ST-segment Elevation Myocardial Infarction in a Patient with Polycythemia Vera Managed with High-dose Tirofiban Pre-treatment, Aspiration Thrombectomy, and Paclitaxel-eluting Stent Implantation

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Abstract

While acute coronary syndromes inclusive of ST-elevation myocardial infarction (STEMI) have been described in patients with polycythemia vera (PCV), optimal pharmacologic and interventional management strategies in the setting of drastically elevated platelet counts remain unclear. To our knowledge this is the first reported case of STEMI with massive thrombus burden in a patient with PCV treated successfully with high-dose tirofiban bolus and infusion, followed by staged aspiration thrombectomy and drug-eluting stent implantation. Whether a strategy of antiplatelet and antithrombotic pre-treatment prior to PCI with or without thrombectomy will consistently yield satisfactory outcomes in PCV patients presenting with acute coronary syndrome (ACS) or STEMI, remains a matter of speculation. Nevertheless, based on the relevant pathobiologic considerations and review of the available literature, we feel the strategy employed in this case to be a reasonable one when clinical circumstances render it feasible.

Keywords
Polycythemia vera (PCV), massive thrombus burden, aspiration thrombectomy, glycoprotein inhibitors, ST-segment myocardial infarction

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underwent repeat angiography. Subsequent angiography demonstrated flow improvement to TIMI 3 in the LAD and decrease in the thrombus burden, which now appeared organized, well circumscribed, and limited to the LAD with no side branch or LMCA extension. Percutaneous coronary intervention (PCI) was performed with aspiration thrombectomy using a 6 French (Fr) Medtronic Export catheter, with resultant removal of a significant amount of atherothrombotic debris and progressive angiographic improvement after 10 aspiration passes (see Figures 2 and 3). Histopathologic analysis of the aspirate subsequently demonstrated abundant aggregates of neutrophils, necrotic and degenerated cells, and fibrin, but notably, scant platelet aggregates. The residual 70% lesion was addressed with the implantation of a 3 x 32mm Taxus paclitaxel-eluting stent, deployed at 18ATM. Excellent results were noted in the treated segment of LAD by angiography and by intravascular ultrasound with no sidebranch compromise or evidence of distal embolization. (see Figure 4). Cardiac biomarkers drawn post-PCI, continued to decline. A pre-discharge transthoracic echocardiogram demonstrated a small area of hypokinesis at the apex, with normal overall left ventricular systolic function. Clinically, the patient did well for the remainder of the hospital course and was maintained on enteric-coated acetylsalicylic acid (ECASA) 325mg and clopidogrel 75mg daily following discharge. The patient has remained asymptomatic and free of cardiovascular events including stent thrombosis for over one year on dual antiplatelet therapy.

Discussion

Polycythemia vera is a myeloproliferative disorder characterized by the overproduction of various cell lines including leukocytes, erythrocytes, and platelets. Thrombotic complications, including MI, remain the primary cause of mortality and have been attributed to increased whole blood viscosity, quantitative, and perhaps qualitative platelet abnormalities, and to the presence of leukocytosis. While coronary thrombosis is the predominant mechanism of MI in patients with PCV, there is evidence that marked intimal proliferation may also play a role.5

Cardiac catheterization and percutaneous coronary intervention in patients with PCV has reportedly been associated with acute total aortic occlusion and recurrent stent thrombosis. Other complications of PCV that have been reported include splenic rupture in the setting of peri-PCI use of glycoprotein IIb/IIIa inhibition, as well as ventricular septal rupture as a complication of a small anteroseptal MI in a patient with only minimal ectasia in the LAD. Varying degrees of thrombus burden have also been described in PCV patients presenting with acute coronary syndromes and acute MI. Angiographically evident intracoronary thrombus may be quantified via the TIMI scoring system and is divided into five grades. Per this schema, thrombus grade zero (G0) represents the absence of thrombus. In grade one (G1), possible thrombus is present with such angiographic characteristics as reduced contrast density, haziness, irregular lesion contour, or a smooth convex meniscus at the site of total occlusion suggestive, but not diagnostic of thrombosis. In thrombus grade two (G2), there is definite thrombus with greatest dimensions less than or equal to half the vessel diameter. In thrombus grade three (G3), there is definite thrombus with greatest linear dimension greater than half but <2 vessel diameters and in thrombus grade four (G4) there is definite thrombus with the largest dimension ≥2 vessel diameters. In thrombus grade five (G5) there is total thrombotic occlusion. A thrombus grade ≥4 as encountered in the case described implies a large thrombus burden. Contrast angiography has a sensitivity of 20% and a specificity approaching 100%. Percutaneous interventions of thrombotic lesions may be associated with such complications as distal embolization, no reflow, side branch occlusion, and abrupt vessel closure. Intracoronary infusions of fibrinolytic agents, adenosine, and verapamil have all been demonstrated in case reports and small studies to diminish no-reflow, however, few definitive data currently exist in support of these adjunctive therapies. Other pharmacologic therapies that have been studied include systemic, intracoronary, and site-specific delivery of glycoprotein IIb/IIIa inhibitors.

