation. There was trace tricuspid regurgitation and an

insufficient tricuspid regurgitation Doppler signal to estimate right ventricular systolic pressure. The findings were highly suspicious for pulmonary thromboembolism; however, tumour could not be excluded. In light of these findings, the patient was admitted to the hospital for further investigations, and placed on intravenous heparin anticoagulation therapy for possible thrombus.

A computed tomography pulmonary angiography (CTPA) revealed a large filling defect in the main pulmonary artery that extended into the left main pulmonary artery and the superior lingular pulmonary artery. Another lobulated filling defect was seen within the right interlobular artery extending to the right lower lobe segmental pulmonary artery branches (Fig. 1, B-E). The patient was also staged with magnetic resonance imaging (MRI) of the head and a CT scan of the abdomen/pelvis, both of which were negative for distant metastasis. After 5 days of anticoagulation and no radiologic improvement in the defects, the suspicion for pulmonary artery intimal sarcoma (PAIS) became higher on our differential. The patient's case was discussed at the sarcoma tumour board in a specialized center in our area, and collectively, there was agreement that the mass needed to be excised first before any

Received for publication May 26, 2020. Accepted July 13, 2020.

Ethics Statement: The research reported has adhered to the relevant ethical guidelines.

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Novel Teaching Points

- PAIS is a diagnosis in disguise and is often mistaken for PTE.
- Special attention needs to be paid when a patient presents with clinical symptoms and several imaging manifestations suspicious for PTE.
- There are no specific guidelines for the management of patients with PAIS. However, combination of surgery and adjuvant chemotherapy seems to provide benefits in relieving clinical symptoms and lengthening survival.

form of treatment was given. Therefore, the patient was taken to the operating room for excision of the mass.

The surgery was performed with aortic and bicaval cannulation, cardiopulmonary bypass, deep hypothermia, and intermittent circulatory arrest. The tumour was found to have a broad-based stalk attached to the left lateral wall of the main pulmonary artery (MPA) above the pulmonary valve. It appeared to be capsulated with lobulations. There were also areas of necrosis and hemorrhage. The patient was noted to have embolization to the right inferior lobar artery and underwent a further distal embolectomy with the MPA incision extended to the right pulmonary artery. This procedure included evacuation of both the superimposed thrombosis and the metastasized embolus in the distal segmental pulmonary arteries. The right MPA was then closed to the level of the pulmonary bifurcation. The MPA between the pulmonary valve and bifurcation including the entire mass was resected and replaced with a 24-mm Dacron graft. The pulmonary valve was examined and found to be a tri-leaflet valve with clearly defined left, right, and posterior cusps. A repeat CTPA 5 weeks after surgery revealed a total resolution of the previously noted intramural mass lesion in the widely open main pulmonary graft and left pulmonary artery with a small defect seen in the right aspect of the MPA likely related to the scar tissue on anastomosis between graft and native tissue (Fig. 1, F-I).

The diagnosis and histologic classification were made by the pathologists at our institution (Fig. 2, A-D). The tumour was composed of variably cellular sheets of epithelioid and pleomorphic cells with coarse chromatic macronucleoli, and multinucleation. Lesional cells showed strong positivity for mouse double minute 2 and vimentin, focal positivity for cluster of differentiation (CD)31, and weak positivity for myoglobin. Pulmonary artery intimal sarcoma was diagnosed after broad consultation within the tumour board.

Based on these findings, the patient was referred to medical oncology to discuss further treatment plans. The patient opted for adjuvant chemotherapy with ifosfamide and doxorubicin for 6 cycles. Repeat CTPA and a CT abdomen scan 7 months postoperation, and completion of 6 cycles of treatment, showed no local recurrence or distant metastasis. Since the operation, the patient has been followed with chest radiographs every 3 months, alternating with CT scans. The medical team following the patient reports that the patient is well and asymptomatic. Repeat imaging with CTPA and CT

of the abdomen/pelvis has shown no evidence of local recurrence or distant metastasis 11 months postoperation.

Discussion

PAIS is a rare but aggressive tumour. The risk factors for developing PAIS are poorly defined. There are case reports in the literature that have looked at the genetics of certain patients, and a hypothesis has been made that individuals who are homozygous for some sequence variants that are responsible for folate levels and DNA methylation can cause instability and maybe potentiate the development of PAIS.

