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IMAGING

CASE REPORT: CLINICAL CASE

Chronic Thromboembolic Pulmonary Artery Hypertension or Fibrosing Mediastinitis?

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ABSTRACT

We report a case of pulmonary hypertension in association with right heart thrombus and mediastinal lymphadenopathy leading to the diagnostic dilemma of chronic thromboembolic pulmonary hypertension vs fibrosing mediastinitis despite of extensive noninvasive workup, considering different treatment strategies and therapeutic implications. Surgical findings provided a conclusive diagnosis and excellent prognosis. (JACC Case Rep. 2024;29:102569)

HISTORY OF PRESENTATION

A 6-year-old girl presented with jaundice associated with progressively worsening abdominal distension and exertional dyspnea over the preceding 2 months. At presentation, she had World Health Organization class III exertional dyspnea. She had no episode of paroxysmal nocturnal dyspnea or orthopnea. The past history was not contributory.

TAKE-HOME MESSAGES

- To be able to approach a case of pediatric pulmonary hypertension.
- To identify features of CTEPH and differentiate from mimickers like fibrosing mediastinitis.

On examination, she was sick looking, had decompensated heart failure with tachycardia, tachypnea, raised jugular venous pulse, pedal edema, abdominal distension, and hepatomegaly. Her cardiovascular examination revealed a normal first heart sound, loud pulmonary component of the second heart sound, and grade III/VI ejection systolic murmur at left parasternal area.

PAST MEDICAL HISTORY

She was developmentally normal and immunized for the age, although she did not have a bacille Calmette-Guerin scar.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included pulmonary hypertension (PH) with right ventricular dysfunction and congestive hepatomegaly.

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ABBREVIATIONS AND ACRONYMS

CTEPH = chronic thromboembolic pulmonary hypertension

PH = pulmonary hypertension

RA = right atrium

RPA = right pulmonary artery

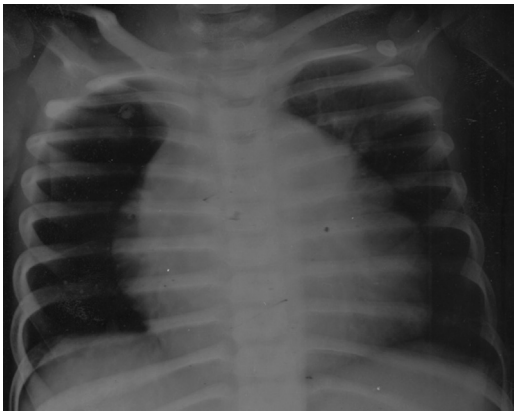
TB = tuberculosis

INVESTIGATIONS

Chest x-ray film revealed cardiomegaly with differential blood flow in the both lung fields (Figure 1). Electrocardiogram showed right-axis deviation, right atrial (RA) enlargement, and right ventricular strain pattern. Echocardiography revealed a large, homogenous, fixed mass at the roof of the RA measuring around 29 × 24 mm (Figures 2A and 2B) and another mass measuring around 23 × 11 mm in the right atrioventricular groove protruding into the coronary sinus (Figure 2C), severe right ventricular dysfunction, and mild tricuspid regurgitation (right ventricular systolic pressure = 56 + RA pressure) with severe PH without any intracardiac congenital abnormality. A series of targeted laboratory investigations and imaging were carried out for evaluating the cause of PH. Computed tomography angiography revealed a diffusely attenuated postostial right pulmonary artery (RPA) (Figures 3A and 3B) and multiple enlarged, calcified mediastinal lymph nodes with normal pulmonary venous drainage. Although diffuse narrowing of the RPA and mediastinal lymphadenopathy pointed toward fibrosing mediastinitis, the unilateral involvement and lack of involvement of the pulmonary veins indicated a possibility of chronic thromboembolic PH (CTEPH). At the radiologic suspicion of CTEPH vs fibrosing mediastinitis, she underwent a positron emission tomography-computed tomography study that revealed ill-defined thickening in the middle mediastinum along the RA and along the large vessels (the possibility of fibrosing mediastinitis may be considered); photopenic areas in the RA are likely thrombus/mass, and nodular opacities in the upper lobes of both lungs are likely postembolic changes (Figure 4). However, the diagnostic dilemma continued, and the possibility of CTEPH could not be ruled out.

