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Case Reports

ST-Segment Elevation Myocardial Infarction and Bleeding Complications in *JAK2*-Negative Polycythemia

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Abstract

Thrombotic and bleeding complications are major causes of morbidity and mortality in patients with polycythemia vera, who predominantly present with an alteration in the *JAK2* gene. Because of their hypercoagulable state and risk of hemorrhage, patients with polycythemia vera who present with an acute myocardial infarction pose a challenge to physicians. This case report describes the presentation and treatment of a Hispanic patient with *JAK2* V617F–negative primary polycythemia who developed cardiac arrest and ST-segment elevation myocardial infarction owing to complete occlusion of the left anterior descending artery as well as bleeding complications and postmyocardial pericarditis.

Keywords: Myocardial infarction; polycythemia; erythrocytosis

Case Report

Presentation and Physical Examination

A 52-year-old Hispanic man acutely developed, while driving, severe substernal chest pain that radiated to the neck and left upper extremity, shortness of breath, and fatigue. During assessment, the emergency medical services team observed electrocardiogram findings of ST-segment elevations in leads V_2 to V_6. While en route to the hospital, the patient went into cardiac arrest. Ventricular fibrillation was documented, and 1 shock was delivered.

Medical History

The patient's past medical history denoted untreated *JAK2* V617F–negative primary polycythemia diagnosed during adolescence. He had previously received intermittent phlebotomy until 6 years ago, when he was last assessed. His brother and mother were diagnosed with polycythemia but had no documented cardiovascular events or bleeding complications. He reported no hypertension, diabetes, or hyperlipidemia and no consumption of tobacco, alcohol, steroids, or recreational drugs.

Technique

On admission, a follow-up electrocardiogram revealed ST-segment elevation in leads I, aVL, and V_2 through V_5 and reciprocal ST-segment depression in leads III and aVF (Fig. 1), which was consistent with an acute, anterolateral, and

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anteroseptal ST-segment elevation myocardial infarction (MI). The patient went into cardiac arrest on 2 additional occasions. Ventricular fibrillation and Torsades de Pointes (Fig. 2) were documented. He was shocked twice, and advanced cardiac life support measures were followed.

Blood analysis showed elevated troponin I (0.060 μg/L), hemoglobin (214 g/L), hematocrit level (65.1%), erythrocyte count (7.51×1,012/L), and leukocytes (15.1×109/L). Platelet count (218×109/L), activated partial thromboplastin time (29.5 seconds), total cholesterol (4 2.9 mmol/L), and low-density lipoprotein (18.98 mmol/L) levels were in the normal range. High-density lipoprotein levels (5.46 mmol/L) were decreased. Triglycerides were elevated (92.82 mmol/L). He had a negative drug urine screening test. A transthoracic echocardiogram revealed mild to moderate concentric left ventricular hypertrophy; severely reduced left ventricular function, with an ejection fraction (EF) of 20% to 25%; severe anteroseptal hypokinesis; anterior wall akinesis; and grade 1 diastolic dysfunction.

During the emergent coronary angiography, an Impella CP pump CPT 33990 (Abiomed) was inserted into the right femoral artery for hemodynamic support, followed by heparin drip and cessation of ventricular fibrillation episodes. The left main coronary artery arose normally from the left sinus of Valsalva, bifurcated into the circumflex (free of significant disease) and into the completely proximately occluded left anterior descending artery (LAD) (Fig. 3). Percutaneous coronary intervention on the LAD included angioplasty, with placement of a drug-eluting stent (XIENCE [Abbott Vascular] 3.25 × 23 mm), postdilated with a 3.5 high-pressure balloon, with evidence of aneurysmal dilation of the proximal LAD, less than 20% residual in the proximal segment, and distal Thrombolysis in Myocardial Infarction grade 3 flow (Fig. 4). Initially, an image suggestive of left main artery disease (with differential diagnosis of stenosis vs thrombotic occlusion) was observed (Fig. 3). This suggestive image, however, was not present upon further contrast injection and after the culprit vessel was repaired (Fig. 4). Thus, the image could have been secondary to the injection model rather than the presence of a thrombus or stenotic lesion. In contrast, the right coronary artery emerged normally from the right sinus of Valsalva as the dominant vessel and was free of significant pathology.

