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Case Report Open Access

Idiopathic Pulmonary Hypertension Induced Thrombocytopenia - A Case Report

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Abstract

Idiopathic pulmonary hypertension (PH) is a diagnosis of exclusion for any patient presenting with pulmonary hypertension (PH). Patient with PH may present with thrombocytopenia along with other signs of PH. We report a case of PH who presented with thrombocytopenia and breathlessness. The possible causes of thrombocytopenia were evaluated and excluded prior to concluding that her thrombocytopenia is due to PH. Various pathogenic mechanisms have been described for thrombocytopenia associated with PH.

Keywords: Idiopathic pulmonary hypertension; Thrombocytopenia; Primary respiratory alkalosis

Introduction

Idiopathic PH is a rare but potentially fatal disease. Multiple pathogenic mechanisms have been described for thrombocytopenia in patients with PH.

Case Report

A 46 year female who was diagnosed to have carcinoma of the breast presented with progressive breathlessness to a state of New York Heart Association functional class IV over 15 days. She was hypotensive (90/64 mmHg) and hypoxic (SpO_2 88% on room air) on presentation. Initial resuscitation with 500 ml of crystalloid and high flow oxygen with a non-rebreathing mask was done. On clinical evaluation the positive findings included a raised jugular venous pressure (JVP), a loud pulmonary component of second heart sound (P2), pan systolic murmur in tricuspid area and clear lung fields on auscultation. There was no organomegaly and no clinical findings suggestive of deep venous thrombosis. Laboratory investigations revealed thrombocytopenia (platelet counts 38000/cc), raised D Dimer (1.5 µg/ml, normal <0.5 µg/ml), primary respiratory alkalosis in arterial blood gas analysis, prominent common pulmonary and right pulmonary artery on X-ray chest anterior-posterior view. The electrocardiogram (ECG) showed Q wave and inverted T wave in lead III. Immediate computerized tomographic pulmonary angiography (CTPA) ruled out any major thromboembolic event, mediastenal compression or mass. A prominent common pulmonary artery (diameter 2.97 cm) (Figure 1) and a dilated RV was marked on CT scan (Figure 2). A two dimension transthoracic echocardiography (2D Echo) showed a dilated right atrium (RA) and right ventricle (RV) and Doppler showed moderate to severe tricuspid regurgitation with a peak velocity of 3.8 m/s. A triple lumen catheter was inserted in the right internal jugular vein and the central venous pressure reading was 21 mmHg which estimated the right ventricular systolic pressure to be 81 mmHg. A working diagnosis of idiopathic pulmonary hypertension was made after exclusion of possible differential diagnoses and treatment with Sildenafil (50 mg orally twice daily) and Bosentan (62.5 mg orally twice daily) started. She received a transfusion of single donor platelet (as the platelet count dropped further to 20000/cc). She became progressively more dyspnoeic and hypotensive. Vasopressor (Noradrenaline) and inotrope (Dobutamine) were started and dose titrated to maintain a mean arterial blood pressure around 65 mmHg. She was stable for the next three hours after which she complained of worsening breathlessness, became irritable and disoriented. The heart rate suddenly dropped to 40/min with no palpable pulse. Cardiopulmonary resuscitation was started, her trachea was intubated and ventilated with 100% oxygen. The endotracheal suction showed frank hemorrhage and the rhythm was now asystole.

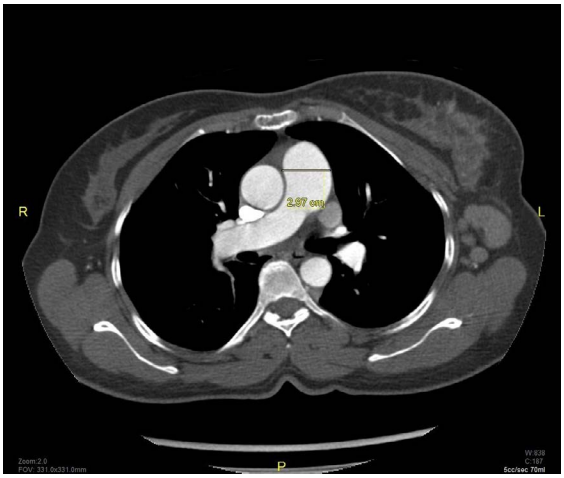

Figure 1: Prominent pulmonary artery in CTPA.

There was no response to all the resuscitation efforts and we were not able to revive her.

Discussion

Our patient could be categorized as Idiopathic pulmonary hypertension (previously categorized as Primary Pulmonary Hypertension (PPH) [1,2]. Idiopathic PH is a rare disease, with varying incidence from 1 to 5.9 cases per million population. Twelve percent of the diagnosed cases are inherited as autosomal dominant [3].

In a cohort study including 576 patients of PH of various etiology, 307 (53%) died during follow-up (the median follow-up time was 3.9 years). The reported 1, 3 and 5 yr survival rates for the PH were 86, 69 and 61%, respectively [4].

