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Primary pulmonary artery sarcoma: A rare and overlooked differential diagnosis of pulmonary embolism. Clues to diagnosis

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ABSTRACT

INTRODUCTION: Primary pulmonary artery sarcoma (PPAS) is a very rare tumor that mimics pulmonary embolism (PE) in clinical presentation and on imaging studies, therefore leading to diagnostic delay and increased patient mortality.

PRESENTATION OF CASE: We discuss the case of 37-year-old man with a rapidly progressing PPAS, which was initially managed as PE. Imaging studies, particularly computed tomography and magnetic resonance imaging, were helpful in reaching the correct diagnosis. Because of the dismal prognosis of such cases, which improves by definite surgery, the patient underwent extensive surgical resection which got complicated by pulmonary reperfusion injury and intrapulmonary hemorrhage, and thus died.

DISCUSSION: Owing to the rarity of the tumor, PPAS is often initially mistakenly diagnosed as PE, leading to a diagnostic delay and increased mortality. Having a high index of suspicion in “atypical PE” cases and a knowledge of the characteristic radiological and clinical features of PPAS may expedite the diagnosis and improve survival. Pulmonary artery distension by the mass on imaging studies and compression of neighboring structures are in favor of a tumor rather than PE. Additionally, tissue characterization on magnetic resonance imaging is particularly useful in differentiating tumor from PE. PPAS has a very poor prognosis which improves by early definitive surgery. Perioperative and late mortality however, remain high.

CONCLUSIONS: Physicians should be alert of this tumor despite its rarity because diagnostic delay increases mortality. In this report, we summarize the features that differentiate PPAS from PE and the importance of imaging in diagnosing the tumor.

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1. Introduction

Primary pulmonary artery sarcoma (PPAS) is a very rare and aggressive malignant tumor. It mimics pulmonary embolism (PE), leading to diagnostic delay and increased mortality. Owing to its rarity, most of our current knowledge is derived from case reports and case series [1,2]. The clinical features, diagnosis, and manage-

ment of this tumor remain controversial [3]. Having a high index of suspicion in “atypical PE” cases may expedite the diagnosis. Knowledge of the characteristic clinical and radiological features of PPAS is paramount. The advances in imaging techniques may improve the rate of premortem detection and the rate of survival [4]. Described below is a report of a case of PPAS. Use of magnetic resonance imaging with tissue characterization was of help in the assessment of the nature of the mass. We reviewed the literature to identify if the clinical, laboratory, and radiological features may distinguish these two conditions. The case is reported in line with the SCARE criteria [5].

2. Case presentation

A 37-year-old man presented to the emergency department with four months' history of progressive dyspnea, cough, and weight loss of more than 20 kg. There was no history of fever

Abbreviations: LA, left atrium; LUPV, left upper pulmonary vein; MPA, main pulmonary artery; MRI, Magnetic resonance imaging; PE, pulmonary embolism; PPAS, Primary pulmonary artery sarcoma; RPA, right pulmonary artery; RUPV, right upper pulmonary vein; RVSP, right ventricular systolic pressure; STIR, short-tau inversion recovery imaging.

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or recent travel or surgery. He was a nonsmoker. Family history was negative for a similar illness. On examination, the patient was found to be tachycardic: 111 beats/minute. His blood pressure was 115/70 mm Hg. Chest examination was unremarkable. The second heart sound was loud. A faint ejection systolic murmur was heard over the base of the heart. Abdominal examination was normal and there was no pedal edema.

The electrocardiogram showed sinus tachycardia with the right ventricle strain pattern. Chest X-ray was unremarkable. The transthoracic echocardiogram detected a mass in the main pulmonary artery. The right ventricle was severely dilated with signs of pressure overload and positive “McConnell’s sign.” The right ventricular systolic pressure was 92 mm Hg (Fig. 1A–C). The D-dimer test was positive. Subcutaneous heparin was started for presumed PE. A contrast-enhanced computed tomography scan of the chest confirmed the echocardiographic findings and showed extension of the main pulmonary artery mass into the main branches (Fig. 1D), appearance suggestive of PE or tumor. A lung ventilation/perfusion scan revealed extensive ventilation-perfusion mismatch (Fig. 1E).

