Case Report

Intimal sarcoma of the pulmonary artery, a diagnostic enigma

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Abstract: Heart malignancies are rare and difficult to diagnose at early stage. Usually they are discovered when they present disease symptoms. CT of the thorax with contrast, MRI of the thorax, endobronchial ultrasound (EBUS) or echocardiography (transthoracic and/or transesophageal) and fluorodeoxyglucose positron emission tomography-CT (FDG-PET-CT) can be used to diagnose this entity. We present a rare heart sarcoma and our diagnostic algorithm.

Keywords: Sarcoma; heart; pulmonary artery

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Introduction

Patients with cardiac tumours present mostly non-specific symptoms which vary according to the location and the infiltration of the tumour. Besides the medical history, the diagnosis is usually based on an echocardiography, a computed tomography and a magnetic resonance imaging. According to autopsy studies, the frequency of cardiac tumours is 0.02%, 75% of which are benign and 25% are malignant. Myxomas are the most common benign tumours (50–70%) while angiosarcomas are the most common malignant neoplasms followed by rhabdomyosarcomas. Sarcomas can be further sub-classified into angiosarcomas, synovial sarcomas, intimal sarcomas, fibrosarcomas, osteosarcomas and pleomorphic sarcomas. The intimal sarcoma is a rare tumour in the area of the pulmonary artery (1). The rather distinctive characteristic of this tumour is its intraluminal growth with obstruction of the original vessel, 80% of the tumours are discovered in the area of the truncus pulmonalis while some of them also affect the pulmonary valve up to the right ventricular outflow tract. The survival time for this type of soft tissue sarcoma is very short; the median survival time without surgical resection is 1.5 months. Due to the rareness of this entity it is not completely clear whether to use surgical resection, chemotherapy or radiation therapy for treatment, or a combination thereof (2).

Case presentation

During the past months, the 61-year-old male patient had been suffering from exertional dyspnoea in response to mild exertion. He was also complaining about a chest pain during the past weeks and about a tickling cough irritation, which had declined in the meantime. There was no weight loss but the frequency of night sweats was increased. The patient worked as a craftsman exposed to glass wool and he had never smoked. The medical history included a left-sided testicular carcinoma orchiectomy, lymph node removal and adjuvant chemotherapy in 1980. Four months prior to his actual hospitalization, he had been given a diagnosis of pulmonary embolism (PE) via a chest CT. The

