Primary pulmonary artery sarcoma differentiated from pulmonary thromboembolism by ventilation-perfusion scan. Long survival of the patient

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Abstract
Primary pulmonary artery sarcoma (PAS) is a rare and highly lethal tumor. Here, we report a case of a 53 years old female with PAS who was initially diagnosed with chronic pulmonary thromboembolism (PTE) based on the results of a transthoracic Doppler echocardiogram, a contrast-enhanced computed tomography angiography, and a ventilation/perfusion lung scan. **Conclusion**: We emphasize the difficulties in diagnosing PAS, the need to investigate this neoplasm in the differential diagnosis of PTE, the diagnostic value of different imaging techniques in the identification of the tumor, and the efficacy of adjuvant chemotherapy in prolonging survival.

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Introduction

Primary pulmonary artery sarcoma (PAS) is rare, with an estimated incidence of between 0.001% to 0.03% in the general population and is also highly lethal tumor. Its signs and symptoms are nonspecific and patients are often misdiagnosed with chronic pulmonary thromboembolism (PTE). This misdiagnosis leads to ineffective management of PAS, as patients are treated with thrombolytics or prolonged anticoagulation. Early diagnosis and radical surgical resection offer the only chance for improved survival in patients with PAS and adjuvant chemoradiotherapy is also worth undertaking in an effort to improve prognosis.

Case report

A 53 years old previously healthy woman presented with exercise-induced chest distress and dyspnea that had been progressively worsening over a period of four months. Physical examination revealed a systolic murmur (grade III/IV) at the pulmonic valve area. Laboratory results showed a normal D-dimer and an elevated N-terminal pro b-type natriuretic peptide (3053pg/mL, normal range 0-100pg/mL). A transthoracic Doppler echocardiogram showed extensive thrombosis in the pulmonary artery trunk. Pulmonary artery systolic pressure (PASP) was 70mmHg. Computed tomography pulmonary angiography (CTPA) demonstrated a large, contiguous filling defect in the main pulmonary artery that extended into the distal bilateral branches (Figure 1). A ventilation/perfusion lung scan (V/Q scan) revealed multiple segmental perfusion deficits with normal ventilation (Figure 2). In view of these findings, a pulmonary embolus was suspected, and the patient was started on oral warfarin for one week. However, this anticoagulation therapy resulted in no improvement. Thus, a surgical intervention was carried out to resect the suspected embolism.

Upon incision into the pulmonary artery, the patient was found to have a whitish-gray, myxoid mass with a maximum diameter of 4.0cm in the lumen of the main pulmonary artery, extended into the artery and its segmental branches. Hematoxylin and eosin staining of a section of the mass demonstrated tumoral necrosis and abundant malignant spindle cells with low to moderate cellularity and frequent mitoses (Figure 3A). Immunohistochemical analysis revealed that the mass was positive for vimentin (Figure

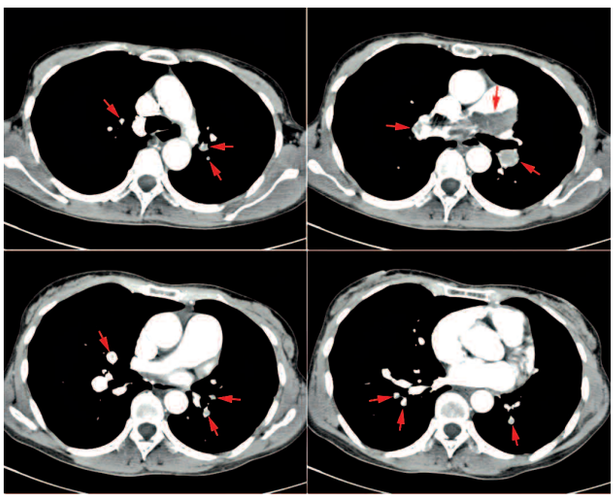

Figure 1. CTPA images show extensive involvement of the main pulmonary artery and the bilateral branches (arrow).