Magnetic resonance imaging was performed (Fig. 2A–D) for tissue characterization of the main pulmonary artery mass. The main bulk of the mass exhibited high signal intensity on T2-weighted short-tau inversion recovery imaging ([STIR], Fig. 2B). There was heterogeneous contrast uptake on first-pass perfusion with early enhancement, and significant late gadolinium enhancement (Fig. 2C). These features were consistent with tumor rather than thrombus. The tumor distended the main pulmonary artery and right pulmonary artery. Compression of the left atrium and right and left upper pulmonary veins by the mass was noted (Fig. 2D). The anatomical site, presence of vessel distension, and rapid progression of the mass on successive imaging were indicative of an aggressive PPAS. A transoesophageal echocardiogram was carried out to clarify the relation of the mass to the left atrium, and pulmonary veins. This showed compression of the left atrium and upper pulmonary veins with infiltration of the left atrial wall by the mass (Fig. 2E and F). No metastases were seen on abdominal computed tomography scan.

Considering that complete obstruction of the pulmonary arteries is eminent, the patient was referred for urgent surgery. Due to the emergency situation, endovascular catheter biopsy was not attempted. A surgical biopsy at the time of surgical resection/debulking was performed. Fresh frozen sections were reported as undifferentiated spindle cell sarcoma. The tumor was found to extend to the hilum of the left lung. Considering the aggressive nature of the tumor and reported improvement in survival with complete resection, a complete removal of the tumor was attempted. Reconstruction of the left atrium and pulmonary veins was performed. Unfortunately, the patient died due to pulmonary reperfusion injury and intrapulmonary hemorrhage.

3. Discussion

PPAS is a very rare malignant tumor. The exact incidence of PPAS is difficult to determine, because a significant number of patients who die of “PE” are not autopsied [4]. PPAS remains a subject of case report [6]; in a recent report from the Cleveland clinic, only 10 cases were identified over a 20-year period [1].

The tumor usually arises from the pulmonary trunk (85%). The right and left pulmonary arteries are involved in 71% and 65% of the patients respectively. Involvement of the pulmonic valve (32%), and right ventricular outflow tract (10%) is also seen. Intimal location of the tumor with intraluminal growth pattern is the most common morphologic subtype [4]. The commonest histopathological type is leiomyosarcoma (21%) whereas liposarcoma is the least common (1%). Spindle cell sarcoma is observed in 15% of the cases [1]. Tumors

Table 1

Summary of the clinical, laboratory, and radiological features that may distinguish PPAS from PE.

Clinical	Clinical features favoring diagnosis of PPAS over PE: <ul style="list-style-type: none"> • Gradual onset of symptoms (may not be of value in CPTe) • Cough and hemoptysis • Presence of systemic symptoms and asthenia • Lack of improvement with adequate anticoagulation • Absence of deep venous thrombosis
Laboratory investigations	<ul style="list-style-type: none"> • D-dimer is elevated in both PPAS and acute and chronic PE. • BNP is elevated in both PPAS and acute and chronic PE, but BNP levels are lower in PPAS. • CRP is higher in PPAS cases compared to CPTe. • ESR values appear similar in both PPAS and CPTe.
Radiological	<ul style="list-style-type: none"> • Echocardiography: Mobility of the mass, attachment to the pulmonary valve or PA wall, bulging rather than linear morphology, and absence of echolucent areas. TEE may additionally show planar invasion of the vessel wall. • CT: Involvement of the entirety of the MPA and one of its branches. Vascular distension, globular appearance of the lesion, and expansion beyond the vessel wall. Heterogenous and delayed contrast enhancement (not present in all cases) and distant metastases. • MRI: Hyperintensity on fat-suppressed T2-weighted imaging (lesion intensity is comparable in CPTe and PPAS). Beaded peripheral PA, eclipse sign, grape-like appearance in distal pulmonary artery the latter and cardiac invasion had 100% specificity for diagnosis of PPAS in one study. Contrast enhancement (although not present in all the cases). • FDG-PET: High metabolic activity (false-negative scans are reported).

with chondroid (chondrosarcoma) and osteoid (osteosarcoma) differentiation have also been reported [4].