She had an elevated erythrocyte sedimentation rate (35 mm/h) and C-reactive protein (19.75 mg/dL), D-dimer (910 ng/mL), and fibrinogen levels (550 mg/dL), suggestive of chronic inflammation. Apart from positive tuberculin skin tests, other laboratory workup findings for prothrombotic states (methylenetetrahydrofolate reductase, factor V mutation, β-2 antiglobulin), viral infections (hepatitis B, hepatitis C, and HIV), histoplasmosis, and SARS-CoV-2 were negative. Lower limb venous Doppler and abdominal ultrasound findings were normal. The identity of the patient has not been divulged in any form. Institutional ethics approval is not required.

FIGURE 1 Chest Radiograph

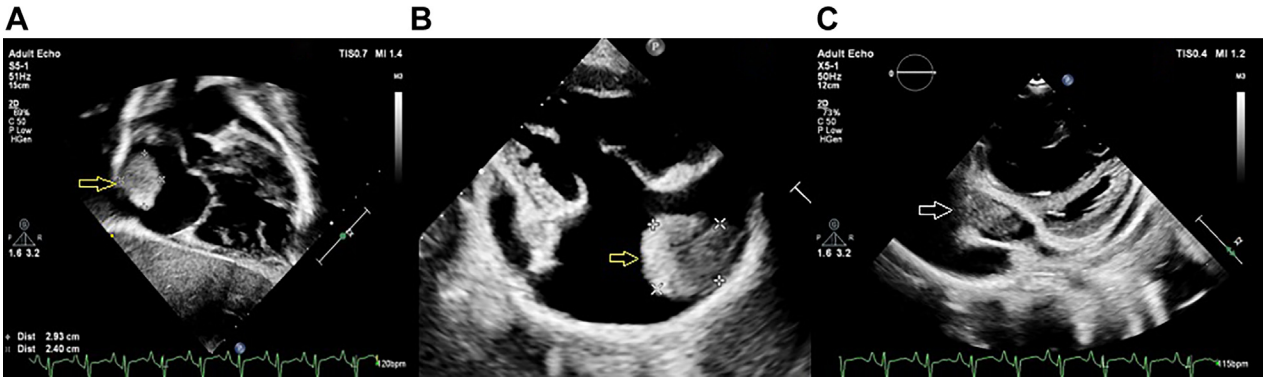


Frontal view showing cardiomegaly, right atrial and right ventricular enlargement, right ventricular type of apex, oligemic lung fields, and prominent bands to the left upper lobe.

MANAGEMENT

She was received symptomatic management (anticoagulation and diuretics). In view of the sick status of the child, a large fixed intracardiac thrombus, and diagnostic uncertainty, we planned for surgical exploration with the aim to establish the diagnosis by providing visual inspection and biopsy of the lymph node close to the RPA and surgical thromboendarterectomy if this turned out be a case of CTEPH. Intraoperatively, there was no soft tissue mass in the mediastinum, and the pulmonary veins were normal. She had large, fibrotic, calcified lymph node around the RPA without any compressive effect. Subsequent exploration revealed an organized cast-like thrombus suggestive of CTEPH in the RPA (Figure 5). Thromboendarterectomy with RPA reconstruction was performed. The lymph node specimen showed large necrotizing granulomas suggesting tuberculosis (TB), although culture did not grow acid-fast bacilli. Nonetheless, considering the common occurrence of TB in the community, positive Mantoux test result, and necrotizing granuloma in the histopathology of the lymph node specimens, a diagnosis of TB-related CTEPH was made. She was started on antitubercular therapy (the isoniazid, rifampicin, pyrazinamide, and ethambutol regimen), oral anticoagulation and pulmonary vasodilators (riociguat).

FIGURE 2 Echocardiography



(A) Subcostal sagittal view and (B) right ventricular inflow view showing a large, fixed, homogenous mass (arrow), likely thrombus, around 29 × 24 mm at the roof of the right atrium. (C) Parasternal short-axis view showing a large, fixed, homogenous mass (arrow), likely thrombus, around 23 × 11 mm at the right atrioventricular groove extending into the coronary sinus.