The prognosis of PAIS is very poor, and in cases in which the tumour is unresectable or already metastasized historically, the median survival has been a month and a half.¹ However, with the use of chemotherapy and advances in radiation, the survival of these patients with even advanced PAIS has improved tremendously, ranging from 8 to 17 months. The use of radiation therapy and chemotherapy after surgical treatment has been found to prolong survival time, compared with surgery alone, for a period of 17 to 26 months.¹

PAIS is a diagnosis in disguise and is often mistaken for pulmonary thromboembolism (PTE). Patients with PAIS often report symptoms of dyspnea, hemoptysis, chest pain, and cough. These clinical symptoms, however, are not specific to PAIS. Most of the time, the clinical diagnosis that is first suspected is PTE. As a result, the diagnosis of PAIS is often made too late after the disease has become advanced. The symptoms of PAIS can mimic those of other diseases as well, such as mediastinal masses, lung cancer, and more likely, acute or chronic PTE.² It is important for clinicians, however, to be aware of these symptoms and consider PAIS in their differential when patients present. The rarity of the disease makes the diagnosis challenging, and often times the disease is diagnosed on autopsy or with surgical specimens.

However, there are certain features that may help clinicians become more suspicious of PAIS. Kim et al., in a retrospective study looking at markers to differentiate PAIS from PTE, revealed that PAIS patients are usually younger than PTE patients, with a mean age of 54 years, compared to 64 years. Another clue was the duration of symptoms, which is significantly shorter in PAIS than in PTE patients (3 months vs 6 months). Half of the patients with PTE have had deep vein thrombosis; however, it is very rare for a PAIS patient to have had a deep vein thrombosis.³

From a radiologic imaging perspective, PAIS and PTE are difficult to distinguish, but there are certain radiologic features that make one more likely. Both PAIS and PTE show enhancement on CTPA images. However, PAIS is more often unilateral and centrally located. The size of the filling defect in PAIS is greater than that in PTE, causing the pulmonary artery to increase in diameter.⁴ Heterogenous densities are characteristic of PAIS, and they represent hemorrhage, necrosis, and ossification within the filling defect, which we have seen in our patient.⁵ Other radiologic features that are more dominant in PAIS are the bulging contours, surface nodularity, single location, and lung ischemia.³

MRI may have a future role to play in the diagnosis of PAIS. However, to date, only a few PAIS patients have

