



CASE REPORT

Essential thrombocythemia presenting with ischemic mitral regurgitation and recanalized coronary artery thrombosis: a case report

Nael Al-Sarraf¹ and Mohammed Hasan²

¹Department of cardiac surgery,
Dabbous Cardiac Center, Adan
hospital, Kuwait.

²Department of cardiology,
Dabbous Cardiac Center, Adan
hospital, Kuwait.

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ABSTRACT

Essential thrombocythemia is a rare myeloproliferative disorder characterized by pathologic expansion of the megakaryocytic elements in the bone marrow leading to persistent thrombocytosis and platelet dysfunction. Coronary artery disease can occur in 9% of cases and there is a high incidence of acute myocardial infarction. Although the association between essential thrombocythemia and coronary artery thrombosis causing acute myocardial infarction was reported, the association between recanalized coronary artery thrombosis and left ventricle remodeling with functional ischemic mitral regurgitation in essential thrombocythemia was not previously reported. Here, a case of essential thrombocythemia in a patient with re-canalized coronary artery thrombosis that presented with ischemic mitral regurgitation secondary to left ventricle dilatation and remodeling is reported. As there are no clear guidelines for best management approach to these patients when cardiac surgery is planned, we report the successful management of such a case. The use of Hydroxyurea to lower the preoperative platelet count close to normal level with Aspirin proved to be effective strategy in our case in combination with the use of arterial grafting and bioprosthetic valve. The patient had uneventful postoperative recovery following coronary artery bypass graft surgery and bioprosthetic mitral valve replacement.

Keywords: Essential thrombocythemia, coronary artery bypass graft, ischemic mitral regurgitation.

Introduction

Essential thrombocythemia (ET) is a rare myeloproliferative disorder characterized by persistent thrombocytosis. It is associated with high incidence of coronary artery disease and can lead to both thrombosis and hemorrhage. Although the association between essential thrombocythemia and coronary artery thrombosis causing acute myocardial infarction was reported, the association between re-canalized coronary artery thrombosis and left ventricle remodeling with functional ischemic mitral regurgitation in essential thrombocythemia was not previously reported. Management of such cases is challenging and requires proper surgical planning with choice of arterial grafting and biological valves and adequate reduction of preoperative platelet count to near normal level to reduce the postoperative complications of thrombosis. Here we present a case of ET that presented with ischemic mitral regurgitation due to recanalized coronary artery thrombosis which was managed successfully with coronary artery bypass graft and mitral valve replacement after full control of platelet count preoperatively. Careful management of such cases when undergoing cardiac surgery is important to avoid the risk of thrombosis and adverse outcomes post-operatively.

Case report

A 50-year-old man with no family history of ischemic heart disease presented with heart failure symptoms in 2019 with shortness of breath on exertion with New York Heart Association (NYHA) class III symptoms with no chest pain. He was a smoker (1 pack daily) for 30 years. He was known for hyperlipidemia and hypertension and was treated medically at that time but with poor compliance. He presented 5 years later to medical side with NYHA class IV symptoms and orthopnea at 45 degrees. He had no hemoptysis and no lower limb edema with no chest pain. Transthoracic echo (TTE) showed severe ischemic mitral regurgitation (MR) with mild tricuspid regurgitation (TR) and pulmonary artery hypertension with pulmonary artery systolic pressure (PASP) of 71 mmHg (Figure 1 and 2). His systemic blood