The central role of platelet activation and aggregation in the pathogenesis of vascular thrombosis has been extensively studied. The glycoprotein (Gp) IIb/IIIa (integrin \( \alpha_{\text{IIb}} \beta_{3} \)) receptor mediates the final common pathway for platelet aggregation via its interaction with soluble fibrinogen. Three parenteral Gp IIb/IIIa inhibitors (GPIs) are currently available for clinical use. Abciximab (c7E3) is a chimeric humanized murine monoclonal antibody fragment directed against the Gp IIb/IIIa receptor, but also binds vitronectin and Mac-1 receptors. Tirofiban and eptifibatide are high-affinity, semi-synthetic inhibitors that are often grouped together as ‘small-molecule GPIs’ in deference to their low molecular weights relative to abciximab. The small-molecule GPIs are associated with high levels of steady-state platelet inhibition especially during longer infusion periods. In contrast, Abciximab evidences
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excellent acute inhibition of platelet aggregation with a slow downward drift during the recommended 12-hour infusion period, with longer infusions rarely used today given data from Global utilization of strategies to open occluded arteries (GUSTO) IV ACS, suggesting higher rates of adverse events when abciximab is used in this capacity. The clinical benefits of the small-molecule inhibitors are most pronounced in patients undergoing early percutaneous intervention after a period of 48 hours. In the case described, the choice of high-dose tirofiban was deliberate and predicated on the previously detailed clinical and platelet inhibition data as well as on specific stoichiometric considerations. While the current abciximab bolus and infusion dosing strategy was developed to provide ≥80% inhibition of stimulated platelet aggregation in individuals with normal platelet counts, the ratio of abciximab molecules to glycoprotein receptor is relatively low (estimated at 2:1) and, therefore, may not provide adequate platelet inhibition in the setting of elevated
platelet count or super-normal receptor expression. In contrast, the analogous ratio with small-molecule GPIs has been estimated to be at least 50:1 but perhaps as high as several hundred to one. Therefore, it was postulated that a small molecule GPI used in the capacity of an aggressive dosing strategy and extended pre-PCI infusion might be a more attractive choice than abciximab in this setting. The near-absence of platelet aggregates upon histologic analysis of the aspirate ostensibly confirms the validity of this strategy. The aggressive use of aspiration thrombectomy facilitated retrieval of a considerable amount of atherothrombotic material with no side branch compromise by angiography and no vessel trauma by angiography and intravascular ultrasound (IVUS). Furthermore, little or no embolization was seen on the angiographic images or evidenced by biomarker release post-PCI.

Long-term management of patients with PCV includes use of low-dose aspirin, which has been shown to reduce the rate of major thrombus and cardiovascular death and is therefore recommended in all PCV patients in the absence of contraindications. However, no data exist with respect to dual antiplatelet therapy with aspirin plus a thienopyridine. There are also no established guidelines for treating patients with ACS or STEMI in the setting of PCV. Phlebotomy with volume replacement and close hemodynamic monitoring has been suggested as an adjunctive approach to standard treatments. Whether a strategy of antiplatelet and antithrombotic pre-treatment prior to PCI with or without thrombectomy will consistently yield satisfactory outcomes in PCV patients presenting with ACS or STEMI, remains a matter for speculation. Nevertheless, based on the relevant pathobiologic considerations and a review of the available literature, we feel the strategy employed in this case to be a reasonable one when clinical circumstances render it feasible. However, we acknowledge that the window of freedom from chest pain encountered in our patient was a fortunate, if uncommon occurrence in STEMI, which allowed us to extend the antiplatelet/antithrombotic pre-treatment regimen for 24 hours prior to definitive mechanical therapy for the infarct-related vessel.

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