Case Report

Thrombosis of Coronary Arteries in a Patient With Polycythemia Vera During the Myocardial Revascularization: A Case Report

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Introduction: Coronary artery bypass grafting in a patient suffering from polycythemia vera is clinically rare and extremely challenging. There is no established protocol regarding the management of these patients because the number of patients in this circumstance is very small. Expressed thrombotic risk in patients suffering from polycythemia vera is highly emphasized in patients with coronary artery disease. Only a few cases have been reported of performing coronary artery bypass grafting, and in those cases a successful outcome seems to be an exception.

Case presentation: We report a case of a 73-year-old male caucasian patient suffering from frequent daily chest pain and unstable angina with a 75% stenosis of the left main coronary artery and a subocclusion of proximal right coronary artery undergoing coronary artery bypass grafting, where despite following all the management algorithms and hematologic and cardiologic guidelines properly during the preoperative workup, the patient had a complex postoperative recovery with thrombosis of native coronary vessels—the left anterior descending artery and right coronary artery.

Conclusion: Further investigation is needed regarding the effect of deciding between strategies in the domain of cardiac surgery as well as in the hematologic domain on the final outcome. It would be absolutely necessary to conduct a global trial to investigate the preferred cardiosurgical procedure (OPCAB or on-pump CABG).
Key words: Coronary artery bypass – Polycythemia vera – Thrombosis – Coronary vessels – Hydroxyurea

Myeloproliferative disease is a group of disorders caused by the clonal expansion of abnormal hematopoietic stem cell. According to the 2016 revision of the World Health Organization (WHO) classification, the disease includes the following types: polycythemia vera (PV), primary myelofibrosis (PMF), essential thrombocythemia (ET), chronic myeloid leukemia (CML), chronic neutrophilic leukemia (CNL), chronic eosinophilic leukemia not otherwise specified (CEL NOS), and myeloproliferative neoplasms unclassifiable.1

PV is a chronic myeloproliferative disorder classified as a clonal stem cell disease that includes myelofibrosis with myeloid metaplasia and CML. Clinically, PV can occur with thrombohemorrhagic complications and is associated with venous and arterial thrombosis. Pathogenesis of thrombotic events related to PV depends on increased blood cell count (erythrocytosis, leukocytosis, thrombocytosis), abnormality of blood cells caused with combined quantity and quality changes, and influence of concomitant factors (age, obesity, hypertension, hyperlipidemia).2,3

Expressed thrombotic risk in patients suffering from PV is highly emphasized in patients with coronary artery disease (CAD). Only a few cases have been reported where coronary artery bypass grafting (CABG) was performed with a successful outcome being an exception. We report a patient with CAD suffering from PV that had undergone CABG having an extremely complex postoperative recovery with thrombosis of native left anterior descending artery (LAD) and right coronary artery (RCA).3,4

Case Report

A 73-year-old male caucasian patient with an unstable angina and frequent daily chest pain was referred from a secondary care institution with a 75% stenosis of the left main coronary artery (LMCA) and a subocclusion of the proximal right coronary artery (RCA) to the Department of Cardiac Surgery in our hospital. Two years ago, he was diagnosed with myeloproliferative disease—PV, grade I myelofibrosis, verified by a bone marrow biopsy. He was not compliant with his hematology check-ups, nor on regular treatment except occasional phlebotomies, last performed 4 months before this referral. He suffered a transient ischemic attack 10 months ago, and was diagnosed with diabetes, hypertension, hyperlipidemia, hyperthyreosis, diffuse hepatic lesion, splenomegaly associated with the myeloproliferative disease, low grade stenosis of both carotid arteries, and a benign prostatic hyperplasia. The day after admittance his red blood cell count (RBC) was \(6.06 \times 10^{12}/L\) (Fig. 1), white blood cell count (WBC) was \(27.1 \times 10^9/L\), platelet count (PC) was \(201 \times 10^9/L\) (Fig. 2) and hematocrit (Ht) was 0.542 (Fig. 3). He was examined by a hematologist who recommended hydroxycarbamide \(2 \times 500 \text{mg}\) and a therapeutic phlebotomy every other day. During the preoperative workup, his RBC, WBC, and Ht increased (Figs. 1–3) but because he was hemodynamically stable, a thorough preoperative preparation was performed. Phlebotomy was performed 3 times, the last one 24 hours before the surgery with the goal to reduce the Ht level to 0.45%, according to the hematologic guidelines.3,5 The patient was on low-dose acetylsalicylic acid the whole perioperative time. The hydroxycarbamid daily dose was reduced to 500 mg/d before surgery. On the day of surgery, RBC was \(5.23 \times 10^{12}/L\) (Fig. 1), WBC was \(13.5 \times 10^9/L\), PC was \(170 \times 10^9/L\) (Fig. 2), and Ht was 0.468 L/L (Fig. 3). These values were satisfying so the patient was ready for operation.