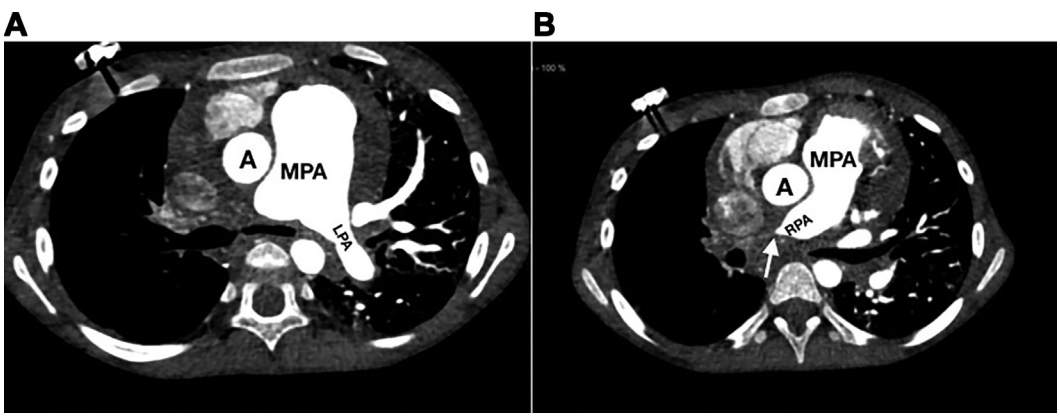
POSTOPERATIVE OUTCOME AND FOLLOW-UP

The patient had an uneventful postoperative recovery, with echocardiography showing no residual thrombus, trivial tricuspid regurgitation (right ventricular systolic pressure = 23 + RA pressure), mild PH, mild right ventricular dysfunction, and normal pulmonary arteries. Antitubercular treatment was stopped at 6 months. At 1 year of follow-up, she is in World Health Organization class I and has gained weight (3 kg in the span of 1 year). Right ventricular function was normal, with no evidence of PH.

DISCUSSION

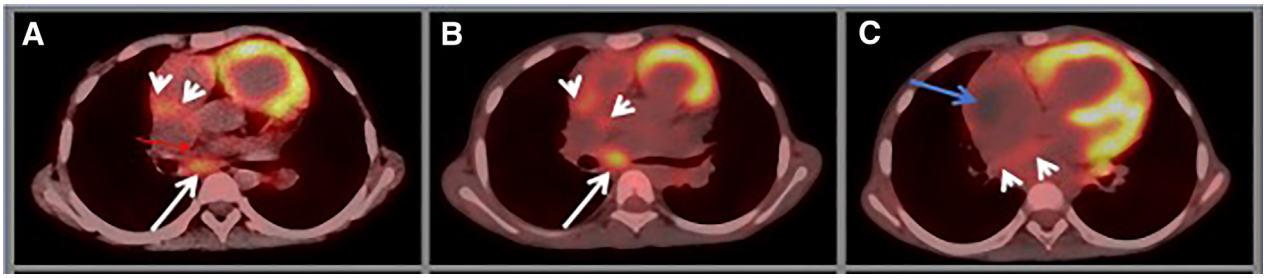
CTEPH is a rare and life-threatening disease[1] contributing <1% of the causes of pediatric PH.[2] Fibrosing mediastinitis is a close mimicker of CTEPH with similar etiologic agents, like TB, and atypical pulmonary artery and mediastinal organ involvement.[3] Different therapeutic and prognostic implications makes differentiation important. CTEPH occurs commonly as a sequela to acute pulmonary embolism and very rarely without any antecedent predisposing factors. It presents in the advanced stages in the form of right heart failure and right heart thrombosis

FIGURE 3 Contrast-Enhanced Computed Tomography



(A) Axial section showing enlarged main pulmonary artery (MPA) and normal-caliber left pulmonary artery (LPA). (B) Abrupt cutoff of the right pulmonary artery (RPA) with diminished flow on the right-side lung.