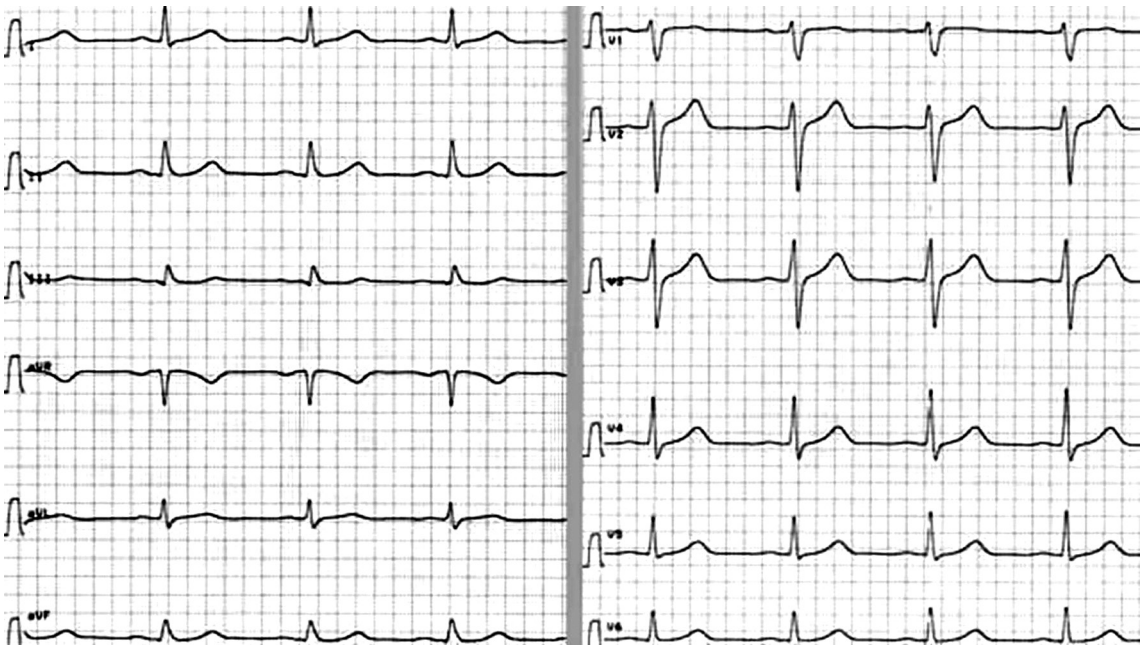

Figure 1 12-Channel ECG, normal sinus rhythm without signs of acute ischemia or signs of right ventricular strain.

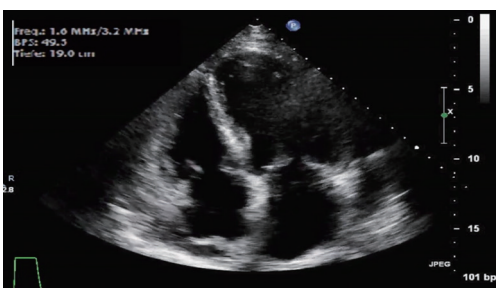

Figure 2 Apical 4-chamber view echocardiogram: normal values of the LV and the RV with normal systolic function of the LV and the RV without signs of right ventricular overload. Except for a mild mitral and pulmonary valve insufficiency there were no further hemodynamically relevant defects. Mild dilatation of the left atrium, indicating a grade I diastolic dysfunction. A small pericardial effusion was also detected. LV, left ventricle; RV, right ventricle.

cause of the PE was unclear at that time. Anticoagulation therapy with Rivaroxaban was needed for paroxysmal atrial fibrillation and a CHA2DS2-VASc Score of 2. It's worth mentioning that the patient had a short stay in Egypt in November 2015 and in South Africa in April 2016.The lab results, apart from a mild "eosinophilia", have not shown any pathological results (*Figures 1,2*).

CT pulmonary angiography (CTPA)

The contrast agent-enhanced chest CT scan showed a contrast defect in the main pulmonary artery with a delayed perfusion in the left lung without demonstrating any perfusion defects in the right lung. Compared with the previous findings of the chest CT, despite an effective oral anticoagulation, there was no decrease in the size of the described mass in the main branches of the pulmonary artery; as a result, the diagnosis of PE seemed unlikely (*Figure 3*).

Cardiac magnetic resonance imaging

Hypodense lesions in the main pulmonary artery were detected on T1w. No structures were found in the lobar segmental arteries. The contrast agent-enhanced filling defects, with consecutively reduced and delayed perfusion in the whole left lung, without perfusion disorders in the right lung, were indicative of an intravascular tumour rather than a recurring PE. Parasitic infestation was also included in the differential diagnosis. The occurrence of eosinophilia was tentatively taken into consideration, but after running extensive diagnostic tests for parasites no relevant findings were found (stool samples for Cryptosporidium parvum, Entamoeba histolytica, Entamoeba dispar and Giardia

