Chronic thromboembolic pulmonary hypertension following pulmonary embolism with a right ventricular thrombus: A report of two cases

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Abstract
Right heart thrombus accompanied by chronic thromboembolic pulmonary hypertension is a rare entity. Right heart thrombus may develop in the peripheral veins or in situ within the right heart chambers. The diagnosis of right heart thrombus is challenging, since its symptoms are typically non-specific and its imaging features resemble those of cardiac masses. Here, we report two cases of right heart thrombus with chronic thromboembolic pulmonary hypertension that presented as right ventricular masses initially. Both patients underwent simultaneous pulmonary endarterectomy and resection of the ventricular thrombi. Thus, when mass-like features are confirmed by imaging, right heart thrombus should be suspected in patients with chronic thromboembolic pulmonary hypertension, and simultaneous right heart thrombus resection is required along with pulmonary endarterectomy.

Keywords
intracardiac thrombus, pulmonary endarterectomy, chronic thromboembolic pulmonary hypertension

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Case description

Case 1
A 41-year-old man presented with an eight-month history of exercise intolerance and fatigue. The patient’s hemodynamic variables were stable, and laboratory tests indicated that he had no abnormalities, except for slightly elevated concentrations of N-terminal pro-brain natriuretic peptide (NT-proBNP) and cardiac troponin (993 ng/L and 15.2 ng/L, respectively). Transthoracic echocardiography (TTE) revealed two non-homogeneous and irregular masses, which were 38 x 23 mm and 10 x 9 mm in size, located at the tricuspid valve chordae (Fig. 1a). Massive tricuspid valve regurgitation was observed, and the right heart was mildly dilated (right ventricular diameter, 37 mm). However, the tricuspid annular plane systolic excursion and inferior vena cava diameter were normal. A pulmonary ventilation perfusion scan revealed perfusion defects. Although the patient had no recorded medical history of pulmonary embolism (PE) or lower-limb deep vein thrombosis, his long history of symptoms and elevated tricuspid valve gradient pressure (110 mmHg) strongly indicated the presence of a right ventricular mass with chronic thromboembolic pulmonary hypertension (CTEPH). After a standard management with three months of anticoagulation treatment, the symptoms persisted. Pulmonary computed tomography angiography (CTA) indicated multiple filling defects in both the right and left pulmonary arteries (Fig. 1b). Considering the mobility of the mass and the CTEPH diagnosis, pulmonary endarterectomy (PEA), right ventricular masses resection, and tricuspid valve repair were performed simultaneously. Fig. 1c shows the thickened intima and fresh thrombi that were resected during surgery. The mean pulmonary artery pressure (mPAP) immediately after surgery decreased from 61 mm Hg to 27 mm Hg, and the patient had an uneventful recovery. Subsequent histopathological analysis confirmed the presence of an organized right heart thrombus (RHT).

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Case 2

A 24-year-old man was presented to the clinic with exertional fatigue and decreased exercise tolerance. He had experienced cough and hemoptysis two months earlier. He did not have a medical history of PE or deep vein thrombosis. Electrocardiography revealed right axis deviation and T-wave inversion in V1–V5 (Fig. 1d). TTE demonstrated a right ventricular mass (39 × 21 mm) attached to the apex with little mobility, while right ventricular and tricuspid valve function were normal (Fig. 1e). Cardiac neoplasm was considered; but laboratory tests showed elevated D-dimer, NT-proBNP, and factor VIII levels (1.43 mg/l FEU and 1825 ng/L, 165%, respectively). The results of protein S, antineutrophil cytoplasm antibodies, and tumor markers were unremarkable. Pulmonary CTA demonstrated a right ventricular filling defect and PE, pulmonary artery luminal stenosis was indicated (Fig. 1f–g). As the origin of the mass was unknown, whole-exome sequencing was performed, and revealed a mutation in the gene encoding factor V, which was indicative of factor V Leiden. Right heart catheterization (RHC) indicated an mPAP of 43 mm Hg. At this point, PE with a right ventricular mass accompanied with thrombophilia was highly suspected. The patient received oral anticoagulation therapy for two months. However, since the symptoms had developed over time and the origin of the ventricular mass was uncertain, we surgically resected the mass. PEA was performed simultaneously according to the intraoperative findings. Fig. 1h shows the thickened pulmonary artery intima and ventricular mass excised during surgery. mPAP was reduced to 20 mmHg after surgery, and histopathological analysis confirmed that the mass was a thrombus. The patient had a smooth recovery and consented to lifelong anticoagulation treatment. No recurrent thrombosis was observed during postoperative follow-up.