FIGURE 4 Positron Emission Tomography-Computed Tomography



Positron emission tomography-computed tomography. (A) Image shows uptake in the middle mediastinum corresponding to the region of the mediastinal lymph node (white arrow), (B) along the right atrium (red arrow), and (C) along the large vessel (arrowheads). Photopenic areas in the right atrium are likely thrombus (blue arrow).

because of the nonspecific nature of the symptoms.[1] CTEPH as a primary manifestation of TB in the absence of specific risk factors is not described in the literature, to our knowledge, and we hereby report such a rare presentation.

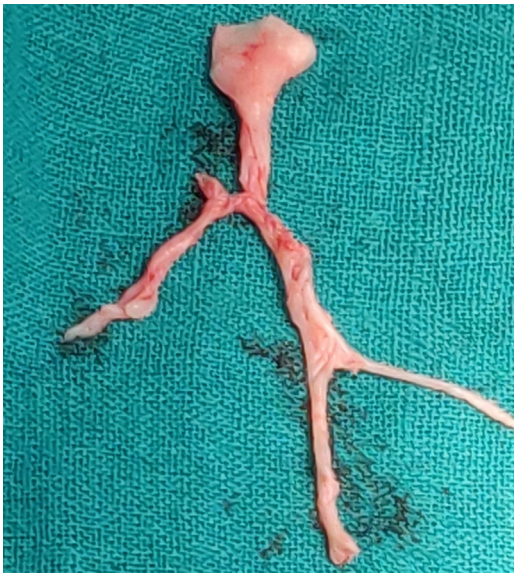
Pediatric PH has an estimated prevalence of 2 to 16 cases per million children,[2] with poor morbidity and mortality. This is far more common in the developing countries with limited health care, and the real burden of PH worldwide is probably underestimated.

Based on the World Symposium of Pulmonary Hypertension, PH associated with CTEPH is classified as group 4.[2] Based on the TOPP (Tracking Outcomes and Practice in Pediatric Pulmonary Hypertension) Registry, it contributes to <1% of the cases of pediatric PH[2]; however, because it is a treatable entity, its identification is important. Diagnosis is delayed until stages of right heart failure because of nonspecific respiratory symptoms akin to our case at presentation, leading to worse prognosis and outcomes.

CTEPH and fibrosing mediastinitis share similar clinical and radiologic features, especially in unilateral pulmonary artery involvement. As in our case, PH and mediastinal lymphadenopathy secondary to systemic granulomatous infection could be misdiagnosed as either, leading to an unfavorable outcome because of the different therapeutic options and prognostication. CTEPH, being treatable, merits extensive evaluation. Pulmonary thromboembolism may be seen in up to one-fifth cases of right heart thrombi.[4] Vasculitis with isolated pulmonary arterial involvement was considered; however, the absence of imaging characteristics of inflammation (viz, wall enhancement on computed tomography angiography and fluorodeoxyglucose-18 uptake on positron emission tomography-computed tomography) made it less plausible.

In CTEPH, about one-third of the cases are associated with underlying thromboembolic conditions, and less than one-third can present without any predisposing factors or past history of pulmonary embolism,[1] further leading to missed diagnosis in the absence of a predisposing factor. Although TB can lead to long-term sequelae of CTEPH secondary to pulmonary embolism caused by the systemic dysfibrinogenemia secondary to local lesion invasion, venous compression, and hypercoagulability,[5] isolated manifestation in the form of CTEPH has not been described in the literature, which further complicates the diagnostic certainty. Because of these uncertain manifestations, the exact incidence and prevalence are not known.

FIGURE 5 Intraoperative Specimen Showing Organized, Web-Like Thrombus of the Right Pulmonary Artery



Pulmonary thromboendarterectomy is the only curative option in CTEPH, with excellent results with early surgery.[6] Riociguat is the only approved drug for CTEPH in the adult population,[1] and use in the pediatric population is limited to case reports and case series lacking long-term data.[7] Early diagnosis and prompt therapy may be difficult in these types of presentations. This case may throw light on the importance of considering TB as a cause of CTEPH in children.

CONCLUSIONS

To conclude, a high index of suspicion is needed in atypical presentation of the common disease, like in our case. Always search for treatable causes like TB, especially in developing countries, where it is a still the prevalent disease with varied clinical manifestations and complications.

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