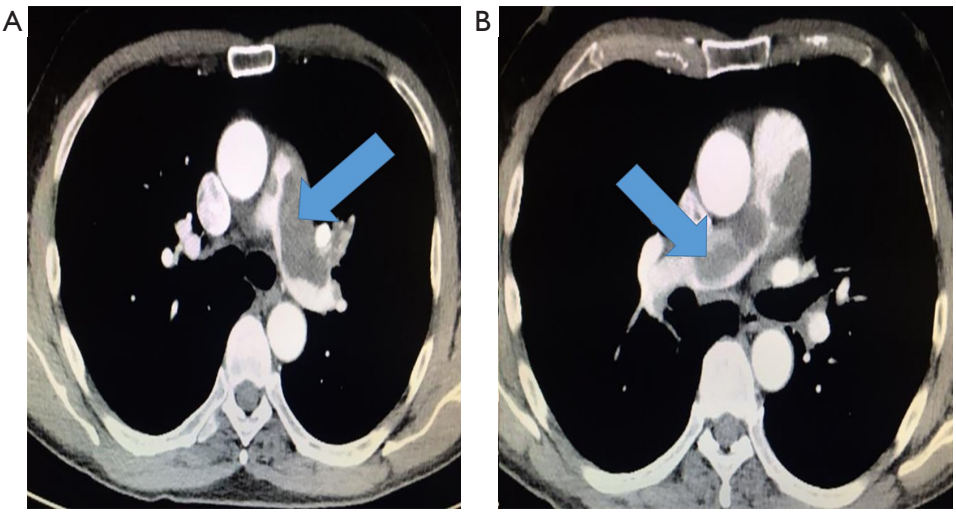

Figure 3 Contrast defect in the (A) left main branch and (B) right main branch of the pulmonary artery (arrow).

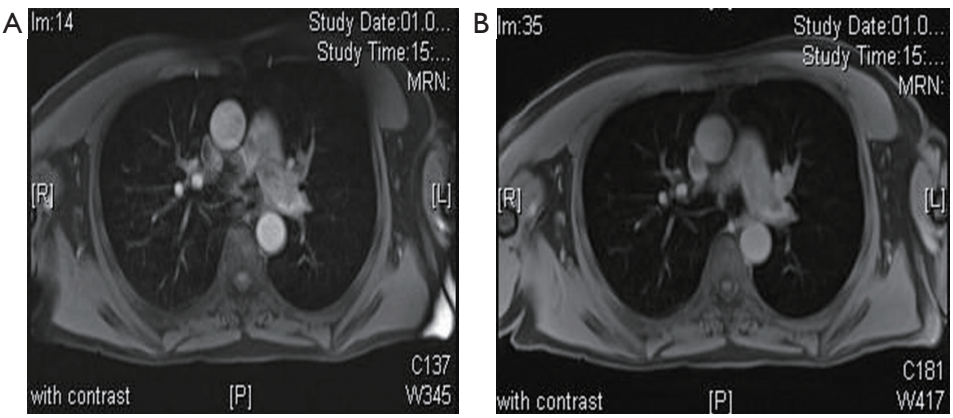

Figure 4 T1w hypodense lesion in the (A) left main branch and (B) right main branch of the pulmonary artery.

lamblia-antigen were negative). In order to exclude vasculitis, a detailed medical evaluation followed without relevant findings (*Figure 4*).

The patient was referred to the Heart Centre of the Heidelberg University Hospital for further diagnosis by means of a biopsy and a possible surgical resection. After discussing the case, a left catheterization and right heart catheterization with biopsy were performed. The results of the coronary angiography excluded hemodynamically relevant coronary heart disease. The final histopathological examination showed an intimal sarcoma of the pulmonary artery. There were no infiltrates of a germ cell tumour (testicular tumour in 1980 orchiectomy and adjuvant chemotherapy), a carcinoma, a lymphoma or an angiosarcoma. We discussed the case thoroughly; no thoracic surgical intervention was possible. Finally, the case was discussed in the Interdisciplinary Tumour Conference of the Heidelberg University Hospital and since a surgery was not possible, palliative radiation was recommended.

Discussion

Because of the clinically common non-specific symptoms and the small number of cases regarding the primary pulmonary artery sarcoma (PAS), in many cases the correct diagnosis is delayed, because this is most commonly confused with PE or chronic thromboembolic pulmonary hypertension (CTEPH) (3). As a result, the patients

