

Therapeutic Challenges in the Management of Acute Myocardial Infarction in Polycythemia Vera

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Introduction

Polycythemia rubra vera (PV) is a chronic myeloproliferative disorder characterized by elevated red cell mass with an increased risk of both thrombosis and bleeding. Thromboembolic events are the most significant and life-threatening complications associated with PV [1]. Here, we report a rare case of PV presenting as acute myocardial infarction (MI) and briefly discuss the applicability of current management strategies for MI in the context of PV.

Case Report

Patient is a 73-year-old white male presented to the emergency department with sudden onset of severe chest pain. He reported history of hypertension and hyperlipidemia but denied use of tobacco or recreational drugs. On admission, physical examination was unremarkable except for splenomegaly. Laboratory data was significant for hemoglobin of 22 g/dl, hematocrit of 66%, and peak troponin of 4.3 ng/ml. White cell count was 9.6×10^3 /dl, platelet count was 357×10^3 /dl and biochemistry panel was normal. Electrocardiogram showed mild ST depression in the inferior leads. Echocardiogram was normal without regional wall motion abnormalities and an ejection fraction of 50-55%. Overall, the clinical picture was consistent with non-ST elevation myocardial infarction and treatment with aspirin, heparin, metoprolol, simvastatin and lisinopril was initiated. Subsequent coronary angiography showed diffuse three-vessel disease and cardio thoracic surgery was consulted for coronary bypass surgery (CABG). Hematology consult was sought in view of polycythemia and further evaluation confirmed polycythemia rubra vera (low erythropoietin, JAK-2 mutation positive and massive splenomegaly). He was treated with intermittent phlebotomy and volume replacement. Three-vessel coronary artery bypass graft (CABG) was done once hematocrit less than 45%. Peri- and post-operative course was uncomplicated and he was discharged with recommendations of long-term intermittent phlebotomy apart from aspirin, statin and beta-blocker. He was scheduled to follow up with hematology for further consideration of myelosuppressive agents.

Discussion

PV is a myeloproliferative neoplasm characterized by clonal proliferation of myeloid cells with predominant elevation in red cell mass. The most common complications of PV include thrombosis, bleeding and transformation to myelofibrosis or leukemia. The thrombotic events could be both arterial and venous. It is often diagnosed incidentally on a routine laboratory testing prior to a major

thrombotic event. However, myocardial infarction as the initial manifestation of PV as in our patient is unusual [2-9]. Although hyper viscosity is commonly considered to be the major pathogenic mechanism for arterial thrombotic complications in PV, a significant number of patients have other risk factors like smoking, hypertension, arguing strongly in favor of additive risk and shared pathogenesis [10].

Cytoreductive treatment with phlebotomy to achieve a goal hematocrit of 45% is crucial in optimizing the outcomes in patients with PV [11]. The role of low dose aspirin in preventing thrombotic complications in PV is well known [12]. The patients with age greater than 60 years and prior history of thrombosis are considered high risk for thrombotic events and are often treated with additional myelosuppressive agents such as hydroxyurea. Recently ruxolitinib, a JAK1/2 inhibitor was also approved to treat these patients.

There is no standard consensus on management of acute MI in patients with PV. In one study, standard anti platelet therapy combined with recurrent phlebotomy reduced the risk of re-infarction by 70% in patients with acute coronary syndrome [13]. In patients with PV presenting with acute coronary syndrome, it was reviewed that cytoreductive therapy along with aspirin provided greatest benefit in mortality reduction with a minimal risk for bleeding [14]. Few studies suggested the use of anticoagulants such as warfarin along with antiplatelet agents will help prevent recurrent thrombosis [8,15,16]. However, the effectiveness of clopidogrel, glycoprotein IIb-IIIa inhibitors and intervention with coronary stents or CABG has not been rigorously studied in patients with PV.

