Isolated Pulmonary Arterial Thrombosis in Patient with Eisenmenger Syndrome Treated with Catheter-directed Thrombolysis: A Case Report and Literature Review

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ABSTRACT

The concept of venous thromboembolism (VTE) has recently been revisited because of evidence of a new spectrum of the disease called in situ pulmonary arterial thrombosis (ISPAT). We present the case of a 40-year-old female with shortness of breath, who was referred from a regional hospital because of a secundum atrial septal defect. Using echocardiography and computed tomography pulmonary angiogram, she was diagnosed with ISPAT. She received catheter-directed thrombolysis with good results. Knowing the difference in diagnostic clues between classical VTE and ISPAT is crucial, especially for managing the patient correctly.

Keywords: *Eisenmenger Syndrome, in situ pulmonary arterial thrombosis, venous thromboembolism, pulmonary.*

INTRODUCTION

Pulmonary thromboembolism is a potentially life-threatening condition. It is one of the most common causes of cardiovascular death and is associated with several systemic diseases and their acquired risk factors. The combined spectrum of pulmonary embolism (PE) and deep vein thrombosis (DVT) is referred to as venous thromboembolism (VTE). However, this concept has recently been revisited because of the evidence demonstrating that a new thrombus may be formed in pulmonary arteries without DVT in the lower extremities, creating a different clinical spectrum of pulmonary thromboembolism called in situ pulmonary arterial thrombosis (ISPAT).[1,2]

In the clinical literature, ISPAT is considered rare. It is often underdiagnosed or cited as isolated PE without DVT. Therefore, we aim to report a case of ISPAT in a patient with Atrial Septal Defect (ASD) and Eisenmenger syndrome, which was successfully treated with catheter-directed thrombolysis (CDT).

CASE ILLUSTRATION

A 40-year-old woman referred from a regional hospital presented at the outpatient clinic with shortness of breath that had worsened 2 weeks before her hospital admission. Shortness of breath was accompanied by fatigue felt after a light to normal activity. There were no

complaints of pounding or chest pain.

From physical examination, the patient's blood pressure was 98/66 mmHg, heart rate was 68 bpm, and respiratory rate was 24 per minute. Peripheral oxygen saturation on room air was only 93%. The jugular vein was distended. Based on heart sounds, the S1 was normal and singular and S2 was wide fixed, split between pulmonic and aortic components, with a grade 3/6 pan systolic murmur heard along the lower left sternal border. The breath sound was vesicular and clear. There was no hepatomegaly, and no peripheral cyanosis or edema was seen. Capillary refill time was under 2 seconds. The electrocardiogram showed normal sinus rhythm with right axis deviation and incomplete right bundle branch block (RBBB) with right ventricular strain pattern (**Figure 1**).

Laboratory test results showed normal complete blood count and renal function. The coagulation profile showed normal platelet count, prothrombin time (PT), activated partial thromboplastin clotting time (aPTT), and international normalized ratio (INR). D-dimer was elevated at 1620 ng/ml, while fibrinogen level was still within normal range, at 409 mg/dl.

The echocardiogram showed a large secundum ASD with a 2.4 cm diameter and a predominantly right-to-left bidirectional shunt. The right atrium, ventricle, and pulmonary artery were dilated, with the left ventricle being D-shaped. A large thrombus was observed in the left pulmonary artery. The pulmonary velocity (PV) acceleration time was 66 msec and mean pulmonary arterial pressure (mPAP) was 49 mmHg.