Discussion

In this report, we describe the cases of two patients who were both admitted with right ventricular masses and diagnosed with RHT. There are two major types of RHT.1 Type A is serpiginous and highly mobile, mostly originates in the peripheral veins, while type B is believed to develop in situ. Type B is immobile and could be related to underlying cardiac abnormalities.2 In Case 1, the morphological features of the mass resembled type A RHT.1 Based on the findings in this case, we hypothesized that peripheral venous clots lead to PE that subsequently develops into CTEPH. Some of these clots got lodged in the tricuspid valve chordae, where they formed a mass-like lesion. The patient received oral anticoagulation therapy for two months. However, since the symptoms had developed over time and the origin of the ventricular mass was uncertain, we surgically resected the mass. PEA was performed simultaneously according to the intraoperative findings. Fig. 1h shows the thickened pulmonary artery intima and ventricular mass excised during surgery. mPAP was reduced to 20 mmHg after surgery, and histopathological analysis confirmed that the mass was a thrombus. The patient had a smooth recovery and consented to lifelong anticoagulation treatment. No recurrent thrombosis was observed during postoperative follow-up.
Although the RHT in Case 2 was eventually classified as type B, the features were hard to diagnose initially. According to the 2019 guidelines for the management of acute PE,3 patients with intermediate-risk PE require at least three months of anticoagulation therapy. However, the treatment strategy was altered in this patient due to the presence of a right ventricular mass and an uncertain diagnosis. Surgery was performed early with the aim of exploration and intracardiac mass excision. Underlying CTEPH was suspected based on the luminal stenosis indicated by CTA and thickened pulmonary artery intima, so PEA was performed simultaneously.

Studies reported a lower incidence of CTEPH and female predominance in Japanese population compared with Caucasian population.4 In China, however, the prevalence of CTEPH among PE patients is about 5%, both sexes are equally affected. The CTEPH epidemiology in Chinese Han population is similar to that of the Caucasian population. In our center, among 32 PEA procedures during recent years, there were 20 male patients (62.50%), which shows a slightly male predominance.

The prevalence of factor V Leiden in the Chinese Han population is extremely rare, the allelic frequency is 0.10% vs. 5.27% in Caucasian Americans.5,6 Despite the similarity of CTEPH epidemiology between the Chinese and western Caucasian populations, it indicates that factor V Leiden is not associated with CTEPH in the Chinese population. In this report, both patients have blood type B, and in Case 2, the plasma level of factor VIII were slightly elevated. Non-O blood group and factor VIII elevation are risk factors for CTEPH, which would help the diagnosis. However, history of venous thromboembolism is absent in these two patients, which made it difficult to diagnose initially.

The optimal strategy for the management of RHT remains unclear. A recent study demonstrated that surgical intervention is not superior to thrombolysis in RHT patients.7 However, RHT patients diagnosed with operable CTEPH require PEA, and simultaneous surgical resection of the RHT should be performed. Both patients in this report did not demonstrate recurrent thrombosis after surgery, and the symptoms improved.

For the diagnosis of pulmonary hypertension, RHC is required. At present, RHC is considered a low-risk procedure, as the reported morbidity and mortality rates at expert centers are 1.1% and 0.055%, respectively.8 However, RHC may have potential risks in patients with RHT, as the catheter tip may cause dislodgement of the RHT and embolize the pulmonary artery. There are no reports on the prevalence of PE as a complication of RHC in RHT patients. Despite this, AbuHalimeh et al.9 suggested that a thorough evaluation including echocardiography and magnetic resonance imaging is required before the RHC procedure is conducted in RHT patients. In the cases reported here, RHC was not performed until multiple clinical features indicated that the probability of pulmonary hypertension was high, and no complications occurred during RHC. In such cases, RHC is necessary for the diagnosis of CTEPH, and for determining the surgical strategy, based on our experience, we recommend that RHC to be performed when the benefit outweighs the risk in RHT patients with suspected CTEPH.

Conclusion
We have reported two cases of RHT accompanied with CTEPH and PE. PEA was performed in both cases due to CTEPH, simultaneous resection of the RHT was also performed. The diagnosis of such patients can be challenging, and RHT should be suspected in any patient who presents with a right heart mass. Additionally, these cases illustrate the difficulty in diagnosing different types of ventricular thrombi and highlight that RHT is an important accompanying diagnosis in CTEPH patients that may necessitate a modified surgical strategy.

Conflict of interest
The author(s) declare that there is no conflict of interest.

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Consent for publication
Written and informed consent was taken from the patient for publication of this case report and the associated images.

Ethics approval
This case report study was carried out respecting the Declaration of Helsinki in its current version. Ethics approval is not applicable.

Contributorship
Zhong Wu: conceptualization, methodology, supervision. Tailong Zhang: writing- original draft preparation, writing-review and editing. Weitao Liang: revision, resources, project administration. Longrong Bian: investigation, data curation.

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