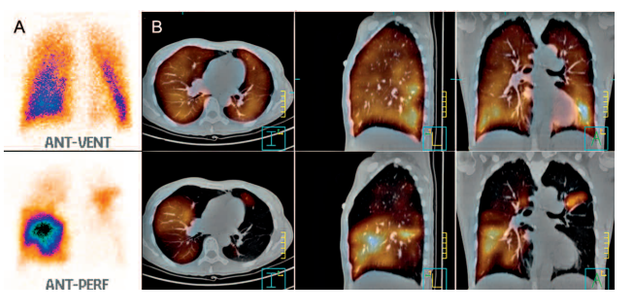

Figure 2. Radionuclide lung ventilation/perfusion scintigraphy shows a wide range of bilateral pulmonary emboli. A: Planar images, anterior position. B: Transaxial, sagittal and coronal views of integrated SPET/CT images (upper row: ventilation; lower row: perfusion).

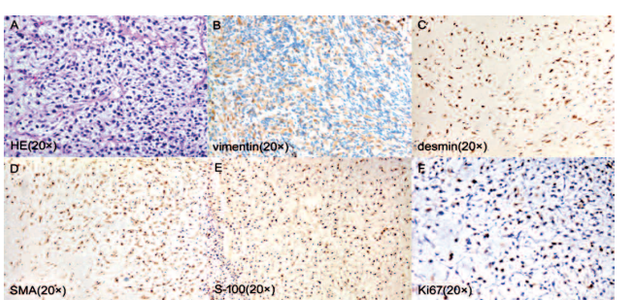

Figure 3. Histopathological findings. A: The resected neoplastic mass was comprised of spindle cells with hyperchromatic nuclei in a myxoid background (hematoxylin and eosin, 20×). B: Vimentin-positive stain (20×). C: Desmin-positive stain (20×). D: SMA-positive stain (20×). E: S-100 protein-positive stain (20×). F: The Ki67 index was approximately 10% (20×).

3B), desmin (Figure 3C), smooth muscle actin (SMA) (Figure 3D), and S-100 protein (Figure 3E). The section was negative for all other markers (pan-CK, CD34, CD31, F8, HMB45, CD1a, CD117, and DOG1). Additionally, the Ki67 index was approximately 10% (Figure 3F). The histopathologic features and immunohistochemical staining pattern were consistent with pulmonary artery intimal sarcoma.

During the postoperative period, the patient received traditional Chinese herbal medicine therapy, but no adjuvant chemoradiotherapy. At a follow-up, 13 months post-resection, the patient demonstrated progressive dyspnea upon effort. Thus, another CTPA was performed, which indicated local recurrence of sarcoma with lung metastases (Figure 4). The patient was then treated with six cycles of a doublet chemotherapy consisted of etoposide (VP-16, 100mg/m^2/day) on days 1-3 and cisplatin (DDP, 75mg/m^2/day) on day 1. The tumors responded favorably to chemotherapy and showed signs of regression. Three years after the initial diagnosis, the patient was still alive.

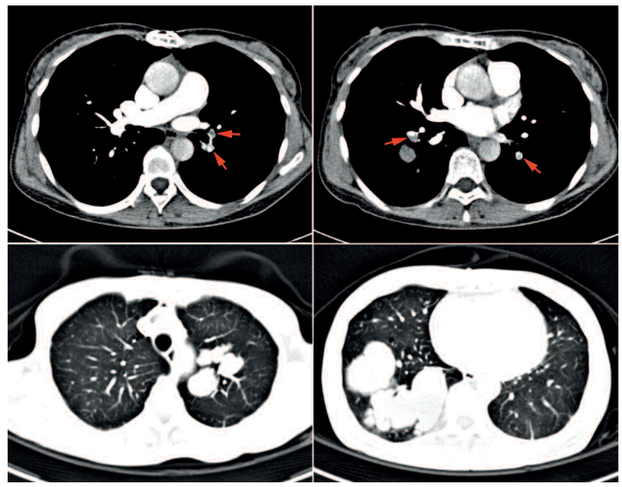

Figure 4. CTPA showing recurrent PAS in the branches of the bilateral lower pulmonary artery (arrow) and metastases in the left upper and bilateral lower lobes, 13 months after surgery.