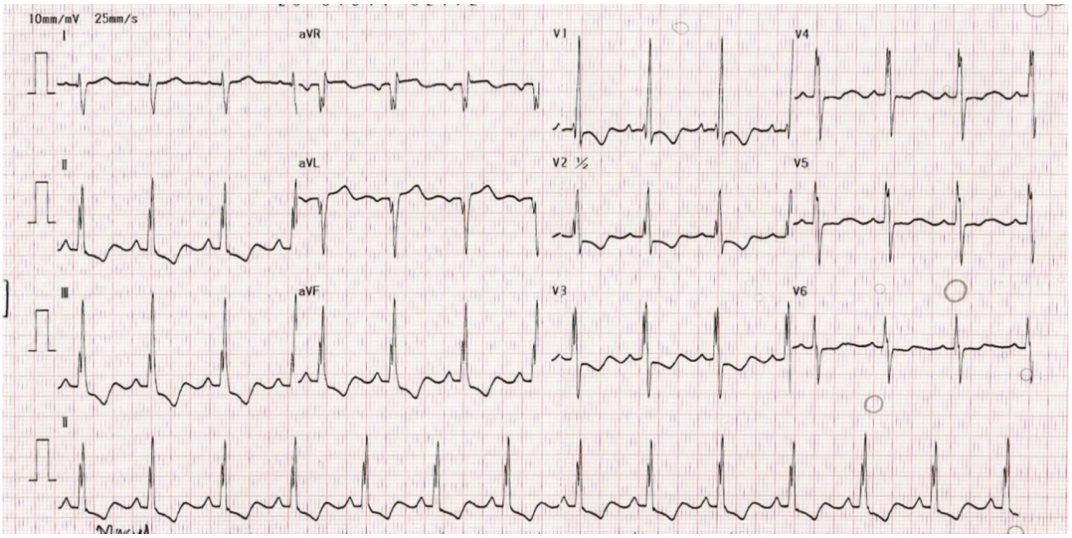

Figure 1. ECG patient shows normal sinus rhythm, right axis deviation, incomplete RB a, andd RV strain pattern

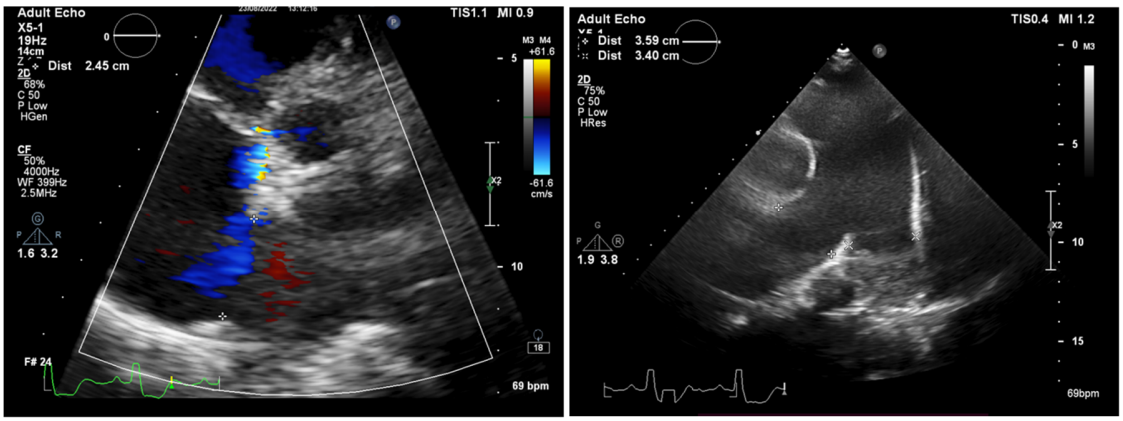

Figure 2. Transthoracic Echocardiography showed ASD secundum with 2.45 diameter and thrombus in LPA

Upper and lower Doppler ultrasound revealed no DVT in both lower extremities (**Figure 3**). The patient was admitted to the critical cardiovascular care unit (CVCU) and received anticoagulation with fondaparinux 7.5 mg subcutaneously. The patient also received sildenafil 3x25 mg and ramipril 1x5 mg.

The computed tomography pulmonary angiogram (CTPA) revealed a large thrombus, approximately 1.5 cm in diameter (**Figure 4**). The patient underwent CDT; alteplase was given intra-catheter 12.5 mg, with a total dosage of 32 mg in 24 hours (**Figure 5**). Invasive pulmonary angiography was carried out the next day with no filling defect. CDT was considered successful. After CDT, the clinical symptoms of the patient improved. The patient then continued on anticoagulants with warfarin, sildenafil, and captopril. Echocardiography was evaluated in the outpatient clinic 1 week after discharge. Thrombus was no longer visible in the left pulmonary artery, accompanied by clinical improvement in shortness of breath. Right heart catheterization revealed a low-flow, high-resistance state with no response to oxygen tests, and the patient then planned for conservative medical treatment.