Preoperative coronarography showed a 75% stenosis of distal LMCA and a subocclusive stenosis.
of the proximal RCA. Echocardiography showed ejection fraction (EF) of 53% with a posterior segment hypokinesia. Based on these results and according to the guidelines, the only possible treatment was aortocoronary bypass procedure. On-pump CABG was done considering the course of events and the complications described in the recent literature. After median sternotomy, an intraoperative sternum and sternal bone marrow biopsy were performed. After cannulation of aorta and right atrium, the heart was stopped in an intermittent warm blood cardioplegia. RCA was calcified along its entire course, so the venous bypass was chosen to be placed to the posterior diagonal artery (PDA), which was slightly less calcified with the distal anastomosis performed. After that, the first obtuse marginal artery (OM1) was prepared and the venous graft was anastomosed to the OM1. LAD was severely atherosclerotic changed in its entire course, except the middle part where there was a short slightly less changed segment, so left internal thoracic artery (LITA)–LAD anastomosis was performed while the LITA itself had a good flow. After removal of the cross-clamp and the construction of the 2 proximal anastomoses to the aorta, the patient was weaned off from the cardiopulmonary bypass (CPB). Flows were measured using a flowmeter (Flash Probe Compatible HT 323 Transonic Flow-QCTM Meter; Transonic Systems Inc, Ithaca, New York). They were good on the PDA and OM1 bypasses, but extremely low on the LITA–LAD bypass (2–3 mL/min). Heart was stopped again and the LITA–LAD bypass was reconstructed. After the removal of the cross-clamp, the measured flow was still low (2–3 mL/min) and additional venous bypass to the distal LAD 2 cm distally from the LITA–LAD anastomosis was administered using a heart stabilizer (tissue stabilizer Octopus 4.3; Medtronic, Inc, Minneapolis, Minnesota). After the opening of the distal LAD, a 1.5 mm diameter intracoronary probe was placed through the proximal and distal LAD, as well as through the LITA–LAD anastomosis and showed that the anastomoses were passable. After that, the distal anastomosis construction was done with the venous graft and the proximal anastomosis was placed to the venous graft for OM1 as Y-graft. The patient was weaned off CPB. Measured, flows were still inadequate (3–4 mL/min) so an intraaortic balloon pump (IABP) was placed through the left femoral artery. Transesophageal echocardiography (TEE) performed intraoperatively after weaning from CPB showed akinesis of the apex and the dyskinesis of the septum, which implied that something was wrong with the native LAD, so an emergency recoronarography was performed. It showed passable venous bypasses on OM1 and PDA with an existing thrombus in the proximal RCA, occluded native RCA and thrombi in the proximal and middle LAD. LAD was occluded on the LITA–LAD anastomosis site and the great saphenous vein (GSV)–LAD anastomosis site. There
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was no visible flow through the GSV–LAD and the LITA–LAD anastomoses. The cardiologist performing the coronarography did not opt for percutaneous coronary intervention (PCI) considering the multiple thrombi in the native LAD. He performed balloon dilatation but there was still no visible flow through the anastomoses.

Patient was on medium dose inotropic support with noradrenaline (0.15–0.20 μg/kg/min) and dobutamine (5–9 μg/kg/min). On that same day levosimendan was administered. Cardioselective enzyme levels were high, suggesting an intraoperative infarction of the LAD. After the hemodynamic stabilization of the patient on the second postoperative day, IABP was removed and warfarin was administered. Pigrel and acetylsalicylic acid were administered on the third postoperative day. Ht was observed during the whole postoperative recovery. Hydroxycarbamid was administered on the fourth postoperative day, considering the complicated course of events. On the fifth postoperative day, the patient was transferred from the intensive care unit (ICU) to a regular ward in a stable hemodynamic condition. RBC was 3.16 × 10^{12}/L (Fig. 1), WBC was 11.5 × 10^{9}/L, PC was 446 × 10^{9}/L (Fig. 2), and Ht was 0.295 L/L (Fig. 3). The postoperative echocardiography showed significantly reduced contractility of the apical anteroseptal segment of the left ventricle, the reduction of the global systolic function of the left ventricle, and a sustained contractility of the right ventricle. Further recovery was uneventful and patient was discharged from the hospital 2 weeks after the surgery.