are often advised to undergo surgical intervention only when the tumour is in an advanced stage, something that obviously has a negative effect on the outcome. The differential diagnosis between an intravascular tumour of the pulmonary artery and a thrombus is challenging but it can be assisted through the imaging of the thorax and the vessels via CT, positron emission tomography (PET)-CT and MRI. Biopsy (transbronchial needle aspiration biopsy) may be considered as the final diagnostic procedure in order to receive the precise diagnosis. The differentiation between thrombus and tumour of the pulmonary artery is not possible with the use of thorax-CT. PET-CT with fluorodeoxyglucose (FDG) should be used in order to differentiate between PAS and PE on the basis of the intensity of increased radiopharmaceutical uptake at the level of the tumor filling defects. It is important to mention at this point, that there are cases where a clear differential diagnosis of these two entities is not feasible because of equivocal results (2,4-6). Cardiac magnetic resonance can also be used in order to provide tissue characterization of the lesions and to help differentiation between the thrombotic and neoplastic components, relying on the degree of vascularity and tissue edema (5). Cardiac magnetic resonance uses specific sequences to differentiate tumors from thrombus, relying on the delayed retention of gadolinium within the extracellular matrix of tumors (5-7). In black-blood T1-weighted sequences after administration of a paramagnetic contrast agent, cardiac masses (e.g., PAS) showed significant contrast enhancement, whereas thrombi did not enhance (2). On the other hand, the lack of echocardiographic signs of a right ventricular dysfunction (e.g., dilatation, hypokinesia or pressure stress of the right ventricle, paradoxical septal motion, increased pulmonary artery pressure, abnormal tricuspid annular plane systolic excursion (TAPSE) and eccentricity index, congestion of the inferior vena cava and the hepatic veins with lack of inspiratory collapse) plus the absence of elevated markers of myocardial damage/strain (cardiac troponins and natriuretic peptides) do not support a PE. Despite all these, the above-mentioned signs may be present in the case of large-sized tumours of the pulmonary artery, causing obstruction of the right ventricular outflow tract. The absence of predisposing factors for PE (no venous thrombosis of the lower limbs on colour Doppler ultrasound, no finding suggestive of hypercoagulable state) and the progressive worsening of dyspnoea in patients with an intraluminal filling defect despite anticoagulation therapy, are factors suggestive of PAS. The lack of response to anticoagulation therapy correlated with the imaging findings may be decisive in the diagnosis. A correct early diagnosis of the PAS is of fundamental importance and the clinician is usually the first to raise a suspicion of PAS in patients with severe dyspnoea and filling defect in the pulmonary artery, unresponsive to anticoagulation therapy. The purpose of this paper is to provide recommendations for the differential diagnosis and treatment of this uncommon and underdiagnosed disease (*Table S1*). Regarding the differential diagnosis, apart from the diseases, we should also take into account possible respiratory motion artifacts or flow related artifacts (caused by inadequate mixing of contrast in the bloodstream) in CTPA. Due to the poor prognosis of the disease, particular awareness is needed to diagnose it at the earliest possible stage and the implementation of a standard protocol in order to establish the differential diagnosis with PE or CTEPH, with which this malignancy is most commonly confused.

Acknowledgments

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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Supplementary