Discussion

Pulmonary artery sarcoma was first described by Mandelstamm in 1923 [1]. The presenting symptoms of this tumor are usually nonspecific and can vary depending on tumor histology, size, and location. Patients may present with dyspnea, cough, chest pain, malaise, and/or hemoptysis. As such, PAS can be frequently misdiagnosed as pulmonary thromboembolism [2].

An early diagnosis of PAS is essential for any hope of survival. However, early diagnosis of PAS is very difficult, since there is no specific diagnostic test including imaging modalities for this disease. Chest radiography may reveal pulmonary nodules, pulmonary artery dilation, reduced pulmonary vasculature, cardiomegaly, and/or pleural effusions [3, 4]. Doppler echocardiography is used for noninvasive investigation of pulmonary hypertension and in cases of PAS may show a dilated right ventricle with obstruction in the ventricular outflow tract or the pulmonary arterial trunk [3, 5]. Pulmonary angiography reveals defects in repletion of the pulmonary artery lumen [3, 6], while contrast-enhanced computed tomography can detect a low-attenuation filling defect that occupies the entire luminal diameter of the proximal or main pulmonary artery, the expansion of the involved arteries, and ex-

traluminal tumor extension. These CT findings are nonspecific as they can also be demonstrated in cases of extensive pulmonary thromboembolism [4, 7]. The ventilation-perfusion scan is not helpful in distinguishing PAS from thromboembolic disease as in this case [1, 8]. Gadolinium-enhanced magnetic resonance is helpful in distinguishing a soft tissue mass from a thrombus by enhancement of the lesion [3, 9]. Fluorine-18 fluorodeoxyglucose (^{18}F-FDG) positron emission tomography scans are very effective in differentiating between these two diseases, as blood thrombi do not take up ^{18}F-FDG, whereas a malignant tumor, such as PAS, does [10, 11].

Although imaging can suggest PAS, definitive diagnosis of PAS is established histopathologically. According to the WHO, there are three types of large blood vessel sarcomas: angiosarcoma, leiomyosarcoma, and intimal sarcoma [9, 12]. They usually extend throughout the lumen as polypoid masses. Less frequently, they grow proximally and affect the pulmonary valve and the right ventricle. Lung metastases occur in 50% and to distant organs in 16%, including kidneys, lymph nodes, brain, and skin, often detected at the time of diagnosis [4]. Death usually results from obstruction of the pulmonary blood flow.

The prognosis of PAS is poor, as the mean survival time without surgery is 1.5 months. Surgical intervention can prolong the survival time to 10 months, regardless of the histological findings. Some medical centers have reported excellent outcomes after treatment. Nakahira's group (2007) reported a patient being well with no evidence or recurrence, 56 months after surgery. Mussot's group (2013) reported that 1, 3 and 5 years survival was 63%, 29% and 22% respectively. Mayer's group (2007) reported that three patients were alive with no evidence of disease 156 months after diagnosis [15-17]. Early diagnosis and radical surgical resection offer the only chance for improved survival. Since PAS has a tendency to cause microembolization in the distal portions of the pulmonary artery, resulting in poor survival outcomes even after radical resection of the tumors, adjuvant chemotherapy and radiation treatment have been recommended for some patients with PAS [18]. However, there are no guidelines for its treatment. We emphasize the relatively long survival of our patient who was alive for at least three years till the time of submitting this paper.

The authors declare that they have no conflicts of interest.

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