Percutaneous coronary intervention (PCI) is the standard of care for treatment of acute MI. Nevertheless, patients with PV presenting with acute MI due to underlying hyperviscosity are reportedly associated with acute aortic occlusion and recurrent stent thrombosis despite appropriate antiplatelet therapy [17-19]. Surgery in patients with PV was notably associated with increased morbidity and mortality. The post-operative mortality was four times higher in patients with elevated hematocrit prior to surgery [17]. It is therefore important to consider pre-procedure phlebotomy to achieve a goal hematocrit of 45% whenever possible. There is limited data on use of other revascularization methods such as fibrinolysis or coronary artery bypass surgery in these patients [3,7,8]. A brief review on the management of acute MI in patients with PV from published case reports in english literature is shown in Table 1. The ideal revascularization strategy in terms of PCI versus CABG remains elusive in these patients. Studies showed that even with adequate control of blood counts in PV patients, thrombotic risk can only be decreased but couldn't be totally ameliorated [17].

Study	Age/ Sex	Presentation	HCT	Initial Treatment	PCI finding	Intervention	Post-op treatment	Long term treatment	Outcome	Remarks
Vengoni et al. [9]	66/F	STEMI	57%	Aspirin Phlebotomy Heparin	Occlusive thrombus in proximal LAD	Urokinase 500,000 units followed by PTCA	Within 24 hours developed refractory cardiogenic shock	Not reported	Dead	Hematocrit 41% prior to first PCI. Repeat PCI showed no thrombosis.
Bahbahani et al. [3]	37/M	STEMI	50%	Aspirin Plavix Lovenox	Not performed due to lack of availability in that facility	Reteplase 10 units bolus, then 10 units given intravenously over 30 min,	-	Aspirin Hydroxyurea Phlebotomy	Alive	Myocardial perfusion scintigraphy one month later was normal
Osada et al. [7]	65/M	Stable angina	59%	Aspirin (until day before surgery) Heparin (until morning of surgery) Phlebotomy intra-op	Proximal LAD showed 99% ; Mid LAD showed 75% , OM showed 90% stenoses	CABG	Post op day 1 developed STEMI . PCI showed thrombosis of native and graft as well s/p PTCA	Aspirin Plavix Warfarin	Alive	
Oz et al. [8]	46/M	Unstable angina	47%	Aspirin Phlebotomy	LAD showed 80-90% ; LCX showed 70%; RCA showed 80% stenoses	CABG	Heparin in early post op period	Aspirin, Plavix, Warfarin	Alive	Diagnosed with PV ~2 years prior. Hematocrit was 42% prior to CABG
Oz et al. [8]	61/F	Stable angina positive stress test	40%	Aspirin Hydroxyurea	LAD showed 80% RCA showed 90% stenoses	CABG	Heparin in early post op period	Aspirin, Plavix, Warfarin Hydroxyurea	Alive	On treatment for PV ~ 3 years prior
Wu et al. [2]	34/M	STEMI	65%	Aspirin Plavix Heparin Phlebotomy	Mid LAD 60% occlusion with a distal thrombotic occlusion	No intervention	Phlebotomy	Not reported	Alive	Discharged with hematology follow up
Chan et al. [4]	42/M	Unstable angina	71%	Aspirin, Heparin, phlebotomy	LAD thrombosis distal to perforating branches otherwise normal coronaries	No intervention	-	Warfarin	Alive	On day 7 echo showed large intraventricular thrombus
Hermanns et al. [6]	30/M	Acute MI	61%	-	Not performed	Tissue plasminogen activator 100 mg/2hr	Developed refractory cardiogenic shock failed resuscitation		Dead	Autopsy showed no evidence of atherosclerosis but marked intimal proliferation noted

Table 1: Information from published case reports on management of coronary artery disease and polycythemia vera.

HCT: Hematocrit on Presentation; PCI: Percutaneous Coronary Intervention; F: Female; M: Male; PV: Polycythemia Vera; MI: Myocardial Infarction; STEMI: ST Elevation Myocardial Infarction; LAD: Left anterior descending artery; LCX: Left circumflex artery; RCA: Right coronary artery; OM: Obtuse Marginal; PTCA: Percutaneous Transluminal Coronary Angiography; CABG: Coronary Artery Bypass Graft.

Conclusion

The management of patients with PV presenting with acute MI is complex. The initial treatment should focus on cytoreductive treatment prior to proceeding with intervention. The superior revascularization strategy (PCI versus CABG) and adequate antithrombotic therapy (single or dual antiplatelet therapy +/- anticoagulants) needs further investigation. It is important to consider adequate use of

myelosuppressive agents such as hydroxyurea or ruxolitinib in high risk patients to prevent future thrombotic events.

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