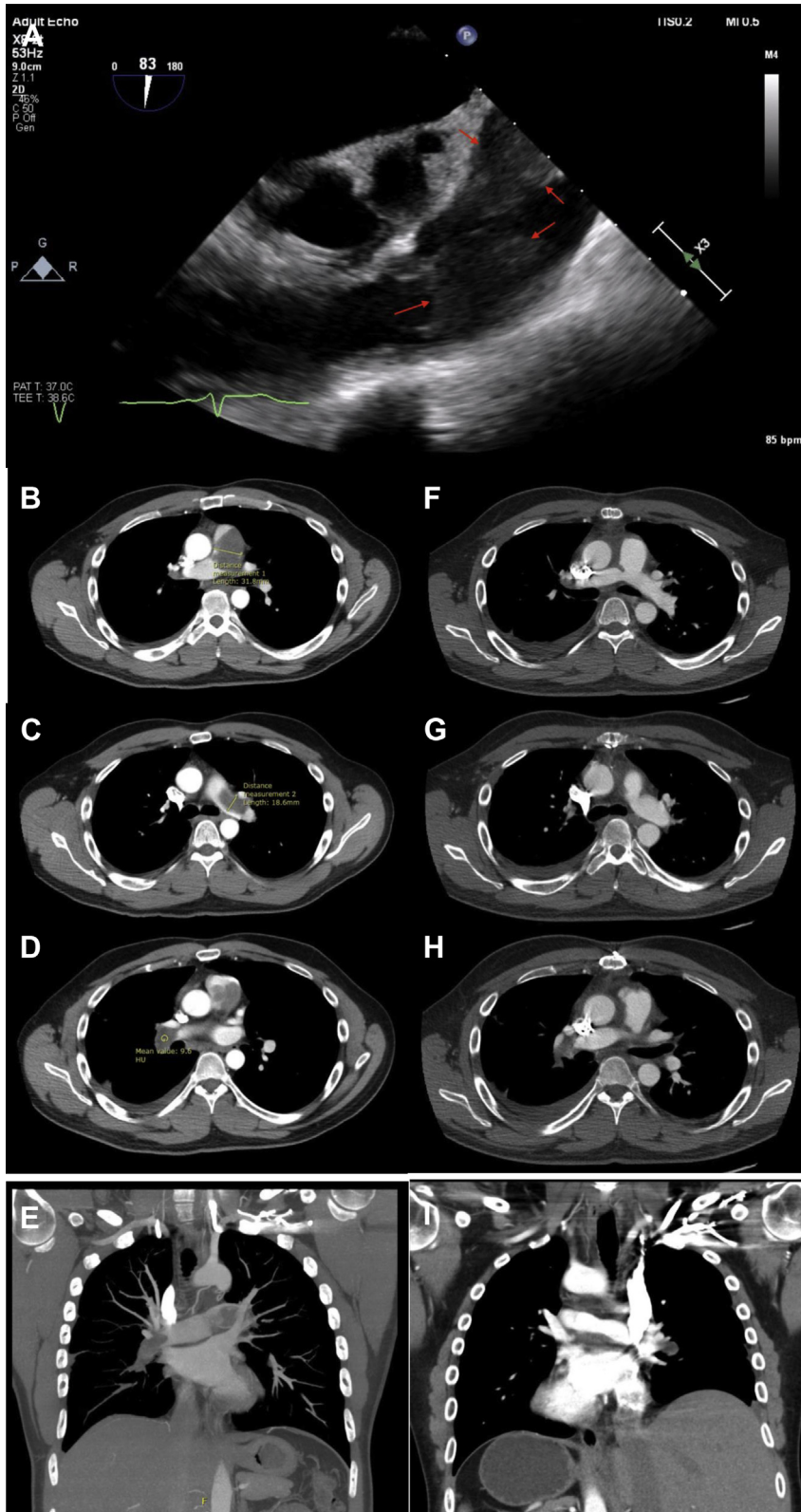


Figure 1. (A) Transesophageal echocardiogram image showing the large mobile mass of 20 × 21 mm in the main pulmonary artery above the pulmonic valve, and a second large fixed mass of 17 × 14 mm in the distal main pulmonary artery. (B-E) Series of images of computed tomography pulmonary angiography taken when the patient presented to the hospital for the first time without any treatment. (B) Large lobulated near-occlusive filling defect in the main pulmonary artery. (C) Filling defect extends into the left main pulmonary artery. (D, E) Another lobulated filling defect, within the right interlobular artery extending to the right lower lobe segmental pulmonary arteries scratch, which appears occlusive. (F-I) Equivalent section of images taken 5 weeks after surgery and before chemotherapy, showing clearing of filling defects.