The patient received dual antiplatelet therapy with 81 mg aspirin, 90 mg ticagrelor, and myelosuppressive

Key Points

- Elevated risk of thrombosis (eg, cardiovascular events) and bleeding is present in patients with PV, who will require detailed and complex management in case of such events.
- Although the majority of patients with PV carry the *JAK2* V617F alteration, a minority may present with somatic mutations involving exons 12 and 13 in the *JAK2* gene or inherited germline mutations involving familial or congenital polycythemia, erythropoietin receptor alteration, or high oxygen-affinity hemoglobin.
- There is no current standard consensus on management of acute MI in patients with PV.

Abbreviations and Acronyms

CAD	coronary artery disease
EF	ejection fraction
LAD	left anterior descending artery
MI	myocardial infarction
PV	polycythemia vera

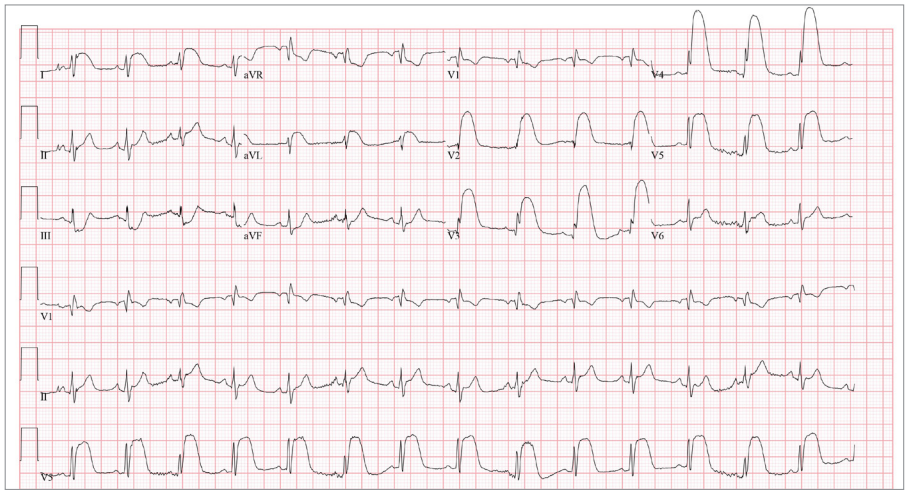

Fig. 1 Initial electrocardiogram at the emergency department with anterolateral and septal ST-segment elevation myocardial infarction evidenced in leads I, aVL, and V_2 through V_5 and reciprocal ST-segment depression in leads III and aVF.

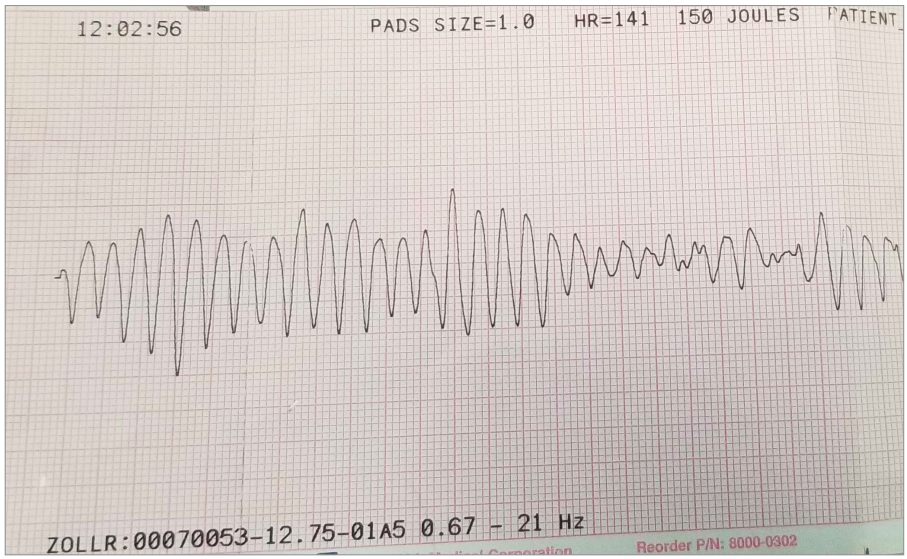

Fig. 2 In-hospital electrocardiogram showing an episode of Torsades de Pointes.