PPAS mimics PE in clinical presentation and on imaging studies. This leads to initial misdiagnoses and treatment as PE in 47% and 39% of the cases, respectively. The confusion with PE delays the diagnosis and increases mortality. Doubling of the time from symptom onset to PPAS diagnosis increases the odds of death by 46% [1].

Knowing the distinguishing clinical and radiologic features is a prerequisite for accurate diagnosis (Table 1). PPAS has a roughly equal sex distribution and a mean age of 51.7 years at presentation. The commonest clinical manifestations are dyspnea (74%), chest pain (31%), cough (23%), and hemoptysis (15%). Weight loss occurs in 10% of the patients [1]. The duration of symptoms may help in distinguishing PE from PPAS as the latter is more insidious [1]. This feature, though, may not distinguish PPAS from chronic pulmonary thromboembolism. The presence of, fever, weight loss, and digital clubbing, however, make PPAS more likely [1,7]. Additionally, cough and hemoptysis are more common in PPAS than in acute and chronic PE [7,8]. It is important to remember that PPAS, like other malignancies can be associated with deep vein thrombosis [9]. The latter association further masks its clinical diagnosis [10].

D-dimer and B-type natriuretic peptide (BNP) can be elevated in both PPAS and acute and chronic PE [7,8]. The values are however lower in PPAS [8]. Elevation of coagulation markers in PPAS is thought to result from a thrombus or inflammation surrounding the tumor [11]. C-reactive protein levels are increased in PPAS more than chronic pulmonary thromboembolism cases. There is no significant difference in the erythrocyte sedimentation rate [7]. Normochromic, normocytic anemia has been reported in some cases [12].