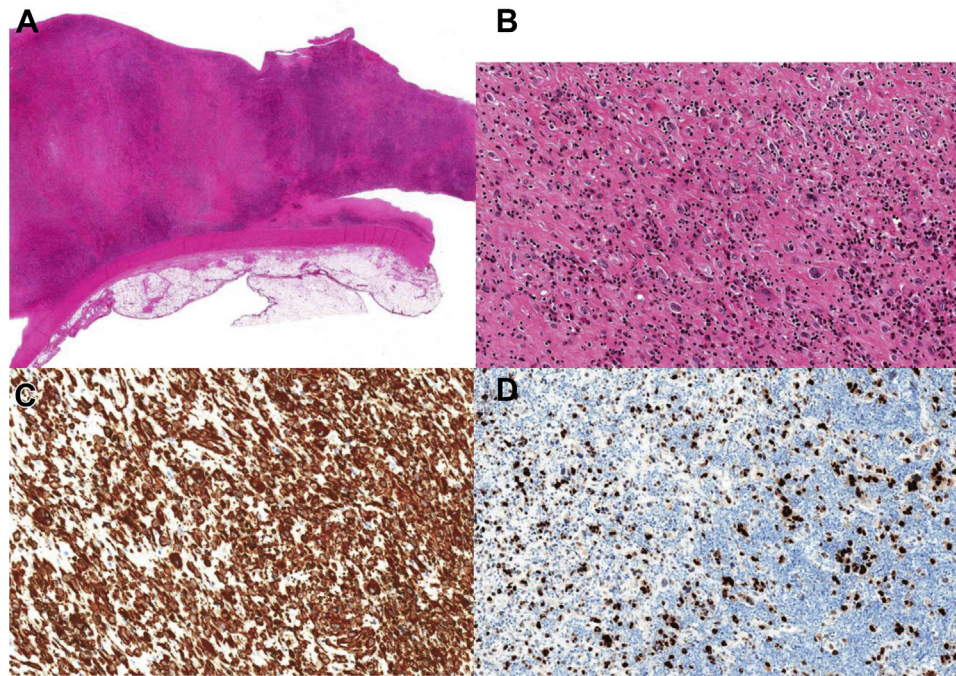


Figure 2. (A) Hematoxylin and eosin staining demonstrating neoplastic growth arising from intimal lining of sampled pulmonary artery ($\times 20$ magnification). (B) Hematoxylin and eosin staining demonstrating poorly differentiated neoplasm composed of epithelioid and pleomorphic cells with abundant background inflammation and no convincing vascular formation ($\times 100$ magnification). (C) Staining for vimentin demonstrated strong positivity ($\times 100$ magnification). (D) Staining for mouse double minute 2 demonstrated strong positivity with nuclear pattern ($\times 100$ magnification).

undergone MRI, and thus, not many associations have been made among radiologic MRI features with PAIS. Moreover, for those who have had an MRI, the radiologic findings are nonspecific. Magnetic resonance angiography, with or without contrast, is one technique used to image the pulmonary arteries. However, there are disadvantages, which include longer acquisition times, the potential need to image acutely ill or unstable patients, and a lack of experience and familiarity with MRI. Many centres lack the MRI technology needed to do more advanced T1-weighted imaging, T2-weighted imaging, fat-suppressed T2-weighted imaging, and transversal diffusion-weighted imaging, which have been studied by Liu et al. in a very small sample size, revealing some differences between PAIS and PTE.⁶

There are no specific guidelines for the management of patients with PAIS. Although some studies have shown effectiveness of chemotherapy in treating PAIS, its role remains unclear. In an observational study done by Bandyopadhyay et al., the group looked at 391 confirmed cases of PAIS in the literature over a 20-year period.⁷ From this group, 89 patients (23%) were noted to have distant metastases, and 34 (9%) were noted to have local recurrence. A multivariable analysis conducted in the study looking at odds of mortality using clinical characteristics revealed that distant metastasis was associated with a more than twofold increase in mortality during follow-up, with an odds ratio of 2.30, and local recurrence was also associated with a more than twofold increase in mortality, with an odds ratio of 2.37. Interestingly, although adjuvant chemotherapy improved survival in distant metastasis, it had no significant effect on local recurrence.

Conclusions

PAIS should be considered when the patients present with nonspecific clinical symptoms and several imaging manifestations suspicious for PTE. Radiology involvement at an early stage in identifying those radiologic features and clinical correlates offers the best way to obtain a diagnosis. Due to the high lethality of this disease, it is essential for clinicians and surgeons to be aware of this diagnosis and the features that differentiate it from PTE. A combination of surgery and adjuvant chemotherapy seems to provide benefits in relieving clinical symptoms and lengthening survival. However, clinical trials to better understand the role of chemotherapy and surgery are required to better inform treatment plans.

Funding Sources

The authors have no funding to declare.

Disclosures

The authors have no conflicts of interest to disclose.

References

1. Krüger I, Borowski A, Horst M, et al. Symptoms, diagnosis, and therapy of primary sarcomas of the pulmonary artery. *Thorac Cardiovasc Surg* 1990;38:91-5.
2. Simpson WL Jr, Mendelson DS. Pulmonary artery and aortic sarcomas: cross-sectional imaging. *J Thorac Imaging* 2000;15:290-4.
3. Kim C, Kim MY, Kang J-W, et al. Pulmonary artery intimal sarcoma versus pulmonary artery thromboembolism: CT and clinical findings. *Korean J Radiol* 2018;19:792-802.

4. Wittram C, Maher MM, Yoo AJ, et al. CT angiography of pulmonary embolism: diagnostic criteria and causes of misdiagnosis. *RadioGraphics* 2004;24:1219-38.
5. Parish JM, Rosenow EC 3rd, Swensen SJ, Crotty TB. Pulmonary artery sarcoma. Clinical features. *Chest* 1996;110:1480-8.
6. Liu M, Luo C, Wang Y, et al. Multiparametric MRI in differentiating pulmonary artery sarcoma and pulmonary thromboembolism: a preliminary experience. *Diagn Interv Radiol* 2017;23:15-21.
7. Bandyopadhyay D, Panchabhai TS, Bajaj NS, Patil PD, Bunte MC. Primary pulmonary artery sarcoma: a close associate of pulmonary embolism-20-year observational analysis. *J Thorac Dis* 2016;8:2592-601.

Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at <https://www.cjcopen.ca/> and at <https://doi.org/10.1016/j.cjco.2020.07.008>.