Discussion

PV is a chronic myeloproliferative disease, which manifests as excessive RBC production. In 50% of patients there is a proliferation of all cell lines. It is more common in males with a prevalence of 4–16 per million.4 For a PV diagnosis, 2 major and 1 minor criteria or first major criterion with 2 minor criteria are required. Major criteria include hemoglobin >18.5 g/ dL in men, or >16.5 g/dL in women, presence of the Janus kinase 2 (JAK2) V617F or similar mutation. Minor criteria include myeloproliferation on bone marrow biopsy, serum erythropoietin level below normal range, and endogenous erythroid colony formation in vitro.5,6 In our patient PV was manifested as an erythrocytosis and leukocytosis with a high Ht level. Elevated RBC, WBC, and hematocrit levels can lead to hyperviscosity and thrombosis. Therapeutic options presented in hematologic management algorithms include controlling RBC, WBC, PC, and hematocrit with phlebotomies, aspirin, cytoreductive therapy such as hydroxyurea, anagrelide, or interferon in some cases.5,5 According to the hematologic guidelines the Ht should be reduced preoperatively to 0.45 L/L in males and 0.42 L/L in females,5,7 which was reached in our patient using hydroxycarbamid and repeated phlebotomies. Hydroxycarbamid should be administered on the first postoperative day, but due to extremely complicated course of postoperative events, we introduced it on the fourth postoperative day. We followed the management algorithms considering postoperative anticoagulation regimen with combination of oral antiplatelet agents with warfarin recommended being more effective in preventing the graft thrombosis.8 We administered warfarin, and clopidogrel and acetylsalicylic acid on second and third postoperative day, respectively.

Although our patient had bone marrow biopsy, and genetic testing results show Janus kinase 2 (JAK2) mutation supporting his PV diagnosis, the hematologist in our team recommended an intraoperative sternum biopsy and a sternal bone marrow biopsy so further classification of PV could be conducted to be able to more precisely plan his further PV treatment. The pathology results of the sternum biopsy confirmed the diagnosis of PV with grade I fibrosis.

There are only a few manuscripts describing the patients suffering from PV that underwent cardiac surgery. It is a very complex condition considering the high frequency of the graft thrombosis and paradoxical bleeding. Complication rate in such cases is not yet known, but is presumably very high.5,7 There are 3 published cases of massive intraoperative thrombosis of heart chambers and a case of thrombosis of the both LITA grafts used.3,9–11 Also there are published cases of aortic valve replacement (AVR), transcatheter aortic valve implantation (TAVI), and PCI in patients suffering from PV with various outcomes.12–14 Considering the multivessel disease and other variables described in the case section, the aortocoronary bypass was a life-saving procedure that had to be done despite the patient’s extremely complicated comorbidity. In compliance with the guidelines in cardiac surgery, this was a patient with indications for an urgent operation and the risk of thrombotic complications had to be undertaken.

We did not find a case in the literature describing off-pump coronary artery bypass (OPCAB) in patients suffering from PV. In all the patients undergoing cardiac surgery with concomitant PV, the
procedure on choice was on-pump CABG. Few cases of OPCAB were described in patients suffering from ET; as ET has different clinical manifestations we did not find it relevant to our case.15 We chose on-pump CABG considering there were no published papers of outcomes in patients undergoing OPCAB who were suffering from PV. Also, there is a preference for on-pump CABG in our department. Although we followed all proposed management algorithms, and hematology and cardiology guidelines during the preoperative workup, we did not succeed to avoid an extremely difficult complication—thrombosis of native coronary vessels, of the proximal RCA where a new thrombus occurred with a presence of thrombi in the proximal and most likely distal LAD that we were not able to surgically resolve in an adequate way. Coronarography showed the thrombosis of LAD and RCA for which we assumed occurred during the CPB. After the administration of heparin the activated clotting time (ACT) was 535 so the CPB was started. Before the CPB the patient was hemodynamically stable and there were no electrocardiographic or TEE signs of myocardial ischemia. Therefore, we believe that maybe OPCAB could be a better solution. The cardiologist decided to perform the emergent coronary revascularization without PCI of the distal LAD because of the multiple thrombi in the LAD. There are papers describing PCI in patients with PV, stating that PV might not represent a prohibitive background for coronary PCI.16