pressure pressure was 100/70 and he was in sinus rhythm. During his preoperative work up, Complete blood count showed (CBC) showed persistently elevated platelet count of $700 *10^9/L$ on multiple occasions. Patient was seen by hematology service. Bone marrow biopsy showed large clusters of megakaryocytes of variable morphology. Janus Kinase 2 mutation (JAK2 V617F) was positive with 16.5% allele burden, and he was diagnosed with essential thrombocythemia (ET). He was started on Hydroxyurea as a cytoreductive therapy in addition to aspirin. Heart failure medications were also started and optimized. Serum ferritin and vitamin B12 were normal. Transferrin was normal and transferrin saturation was low. His renal and liver function tests were normal. Coronary Angiography showed re-canalized thrombus in Circumflex (figure 3) and left anterior descending (LAD) arteries with chronic subtotal occlusion in mid LAD (figure 4). Ultrasound abdomen was normal. Carotid duplex showed < 70% stenosis in left internal carotid artery (ICA) with normal right side. Computed tomography (CT) of the neck showed LICA stenosis of 60% with left common carotid stenosis 40 % and mild stenosis of left vertebral artery. Right ICA was normal. Computed tomography (CT) of chest ruled out pulmonary embolism and ultrasound duplex of his lower limb ruled out deep vein thrombosis. Patient accepted surgery and he underwent sternotomy with coronary artery bypass graft (CABG) using left internal mammary artery to LAD and mitral valve replacement (MVR). Mitral valve was replaced with bioprosthetic size 29 Magna Ease valve was the patient did not want to be on long term warfarin treatment. Mitral valve was approached through superior trans-septal approach with preservation of posterior leaflet and excision of A2 with preservation of A1 and part of A3. There was no intra-operative complication and patient was weaned from cardiopulmonary bypass on small doses of inotropic support. Transesophageal echo (TEE) showed well-functioning mitral valve with no para valvular leak and mild TR. Post-operative course was uneventful with two days stay in intensive care unit and hospital stay of 7 days. Aspirin and warfarin were started day 1 postoperatively with therapeutic

dose of low molecular weight heparin as a bridge. Hydroxyurea was started day 3 postoperatively once platelet count reached 400 and continued thereafter. His platelet count remained within normal range around $300-400 \times 10^9/L$. Pre-discharge TTE showed well-functioning mitral valve and no para valvular leak. He was discharged on Hydroxyurea

500 mg daily for his ET with Aspirin 81 mg po daily and warfarin. In addition, he was on beta blockers, statin, and loop diuretic. Patient was followed up for 6 months following his surgery and his Warfarin was discontinued 3 months post-operatively. He remained symptom free and in sinus rhythm.