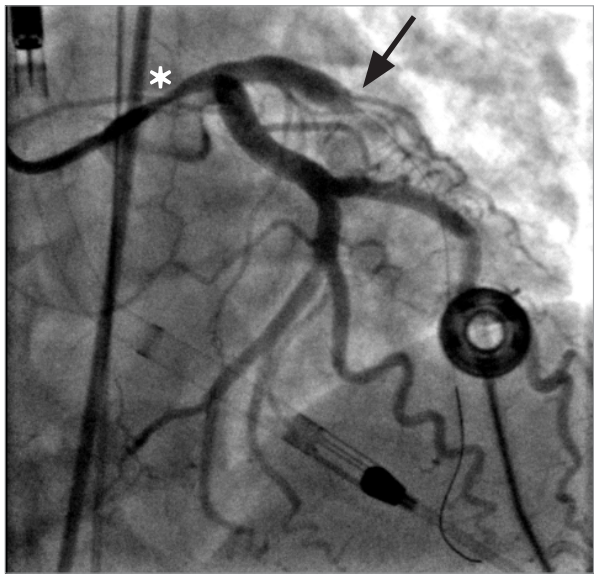

Fig. 3 Right anterior oblique caudal projection of coronary angiography showing complete occlusion of the left anterior descending artery (arrow) and suggestive left main artery disease (asterisk).

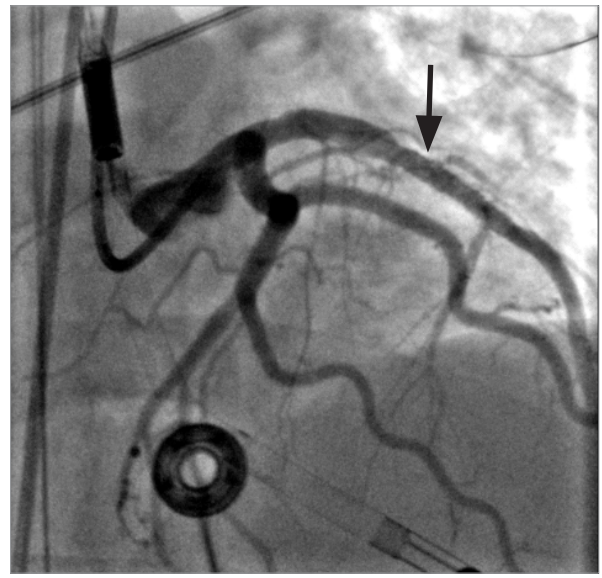

Fig. 4 Right anterior oblique caudal projection of coronary angiography showing patent left anterior descending artery after percutaneous coronary intervention with drug-eluting stent placement (arrow) and normal left main coronary artery.

therapy with hydroxyurea, 1 g daily. Postoperative physical examination was significant for excessive bleeding from the catheter insertion site in the right groin as well as gross hematuria without clots from a Foley catheter. Heparin drip was discontinued, and the Impella CP pump was removed with resolution of bleeding.

A hematology workup was initiated in response to the patient's elevated hemoglobin levels and hematocrit levels as well as the excessive bleeding episode. The patient, however, deferred genetic testing for alterations in *JAK2* exons 12 and 13, erythropoietin receptor, and high-affinity hemoglobin workup.

His postoperative stay at the coronary care unit was complicated by intermittent sharp chest pain radiating to the left scapula, a nonsustained fever of 100.9 °F, and loud pericardial rubbing. Serial electrocardiograms revealed new ST-segment elevation in precordial leads (Fig. 5, Fig. 6). Blood analysis revealed marked troponin I elevation in the first (93.700 μg/L) and second (56.500 μg/L) sets and elevated creatine kinase–MB