Differential diagnosis considered were medical conditions

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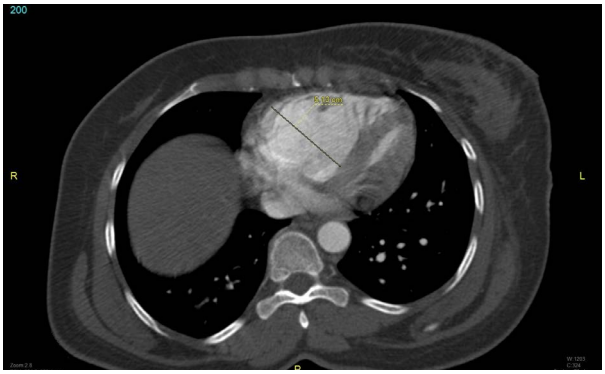

Figure 2: Dilated RV compressing into LV.

associated with PH (including portal hypertension, [5] and connective tissue disease (most commonly systemic sclerosis) [6]. Other possible etiologies considered include human immunodeficiency virus infection [7], chronic hemolytic anemias [8], and congenital heart disease (Eisenmenger syndrome). The diagnosis of idiopathic PH was made by careful exclusion of the above possibilities by detailed clinical history, family history, clinical examinations and specific laboratory parameters.

Pathology behind the worse outcome in PH includes the following. RV is a thin walled chamber structured to handle a low pressure pulmonary circulation [9,10]. Unlike the normal physiology, in PH the perfusion to the RV is gradually restricted only to diastole with the progression of severity of PH resulting in progressive ischemia and failure of RV [11]. Though there may be a disparity of 10-20 mmHg of PASP measurement invasively as compared to 2D Echo, the latter is the preferred initial modality to diagnose, quantify and follow-up PH [12].

Expert panel recommends invasive measurement of pulmonary artery systolic pressure (PASP) as the gold standard but feasibility in each case needs evaluation [13].

In our case PH was diagnosed and quantitated by 2D Echo.

The recommendations for the use of Pulmonary vasodilators (Sildenafil and Bosentan) are restricted to WHO group I pulmonary hypertension (i.e., primary PH or idiopathic PH) probably because, this is the most commonly studied group in clinical trials [14].

The recommended therapies for PH fall into 3 classes of pulmonary vasodilators: phosphodiesterase-5 inhibitors, endothelin receptor antagonists, and prostacyclin analogues. The appropriate choice of the agent should be made judiciously as an erroneous administration of vasodilators in pulmonary venous hypertension may lead to worsening of venous pressure and possible pulmonary edema [14].

Mortality in PH is directly related to RV dysfunction. Hence optimal management of RV dysfunction in all subsets of PH is important. PH with chronic right heart failure is managed by diuresis, sodium and water restriction. Aggressive fluid resuscitation is avoided. Early administration of vasopressors and inotropes are indicated for correction of hypotension and shock [14]. Treatment measures are targeted to augment the supply and decrease the demand for myocardial oxygen. These include oxygen supplementation, maintenance of adequate hematocrit, avoidance of acidosis, reduction in the RV afterload using specific pulmonary vasodilators like inhaled nitric oxide and reducing RV volume load by dieresis and/or ultrafiltration in refractory cases [14]. Our patient received a fluid resuscitation of

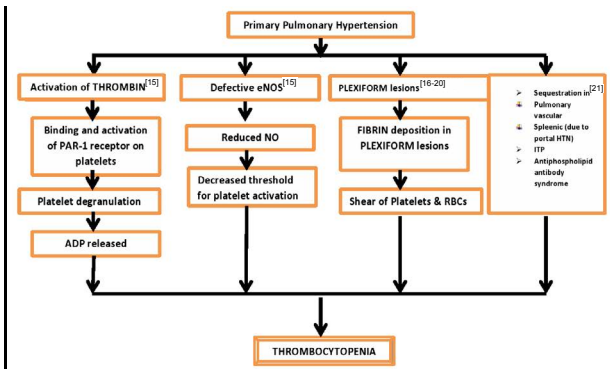

Figure 3: Pathogenesis of Thrombocytopenia in pulmonary hypertension.

500 ml followed by early administration of Noradrenaline (to increase the coronary perfusion pressure), Dobutamine (to support the compromised RV), pulmonary vasodilators-Sildenafil and Bosentan (to reduce RV afterload) and oxygen supplementation. We were unable to use NO as it was not available with us and inhaled prostacyclin was not considered because of thrombocytopenia. We transfused one unit of single donor platelet though there was no evidence of bleeding clinically in view of decreasing trend of platelet count (38000 to 20000/cc).

The possible pathogenic mechanisms for thrombocytopenia in our patient are as described (Figure 3). Blood flow through the pulmonary vasculature in presence of PH can lead to activation of thrombin which binds to protease-activated receptor-1 (PAR1) on platelets. It leads to platelet degranulation and release of factors like adenosine di-phosphate (ADP) leading to platelet aggregation [15]. Nitric oxide (NO) prevents premature activation of platelets. Due to defective endothelial nitric oxide synthases (eNOS), the production of NO is decreased in idiopathic PH. It causes a decreased threshold for platelet activation in patients with idiopathic PH [15].

Pathological "Plexiform" lesions in vasculature of lung have been described in patients of idiopathic PH. Fibrin deposition occurs in these plexiform lesions. Red blood cells (RBCs) and platelets experience injury to their cell membranes while passing through these lesions leading to increased cell damage [16-19]. Moreover, concurrent association of diseases such as portal hypertension leading to splenic sequestration, idiopathic thrombocytopenic purpura (ITP) and antiphospholipid antibody syndrome may present with thrombocytopenia along with idiopathic PH [20].

Conclusion

PPH presenting with thrombocytopenia though rare and reported anecdotally, they are known to have worse prognosis. Other causes of possible thrombocytopenia needs to be excluded prior to concluding idiopathic PH as the cause for it. The treatment modality for PH is still not clearly defined.

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