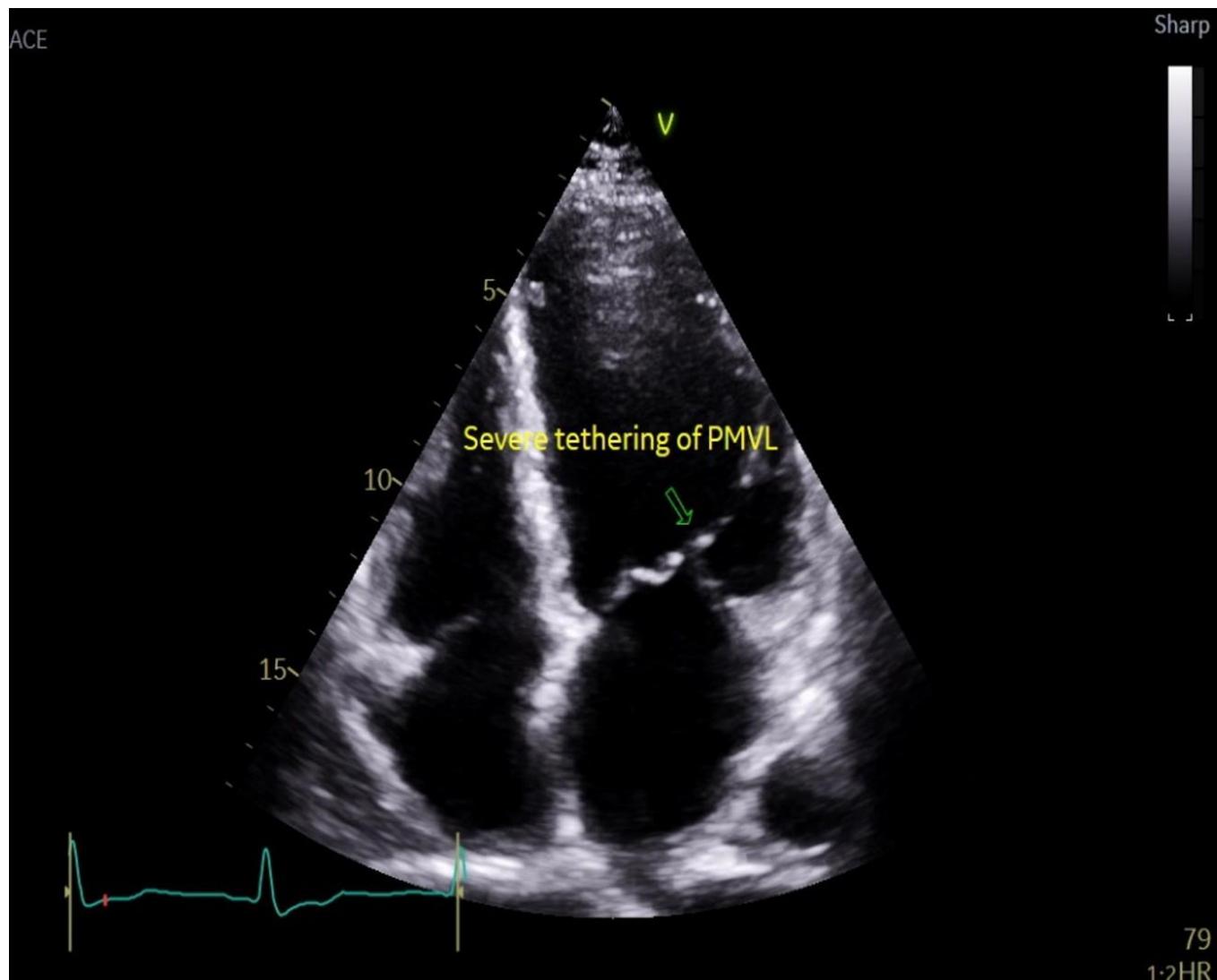


Figure 1: Transthoracic echocardiography apical 4 chamber view showing tethering of posterior leaflet of mitral valve.