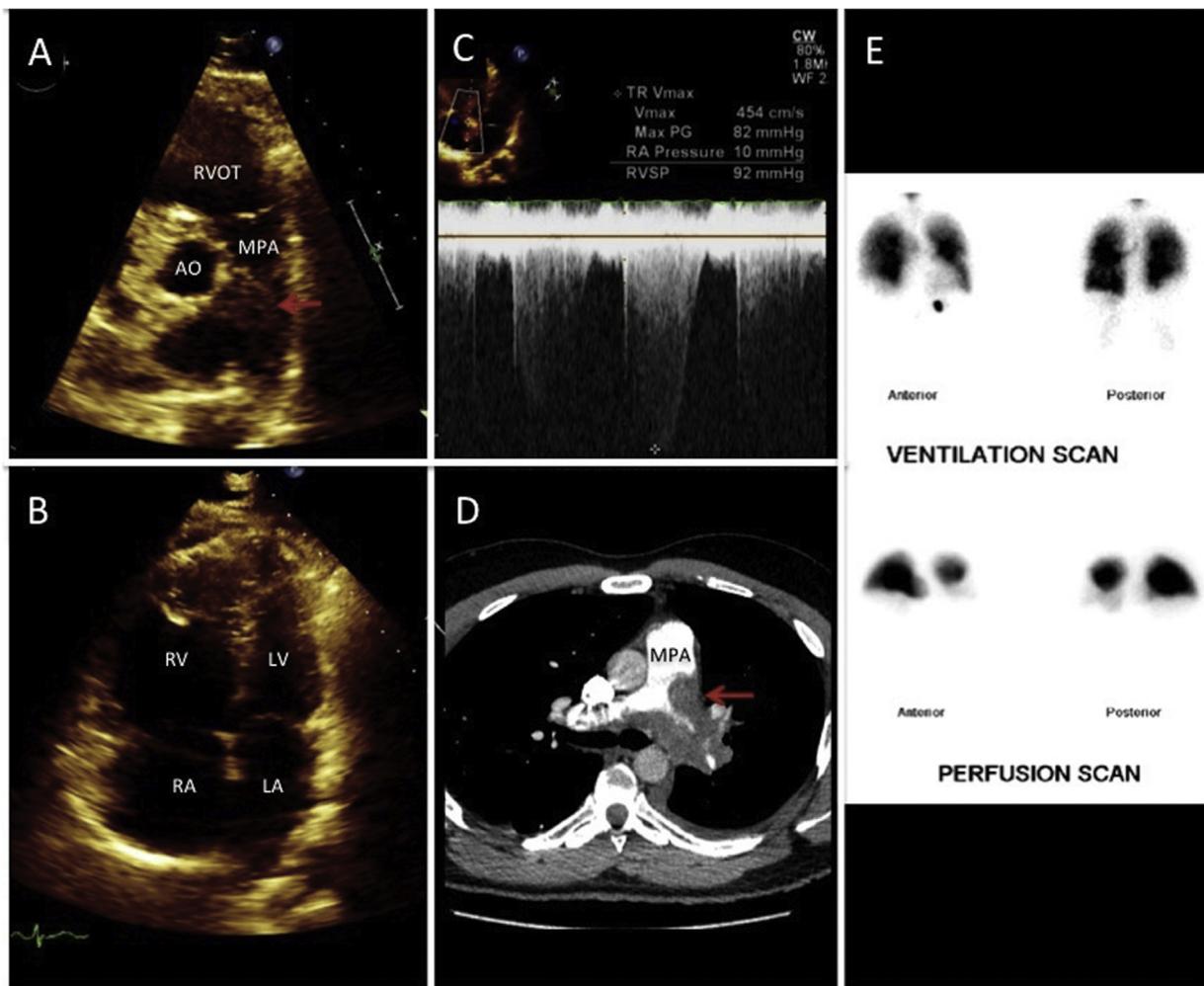


Fig. 1. TTE, CTA and perfusion scan findings. (A) Parasternal short-axis view showing a mass within the lumen of the MPA (red arrow). (B) Apical four-chamber view demonstrating severely dilated RV. (C) Continuous-wave doppler of the tricuspid valve; the RVSP is severely elevated. (D) CTA, axial section demonstrating a columnar filling defect extending from the bifurcation to the RPA (red arrow). (E) A ventilation/perfusion scan showing extensive ventilation/perfusion mismatch. Ao: Aorta, CTA: Computed tomography angiography. LA: left atrium, LV: left ventricle, MPA: main pulmonary artery, RA: right atrium, RPA: Right pulmonary artery, RV: right ventricle, RVOT: Right ventricular outflow tract, RVSP: Right ventricular systolic pressure, TTE: Transthoracic echo.

Multimodality cardiac imaging is paramount for diagnosis. On transthoracic echocardiography, mass mobility, attachment to the PA wall or pulmonic valve, absence of echolucent areas, and bulging rather than linear morphology, favors diagnosis of PPAS over PE [13]. Transesophageal echocardiography may show invasion of the vessel wall [1,12]. Clinical, laboratory, and radiological features of the PPAS are summarized in Table 1 [1,14–17]. About 5% of patients have a concurrent large thrombus burden surrounding the tumor [1].

The diagnosis of PPAS cannot be based on laboratory tests alone [10]. Definitive tissue diagnosis is important for exclusion of other diagnosis; and selection of appropriate chemotherapy regimen. Endovascular catheter biopsy (aspiration and forceps biopsy) is a safe and useful technique for confirming PPAS diagnosis and should be attempted when the tumor is suspected [18].

Management options of PPAS have included palliative pulmonary artery stenting, debulking, pneumonectomy, tumor endarterectomy and wide surgical resection [19]. Chemotherapy alone is associated with poor outcomes [19] and lack of treatment with chemotherapy increases the risk of death [1]. The combination of neoadjuvant chemotherapy with surgical resection is considered the therapy of choice for PPAS [16].