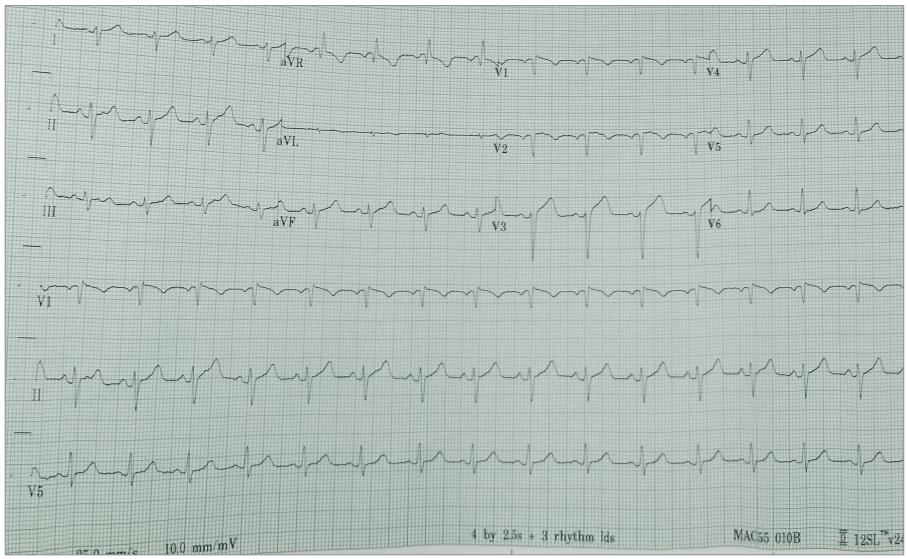

Fig. 5 Electrocardiogram performed during recurrence of chest pain. The ST segment is starting to elevate in precordial leads. The low-voltage QRS interval in aVL might suggest pericardial effusion.

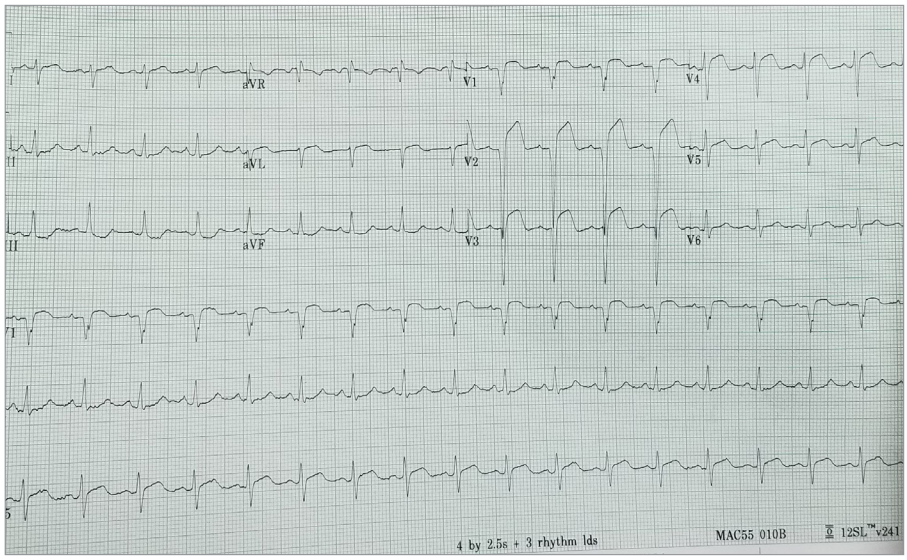

Fig. 6 Follow-up electrocardiogram performed because of increased intensity of chest pain. Note the extension of the ST-segment elevation in precordial leads.

fraction (1.11 μmol/L). He was assessed as having post-MI pericarditis and was treated with high-dose aspirin (650 mg twice a day) with resolution of symptoms. Additionally, hydroxyurea was increased to 1 g twice a day because the patient also deferred phlebotomy as treatment for his polycythemia.

Outcome

Follow-up studies showed downtrending erythrocyte count (6.43×1,012/L), hemoglobin (189 g/L), hematocrit (53.7%), and activated partial thromboplastin time (21.2 seconds). Transthoracic echocardiogram evidenced improvement in EF to 35% with no pericardial effusion. As part of his postdischarge treatment, the patient was fitted with a wearable cardioverter-defibrillator because of his previous episodes of ventricular fibrillation and reduced EF. He was discharged home on 81 mg aspirin orally daily, 75 mg clopidogrel orally daily, 3.125 mg carvedilol orally twice daily; 2.5 mg lisinopril orally daily, 20 mg rosuvastatin orally once a day at bedtime, 1 g hydroxyurea orally twice daily, and follow-up appointments.

Latest Follow-Up

One week later, the patient was found to be euvolemic and without pulmonary edema or other positive physical examination findings. He continued medical therapy and was referred to electrophysiology for evaluation for implantable cardioverter-defibrillator placement. The patient continued to defer any hematology follow-up. Three months later, he reported moderate exertional dyspnea and intermittent orthopnea, which promoted

initiation of 40 mg furosemide orally daily. Medical therapy for cardiomyopathy was optimized by increasing carvedilol to 6.25 mg orally twice a day. Implantable cardioverter-defibrillator placement was not indicated because the episodes of ventricular fibrillation were secondary to the MI. A chest x-ray and echocardiography were requested for the evaluation of left ventricular EF, pulmonary edema, and pleural effusion, but the patient declined any further management of his condition.