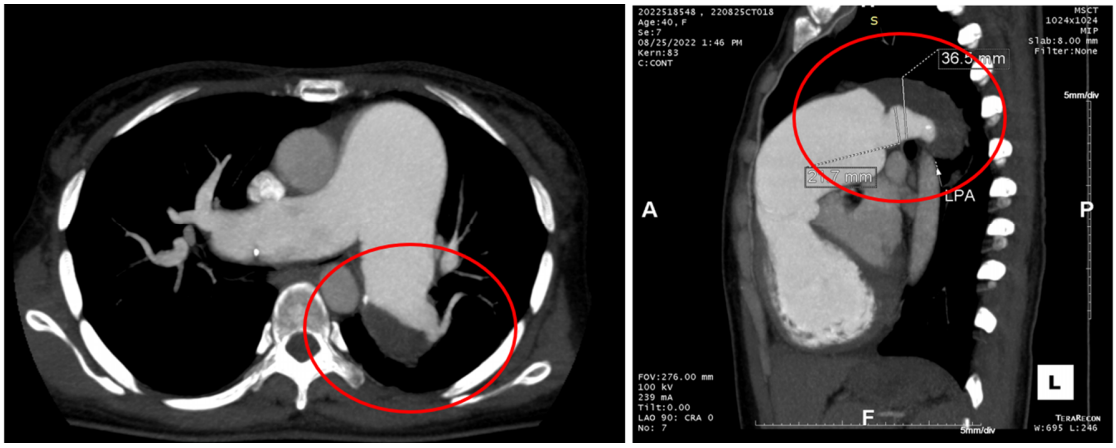

Figure 3. Computed Tomography Pulmonary Angiography revealed a large thrombus in LPA, with a diameter size of approximately 1.5 cm

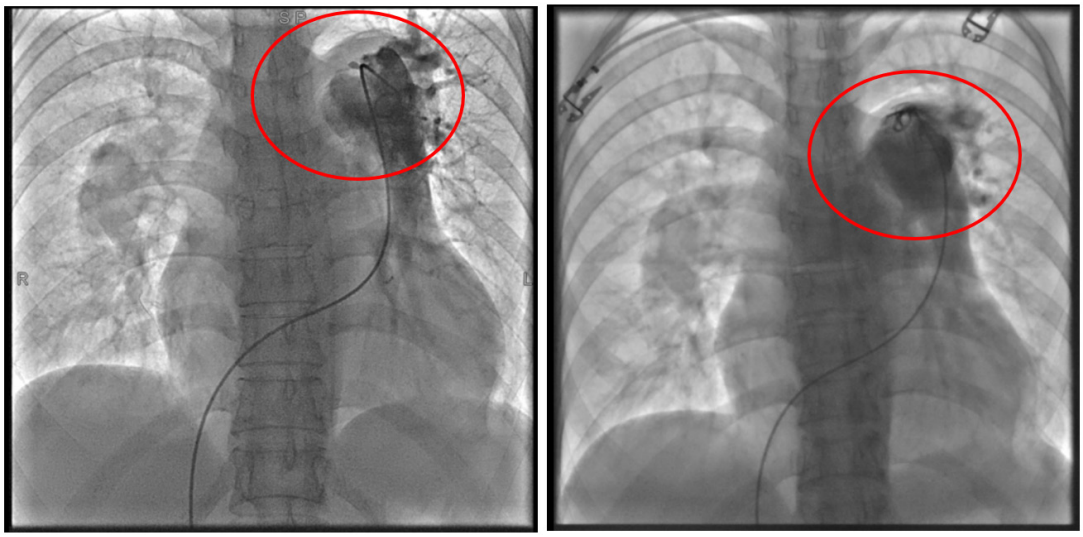

Figure 4. Invasive pulmonary angiography. **Left –** pre CDT, notice the filling defect in LPA. **Right –** post-CDT, the filling defect was no longer visible