Pre-operative chemotherapy may shrink the tumor size, which facilitates its resection, and neutralize metastatic foci. It also aids in identifying chemo-responders. Patients experiencing disease progression despite chemotherapy have poor prognosis and are considered poor surgical candidates. Few patients however, receive pre-operative chemotherapy [19]. There are no standard chemotherapy guidelines currently available. Doxorubicin and ifosfamide are advocated as first choice for neoadjuvant chemotherapy [19]. Failure of doxorubicin-based chemotherapy is reported [20,21]. Platinum-vinorelbine regimens have shown efficacy of in two case reports [21].

Surgical treatment offers a chance for improved symptoms and long-term outcome [3]. Surgery is considered successful only when tumour resection is complete [12]. Comparison between endarterectomy and complete resection is difficult due to scarcity of cases [22]. Observational evidence however, indicates increased risk of local recurrence (up to 30%) after endarterectomy. A complete, full thickness resection is therefore preferred whenever possible [19,22]. As PPAS usually begins in the pulmonary root [3,22] and expands the pulmonary arteries without penetrating them, complete resection of the pulmonary trunk and main pulmonary arteries is advised [19,22]. This full thickness resection is believed to lead to more radical cancer resection and lower risk

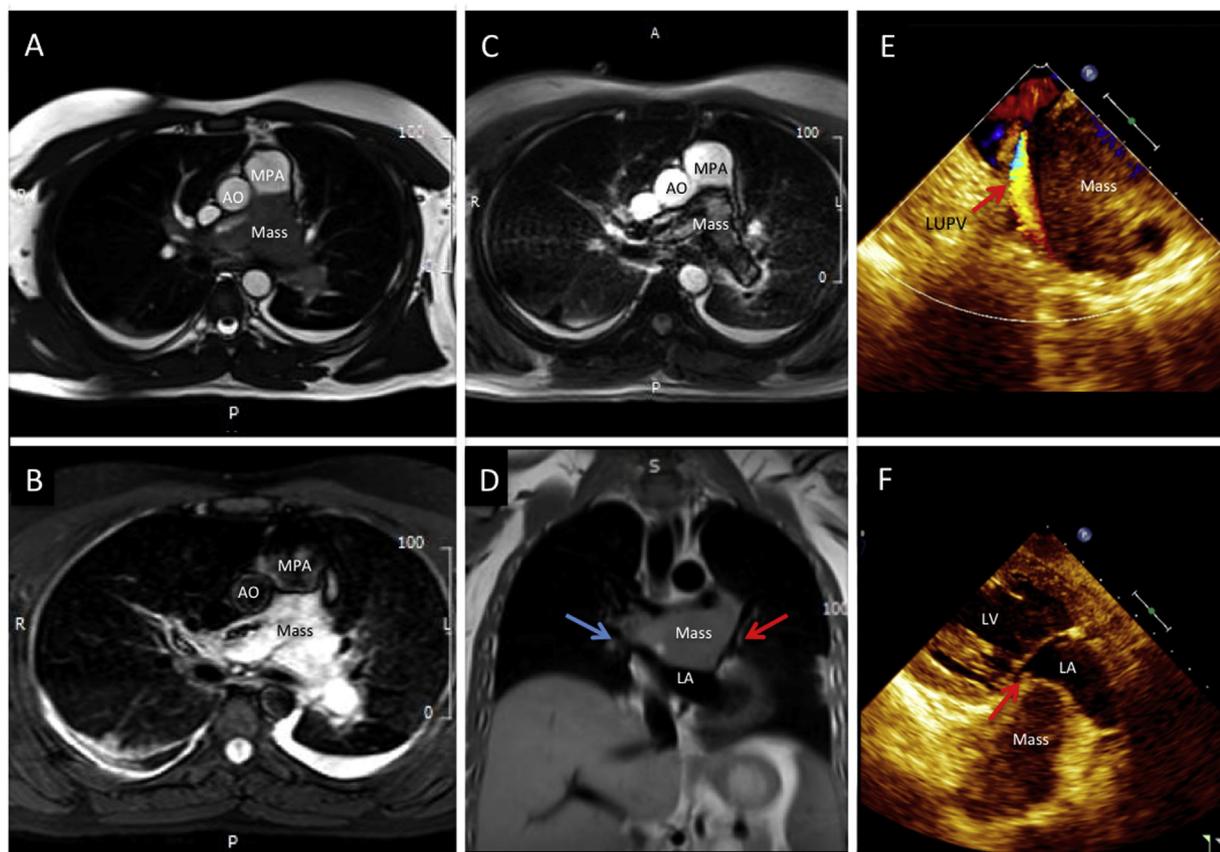


Fig. 2. MRI (axial [A–C], coronal [D]) and TEE (E and F) images. (A) Cine image showing a saddle-shaped filling defect occupying the lumen of the MPA and bifurcation. (B) The mass is hyperintense on short-tau inversion recovery imaging (STIR) image. (C) Significant late gadolinium enhancement of the mass. (D) MRI dark blood, coronal view showing an expanding mass within the MPA-RPA, compressing LUPV (red arrow) and RUPV (blue arrow). (E) Midesophageal view with color Doppler showing flow within the mass indicating vascularity; the LUPV is compressed. (F) Transgastric view showing LA compression by the mass with a small intra-atrial mass (red arrow) most likely representing tumor invasion. Ao: aorta, LA: left atrium, LV: left ventricle, LUPV: left upper pulmonary vein, MPA: main pulmonary artery, MRI: magnetic resonance imaging, RPA: right pulmonary artery, RUPV: right upper pulmonary vein.

of local recurrence [22]. Reconstruction is often performed with a Dacron graft. When the proximal pulmonary artery and pulmonic valve are involved, a pulmonary artery allograft offers an excellent alternative [19]. Tumour extension beyond the upper lobe branch however, will require either endarterectomy or pneumonectomy for removal [22]. Pneumonectomy likely offers the only option of complete resection [19].