Discussion

Polycythemia vera (PV) is a chronic myeloproliferative neoplasm, characterized by erythrocytosis, some degree of leukocytosis, and thrombocytosis in 40% of patients.[1] Blood hyperviscosity caused by persistently high levels of hematocrit and hemoglobin places patients with polycythemia at an increased risk of cardiovascular events, such as thrombosis,[2,3] and subsequent coronary artery disease (CAD).[4,5] Bleeding, thrombotic, and vascular complications are the major causes of morbidity and mortality in PV.[2] This patient presented with acute MI, cardiogenic shock, recurrent ventricular fibrillation, bleeding, and pericarditis, which significantly affected his quality of life.

Research has elucidated the mechanisms of thrombogenesis that lead to this increased risk. Elevated hematocrit levels induce platelets to be pushed centrifugally and adhere to vessel wall collagen, initiating thrombus formation.[6] Vascular damage and elevated erythrocytes directly enhance platelet adhesion and activation, promote leukocyte-platelet interactions, and contribute to activation of the coagulation system.[6] As seen in this patient, these summative events, which can be complications of untreated PV, can lead to MI and even sudden death.[2]

Men with hematocrit levels of 50% or higher are 2.4 times more likely to die from CAD, which correlates borderline polycythemia to an increased cardiovascular mortality risk.[7] Likewise, hemoglobin levels of 17.0 g/dL or greater are associated with an increased risk for CAD and new cardiac events.[8] In addition to maintaining hematocrit levels over 50% and hemoglobin levels over 180 g/L, the patient in this case had an intermediate thrombotic risk level as a result of his age being between 40 and 60 years and having an altered lipid profile (a traditional risk factor).

Increased leukocytes and *JAK2* V617F alteration are potential determinants of thrombotic risk in PV.[2] The V617F alteration in exon 14 of the *JAK2* gene is detected in 97% of patients with PV.[9] Cases have been reported of patients with *JAK2*-positive PV developing MI with single vessel involvement and cardiac arrest.[10-12] Although only a minority of patients with PV do not carry the alteration, this proportion is higher in familiar cases.[13] This patient tested negative for *JAK2* V617F alteration; therefore, other somatic mutations involving exons 12 and 13 in the *JAK2* gene[14] and inherited germline mutations involving familial or congenital polycythemia, erythropoietin receptor alteration, and high oxygen-affinity hemoglobin[9] must also be assessed. Considering the long duration of his polycythemia and his family history, the determination of serum erythropoietin level can also be part of the initial diagnostic approach for *JAK2*-unaltered erythrocytosis in this patient.[15] He also presented with an elevated leukocyte count, which is considered another diagnostic criteria in *JAK2*-unaltered erythrocytosis.[16]

Even though there is no current standard consensus on the management of acute MI in patients with polycythemia, percutaneous coronary intervention continues to be the gold standard.[17] These patients should be treated similarly to those without hematologic diseases because there appears to be a sizable outcome advantage with this approach.[18] Thus, this patient received percutaneous coronary intervention with a drug-eluting stent to a completely occluded LAD with successful flow recovery.

In PV, standard antiplatelet therapy combined with recurrent phlebotomy reduced the risk of reinfarction by 70% in patients with CAD.[19] Cytoreductive therapy, along with aspirin, has also provided the greatest benefit in mortality reduction with minimal risk for bleeding.[20] The patient was initially treated with dual antiplatelet therapy (ticagrelor and aspirin) to prevent stent thrombosis, along with cytoreductive therapy. Considering that this patient's condition evolved to a high-risk polycythemia[21] and that he deferred phlebotomy, he was discharged with dual antiplatelet therapy (clopidogrel and aspirin) to prevent new thrombotic events as well as hydroxyurea at increased dose to achieve a goal hematocrit level of 45%.[22]

This case report illustrates the complex presentation and treatment of a patient with *JAK2* V617F–negative primary polycythemia, noncompliant to hematologic

treatment, with a thrombotic event and bleeding complications, who developed ST-segment elevation myocardial infarction and cardiac arrest. To improve clinical outcomes, it is imperative to take a multidisciplinary and patient-centric approach to the management of acute MI in patients who present with either erythrocytosis or PV. This report is presented to contribute valuable information to clinicians who encounter a similar complex case.

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