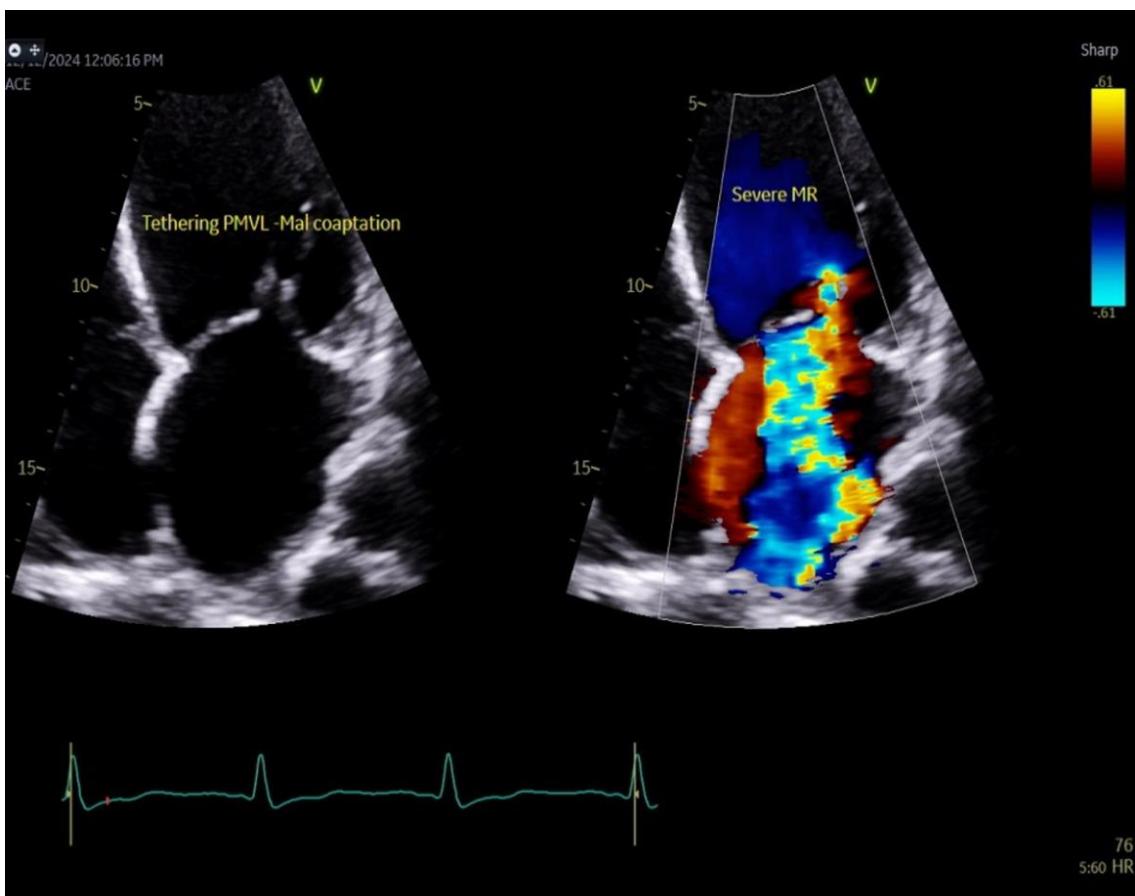


Figure 2: Transthoracic echocardiography focused 4 chamber view with color Doppler showing severe ischemic mitral regurgitation.

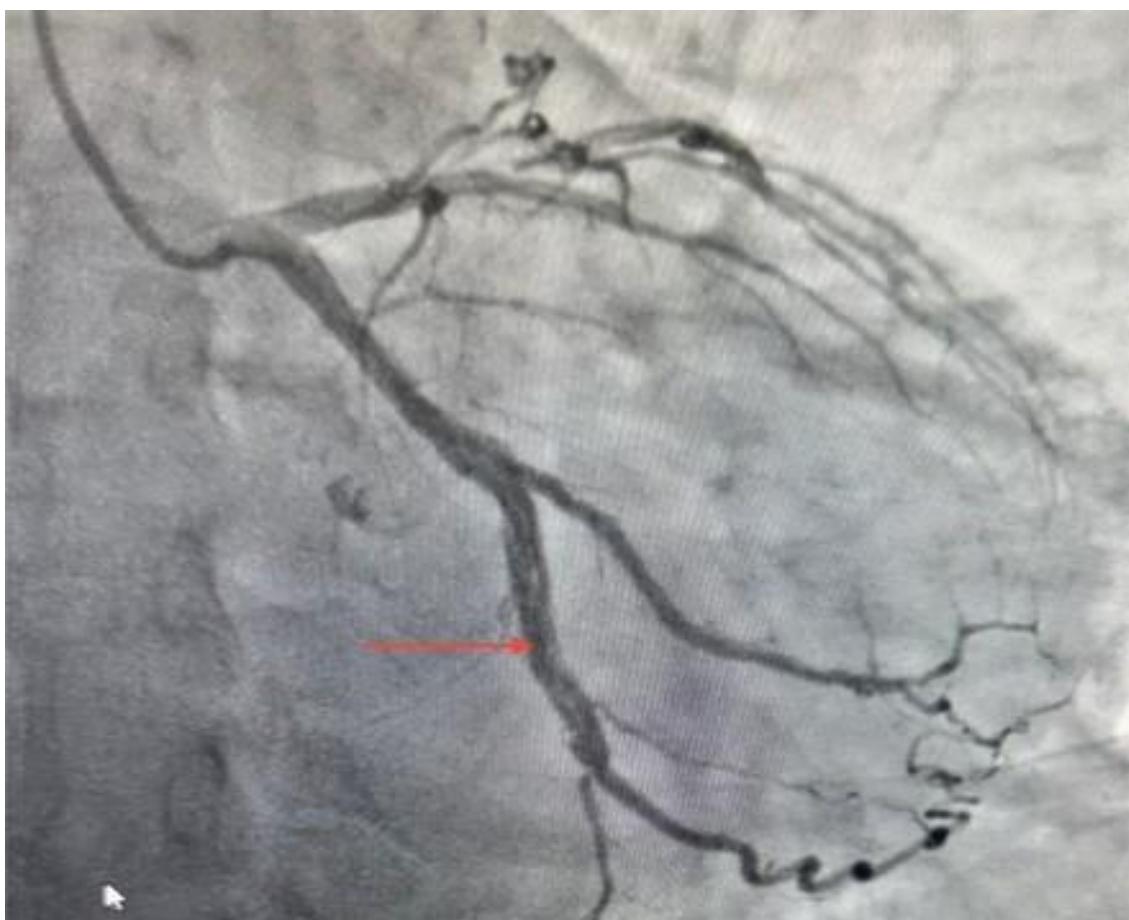


Figure 3: Coronary angiography appearance of the recanalized thrombus in distal part of circumflex artery (red arrow).