PPAS has a very poor prognosis. Prognosis is significantly better in patients who undergo definitive surgeries compared to those who have partial resections [1,16]. Death from uncontrolled internal bleeding postoperatively is a known complication [3]. Late deaths are usually due to recurrence in distal pulmonary arteries, local recurrence, and metastasis [3].

Multimodality treatment (surgery, chemotherapy, or radiotherapy) is associated with better prognosis compared to single-modality therapy (median survival up to 28 months compared to 8.0 ± 1.7 months, respectively) [3,16]. In patients with right heart sarcomas, neoadjuvant chemotherapy led to a doubling of survival (20 versus 9.5 months) in one series [23]. However, although adjunctive chemotherapy improves survival and occurrence of distant metastasis in one analysis, it has no effect on local recurrence [1].

4. Conclusion

Consideration of PPAS in the differential diagnosis of PE, despite its rarity, is important to improve affected patients' survival. Once

PPAS is clinically suspected, expedited investigations with echocardiography, computed tomography or magnetic resonance imaging (and positron emission tomography) are recommended for early diagnosis/rule out. Multimodality imaging is usually necessary for mass characterization. Endovascular catheter biopsy provides definitive tissue diagnosis. Limited available evidence favours complete resection whenever possible. Neoadjuvant chemotherapy improves survival. Further data particularly in relation to optimal chemotherapy treatment are needed.

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Ethical approval

This manuscript does not refer to research involving patients, so it does not need ethical approval.

Consent

The patient is deceased. Written informed consent was obtained from the patient next of kin (brother) for publication of this case report.

Authors contribution

RA and MA identified the subject and selected the case report; MA conducted and wrote the literature review, RA wrote the case presentation. WA collected the patient data. KA and ZA provided clinical and surgical care of the patient. All Authors approved the final version of the manuscript.

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Declaration of Competing Interest

No conflict of interests.

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