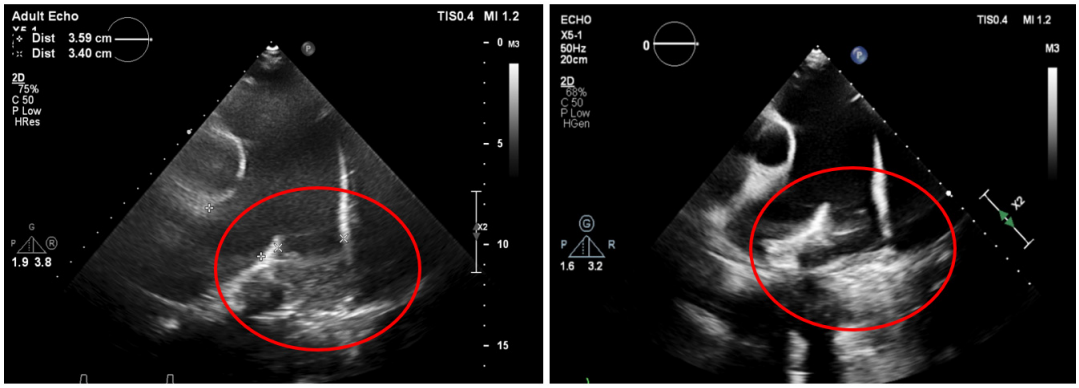

Figure 5. **Left –** Echo pre-CDT. **Right –** Echo post-CDT. Notice the thrombus was no longer visible

DISCUSSION

Evidence suggests the possibility of a new kind of thrombosis, called ISPAT, in the pulmonary arteries without evidence of DVT in the lower extremities. In the clinical literature, ISPAT is considered rare. Moreover, ISPAT lacks standard guidelines for practical diagnosis and management, which limits clinicians' ability to diagnose it.[2]

Pathomechanism of ISPAT

In the reported case, untreated secundum ASD led to chronic pulmonary vascular disease remodeling, pulmonary arterial hypertension (PAH), and eventually Eisenmenger syndrome. Vascular remodeling is associated with alterations in vasoconstriction, inflammation, apoptosis, angiogenesis, coagulopathy, and thrombosis. It leads to the muscularization and occlusion of the lumen of pulmonary arteries.[3] PAH is characterized by remodeling of pulmonary arteries, causing a progressive increase in vascular resistance.

Furthermore, in end-stage PAH, such as in Eisenmenger syndrome, endothelial activation can be induced by hypoxia, which provokes the secretion of reactive oxygen species (ROS), production of hypoxia-inducible factors (HIFs), and induction of pro-inflammatory factors, such as interleukin 6 (IL-6) and tumor necrosis factor-alpha (TNF α), and hypercoagulable state. ROS increases the expression of TNF on endothelial cells and monocytes, inactivates protein C and its agonist thrombomodulin, and promotes oxidation of fibrinogen, which increases its conversion to fibrin, thus promoting thrombus formation. [3–5]

Predictor of ISPAT

In the study by Broberg et al.,[6] lower left and right ventricular functions were found to be related to ISPAT incidence. Those with thrombus also had a larger main pulmonary artery (mPA) diameter and a lower peak systolic velocity in the pulmonary artery. The study also stated a main PA diameter of 40–48 mm was a risk factor for ISPAT.

Our patient had secundum ASD with signs of PAH, along with an mPA diameter of 51 mm and a history of contraceptive hormonal therapy, which acts as a risk factor for ISPAT. There was no history of cancer or malignancy. The patient had a normal menstruation period and no known coagulopathy disorder, no history of stroke or DVT, no history of previous surgery or trauma, and no last known renal or liver disease.

Management of Patients with ISPAT

The clinical status of patients with CT evidence of pulmonary thrombus has been variable. More distal thrombosis raises the concern that the ISPAT may contribute to the progression of patients' pulmonary vascular disease through distal emboli and microinfarction of lung vasculature, leading to progressive loss of their pulmonary vasculature.[6,7]

Thrombus evacuation can be quite challenging. Surgical intervention such as a thrombectomy requiring a bypass could be an extremely high-risk operation. While anticoagulation alone may not be sufficient because of patients being prone to labile INR, the risk of inadequate therapeutic range of INR

would be prominent.[8,9] CDT is a relatively safe and highly effective treatment for VTE such as massive PE. It has lower known complication rates than systemic thrombolysis.[10]

Within the Eisenmenger syndrome population, especially in Indonesia, this is the first reported case of ISPAT managed by CDT. The patient was started on warfarin, achieving a target INR of 2.0–3.0, and then discharged on lifelong warfarin with regular INR follow-ups.

CONCLUSION

We report an uncommon case of ISPAT in a patient with secundum ASD and Eisenmenger syndrome. ISPAT can contribute to the progression of a patient's symptoms such as dyspnea or chest discomfort through microembolization. CDT could offer an effective and safer option than systemic thrombolysis or surgical thrombectomy

DISCLOSURE

The author reports no conflicts of interest in this work.

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