Table S1 Differential diagnosis of filling defect in the pulmonary artery

Diseases	Diagnostic approach	Common CT angiography findings
Acute PE	❖ Clinical Symptoms suggestive of PE	❖ Filling defect in the center of the pulmonary artery lumen or its branches
	❖ Simple investigations such as chest radiograph, electrocardiogram, echocardiogram (signs of a right ventricular dysfunction e.g., dilatation, hypokinesia or pressure stress of the right ventricle, paradoxical septal motion, increased pulmonary artery pressure, abnormal TAPSE and eccentricity index, congestion of the inferior vena cava and the hepatic veins with lack of inspiratory collapse), markers of myocardial damage (e.g., not increased Trop T and BNP or NT-proBNP) and arterial blood gas—enhance the clinical probabilities	
	❖ V/Q scan and CTPA—the main screening tests used for patients with suspected PE. Recently CTPA has largely replaced V/Q scan, in many centres	
	❖ As both V/Q scan and CTPA have their limitations, other diagnostic modalities, such as D-dimer and CUS of the legs, are used as adjunctive diagnostic investigations	
	❖ Although it has been regarded as the gold standard test, pulmonary angiography has not been tested against a reference standard and thromboembolic events have been reported after a normal study	
CTEPH	❖ Clinical symptoms suggestive CTEPH—history of thromboembolic diseases	❖ Filling defect in the periphery of the pulmonary artery lumen or its branches can show calcification in the chronic thrombus
	❖ Echocardiography—first estimation of pulmonary arterial pressures	❖ May show pulmonary arterial bands/pulmonary arterial webs
	❖ V/Q scan—basic toll for CTEPH screening	❖ Signs related to pulmonary hypertension can be seen (such as pulmonary artery dilation and/or calcification, narrowing of the peripheral pulmonary arteries, and right ventricular hypertrophy/enlargement)
	❖ CT angiography	
	❖ MRI	
	❖ Pulmonary angiography/right heart catheterization—diagnostic confirmation; surgery option	
Vasculitis	❖ Clinical symptoms suggestive of systemic vasculitis	❖ Can mimic a filling defect but has a swirling appearance which can be helpful in differentiating it from a real defect
	❖ Assessing inflammation ◆ Blood count and differential—total WCC—leucocytosis consistent with infection and primary vasculitis—leucopaenia associated with CTD's ◆ Eosinophils—elevated in CSS, drug reaction ◆ Acute phase response ESR/CRP ◆ Liver function—often nonspecific—may also suggest viral infection ◆ Urine analysis—proteinuria—haematuria—casts ◆ Renal function—creatinine clearance—24 h protein excretion—biopsy	
	❖ Assessment of organ involvement ◆ Chest radiograph ◆ Liver function ◆ Nervous system—NCS ◆ Cardiac function—ECG—echo ◆ Gut—angiography	
	❖ Immunological tests ◆ Anti-neutrophil cytoplasmic antibodies—proteinase 3—myeloperoxidase ◆ Other autoantibodies—rheumatoid factor—ANA nuclear antibodies—antibodies to extractable nuclear antigens—anti-dsDNA—anticardiolipin	
Parasitosis	❖ Clinical symptoms suggestive of parasitosis	❖ Can mimic a filling defect on thicker cuts
	❖ Stool samples for Cryptosporidium parvum, Entamoeba histolytica, Entamoeba dispar and Giardia lamblia-antigen	
Systemic to pulmonary artery shunt	❖ Clinical symptoms suggestive of systemic to pulmonary artery shunt	❖ Filling defect in the pulmonary artery with extension of the defect to the more proximal portion of the pulmonary artery
	❖ CT scan enable demonstration of these shunts and confirming the diagnosis	
	❖ Conventional angiography has been used for definitive diagnosis but it is relatively expensive, invasive and time-consuming. It is also associated with higher incidence of complications such as access site hematoma or embolic events	
Tumors of the pulmonary artery	❖ Clinical symptoms suggestive of tumor of the pulmonary artery	❖ Large tumor emboli in the main, lobar, and segmental pulmonary arteries cause filling defects that mimic acute pulmonary thromboembolism
	❖ Simple investigations such as chest radiograph, ESR, electrocardiogram, echocardiogram enhance the clinical probabilities	❖ Small tumor emboli that affect subsegmental arteries produce multifocal dilatation or beading of vessels. Reconstruction in coronal and sagittal formats will be useful in showing the tumoral nature of the filling defect
	❖ Transesophageal echocardiography can show mass in the lumen of the pulmonary artery	❖ The filling defect may show enhancement. In the case of primary pulmonary artery sarcoma, the border of the tumor may be irregular. There may be also extension of the tumor beyond the vascular margin. May show enhancement
	❖ CT angiography	
	❖ Gadolinium-enhanced magnetic resonance imaging is a sensitive technique for the differentiation of tumors and thrombi	
	❖ PET-CT scan shows increased metabolic activity. The 18-FDG positron emission tomography is used to differentiate tumors from thromboembolism. Even in a small intake, malignancy should be suspected	
	❖ Pulmonary angiography/right heart catheterization/Biopsy—diagnostic confirmation; surgery option	

PE, pulmonary embolism; TAPSE, tricuspid annular plane systolic excursion; BNP, brain natriuretic peptide; NT-proBNP, N-terminal pro-brain natriuretic peptide; V/Q, perfusion/ventilation; CTPA, CT pulmonary angiography; CUS, compression ultrasound; CTEPH, chronic thromboembolic pulmonary hypertension; WCC, white cell count; CTD, connective tissue disease; CSS, Churg–Strauss syndrome; ESR, erythrocyte sedimentation rate; CRP, c-reactive protein; NCS, nerve conduction studies; ANA, antinuclear antibodies; PET, positron emission tomography; FDG, fluorodeoxyglucose.