During further perioperative recovery we did not encounter additional complications such as pulmonary embolism, tamponade, renal dysfunction, neurological complications, and so on that are described in the literature.8,15

Conclusion

Management of patients suffering from myeloproliferative disease undergoing cardiac surgery is very challenging. This patient had adequate medical therapy, but had frequent daily chest pain. Considering the results of the preoperative coronaryography, the only option, based on the guidelines, was operative treatment. Prevalence of patients with such condition is so small that there is no established protocol. Hematology guidelines and management algorithms must be followed preoperatively and postoperatively. Close cooperation of cardiac surgeon, anesthesiologist, hematologist, and cardiologist is essential in such complicated cases. It would be absolutely necessary to conduct a global trial to investigate the preferred cardiosurgical procedure (OPCAB or on-pump CABG) for the final outcome in such cases.

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References

1. Arber DA, Orazi A, Hasserjian R, Thiele J, Borowitz MJ, Le Beau MM et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood 2016;127(20):2391–2405
2. Barbiu T, Finazzi G, Falanga A. Myeloproliferative neoplasms and thrombosis. Blood 2013;122(13):2176–2184
3. Bhandary SP, Papadimos TJ, Essandoh MK, Apostolakis J. Massive intracardiac thrombosis during coronary artery bypass grafting surgery. Int J Crit Illn Inj Sci 2015;5(1):56
4. Al-Fadhli J, Al-Shammari F, Al-Duaij A, Al-Sarraf N. Coronary artery bypass grafting in a patient with polycythaemia rubra vera - a rare indication with a spectrum of complication: a case report. Cases J 2009;2(1):8126
5. Teferi A, Solberg LA, Silverstein MN. A clinical update in polycythemia vera and essential thrombocythaemia. Am J Med 2000;109(2):141–149
6. Im H, Min JJ, Yang J, Lee SM, Lee JH. Anesthetic management of a patient with polycythaemia vera undergoing emergency repair of a type-A aortic dissection and concomitant coronary artery bypass grafting; a case report. Korean J Anesthesiol 2015;68(6):608–612
7. Elliott MA, Tefferi A. Thrombosis and haemorrhage in polycythemia vera and essential thrombocythaemia. Br J Haematol 2005;128(3):275–290
8. Oz BS, Asgun F, Akay HT, Kaya E, Kuralay E, Tatar H. Anticoagulation after coronary artery surgery in patients with polycythemia vera: report of two cases. J Card Surg 2007;22(5):420–422
9. Yuan SM, Shinfeld A, Raanani E. Massive intraventricular thrombus in polycythemia vera. J Card Surg 2009;24(2):110–112
10. Lima B, Soltesz E. Management of extensive intracardiac thrombosis in a patient with polycythemia vera undergoing coronary artery bypass grafting. J Card Surg 2012; 27(3):320–322
11. Osada H, Nakajima H, Meshii K, Ohnaka M. Acute coronary artery bypass graft failure in a patient with polycythemia vera. Asian Cardiovasc Thorac Ann 2016; 24(2):175–177
12. Erkan H, Korkmaz L, Kiriş G, Celik S. Transcatheter aortic valve implantation in a patient with myelofibrosis and severe thrombocytopenia. J Heart Valve Dis 2015; 24(2):263–265
13. Matsuyama N, Asada K, Kondo K, Kodama T, Minohara S, Hasegawa S et al. Surgical treatment of aortic stenosis with polycythemia vera: a case report. Kyobu Geka 1996; 49(13):1097–1099
14. Hvelplund A, Hansen PR. Subacute intracoronary stent thrombosis in a patient with polycythemia vera. Ugeskr Laeger 2006; 168(47):4104–4105
15. Darwazah AK, Madi H, Zagha R, Hawash Y. Off-pump myocardial revascularization in a high-risk patient with essential thrombocythemia. Tex Heart Inst J 2014; 41(5):537–542
16. Guazzi M, Esposito G, Loaldi A. Long-term successful coronary artery angioplasty in polycythemia vera. J Invasive Cardiol 1995; 7(8):243–247