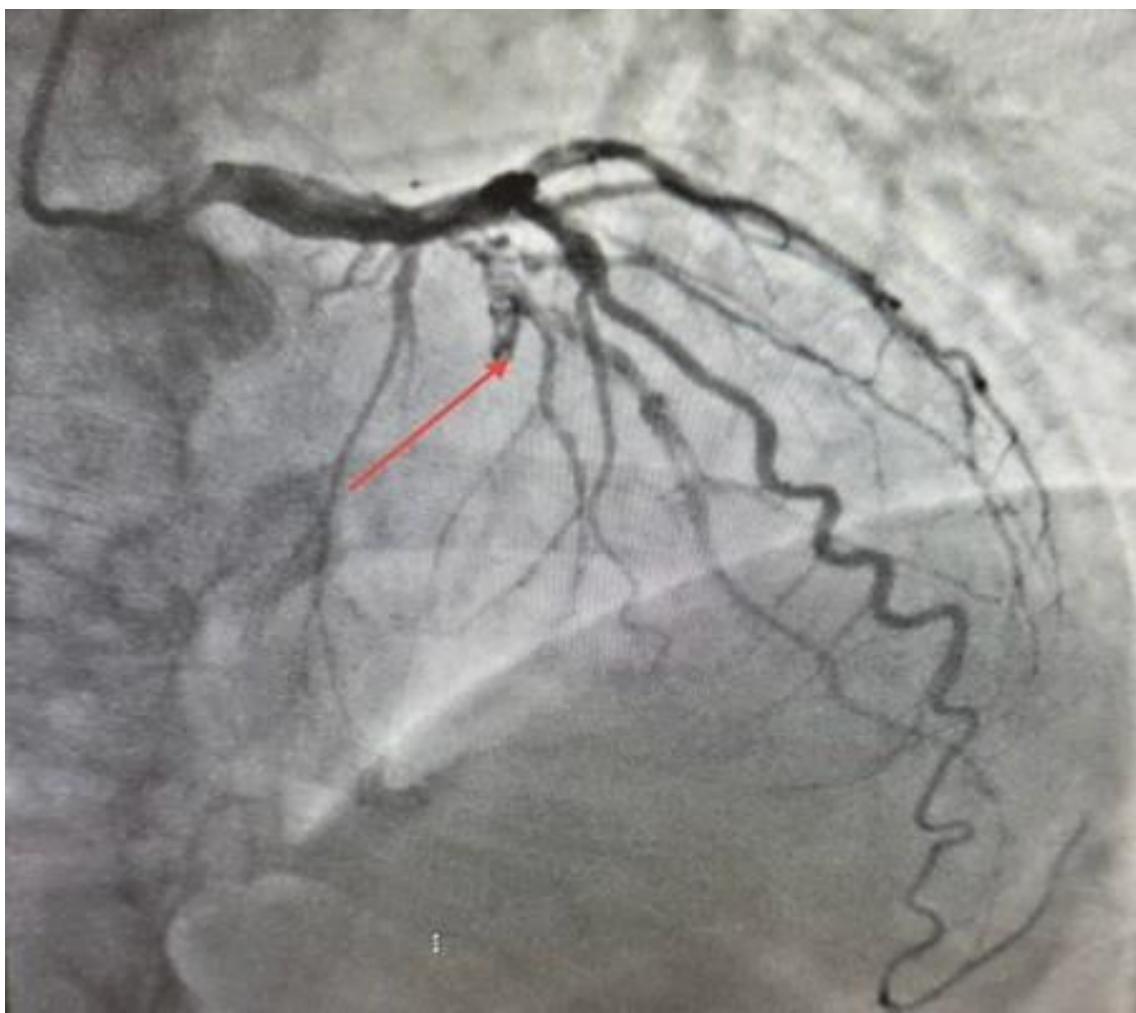


Figure 4: Coronary Angiography appearance of the chronically sub totally occluded left anterior descending artery (red arrow).

Discussion

Essential thrombocythemia (ET) is a rare myeloproliferative disorder (MPD) characterized by pathologic expansion of the megakaryocytic elements in the bone marrow leading to persistent thrombocytosis and platelet dysfunction. It is commonly associated with somatically acquired mutations in the JAK2, CALR (Calreticulin) or MPL (Myeloproliferative leukemia virus oncogene) genes. Patients are asymptomatic but can develop hemorrhagic &/or thrombotic events leading to cerebral, myocardial and peripheral arterial thrombosis^(1,2). The incidence of ET is 9.6 new cases per million people with higher incidence in females and African American⁽¹⁾. Thromboembolic complications are seen in 17-44% of ET patients and these account for 1/3 of deaths and mostly occur in coronary, peripheral arteries, pulmonary, portohepatic, cerebral and deep veins⁽³⁾. World Health

Organization diagnostic criteria for ET requires the presence of four elements for diagnosis. These include: sustained platelet count $> 450 \times 10^9 / \text{L}$, absence of reactive causes, specific bone marrow biopsy findings of primarily megakaryocyte lineage proliferation (not meeting the criteria for other myelodysplastic syndromes or other myeloid neoplasms) and finally the presence of JAK2, CALR or MPL mutation. The presence of JAK2 V617F mutation is seen in 50% of patients with ET and is associated with an increased risk of thromboses^(4,5). Cardiac involvement in MPD was previously examined echocardiographically in 30 patients (8 of them had ET). The study found that 63% of MPD patients had valvular lesions compared to 4.5% in control group. In essential thrombocythemia subgroup alone, valvular lesions were found in 50% of cases. The aortic and mitral valves were most commonly involved and the most common echocardiographic lesions

seen was leaflet thickening. The study also found that 47% of MPD patients had arterial/venous thrombosis or embolism. The authors concluded that the heart is frequently involved in MPD patients particularly when their history was complicated with thromboembolic event⁽⁶⁾. Another study showed the incidence of mitral regurgitation in ET patients was 27% with 13% incidence of pulmonary hypertension⁽³⁾.

Management of ET is focused on thrombotic risk stratification⁽⁷⁾. Patients are risk stratified based on history of thrombosis, age < or > 60 years old, and presence of JAK2/MPL mutation. Patients without these risk factors and without CV risk factors are managed with observation only. All other patients are offered anti-platelet therapy (Aspirin). Patients who have experienced a previous thrombotic event or are above 60 years old with or without JAK2/MPL mutation are offered cytoreductive therapy with a target to return platelet levels to normal range. In terms of cytoreductive therapy, Hydroxycarbamide and Aspirin is the recommended first therapy for ET patients at high risk of vascular events^(4,7). Some reports of surgical complications following CABG were reported including coronary thrombosis with tamponade and pulmonary embolism⁽⁸⁾. A series of 25 ET patients undergoing cardiac surgery had mortality rate of 12% and thrombotic events in 8%⁽¹⁾. Similarly coronary artery stent thrombosis was reported immediately following procedure^(5,9). Some surgical techniques that were reported with successful outcomes in ET patients undergoing cardiac surgery included the use of arterial grafting⁽¹⁰⁾, the use of intra-operative autologous transfusion technique before starting cardiopulmonary bypass (CPB) with administration of intravenous Cangrelor therapy that blocks platelet activation and aggregation to limit the thrombotic complication in perioperative period⁽²⁾. The use of bioprosthetic valve is a good option in ET patients to further limit the risk of valve thrombosis in such cases. We have reported previously the successful use of arterial grafting in ET patient with coronary artery stent occlusion with no postoperative morbidity⁽¹⁰⁾. The use of CPB machine in cardiac surgery is a complex physiological event

that leads to hemostatic alteration in many different mechanisms including platelet activation and aggregation upon exposure to the CPB circuit^(11,12). These mechanisms in ET patients are not well understood raising concerns of higher thrombosis risks in ET patients with uncontrolled platelet count.

Our case is unique in many ways. The presentation of our patient was ischemic cardiomyopathy with associated ischemic mitral regurgitation. In addition, coronary artery had recanalized thrombosis in two major coronary arteries (circumflex and left anterior descending arteries) with chronic subtotal occlusion of mid segment of left anterior descending artery leading to left ventricular geometry remodeling with ensuing ischemic mitral regurgitation consequently and reduced ejection fraction.

Conclusion

Essential thrombocythemia is a rare MPD that carries a risk of thrombosis. Proper diagnosis and prompt treatment of the high platelet count can result in improved outcome of these patients when undergoing cardiac surgery. The use of combination therapy of Aspirin and hydroxyurea have proved to be successful strategy when dealing with such patients.

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Conflict of interest:

No conflict of interest.

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