

## Cardiac surgery in patients with essential thrombocytosis: a report of three cases

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### ABSTRACT

Essential thrombocytosis has been classified as a chronic myeloproliferative disorder. Patients with essential thrombocytosis undergoing cardiac surgery are at increased risk for bleeding and thrombosis. However, the incidence and treatment for this condition are not well known. There are profound implications of essential thrombocytosis in patients undergoing cardiac surgery with the use of cardiopulmonary bypass, where heparin is used for anticoagulation. We want to present successful cardiac surgery in three patients with essential thrombocytosis. Patients received hydroxyurea and antiagregant treatment preoperatively and the thrombocyte counts were lowered to reference ranges. There were no cardiac or systemic complications due to essential thrombocytosis during the postoperative period.

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**Keywords:** Cardiopulmonary bypass; essential thrombocytosis; cardiac surgery

### Introduction

Essential thrombocytosis may cause life threatening complications such as thrombosis or bleeding, particularly in older patients or in patients with high cardiovascular risk factors [1]. There are no brief guidelines for patients with essential thrombocytosis undergoing cardiac surgery [2]. Patients with essential thrombocytosis may suffer intraoperative and postoperative thrombosis or postoperative uncontrollable bleeding, however incidence and therapeutic options of these risks are not well known [3]. Therefore, it is a matter of concern for

cardiac surgeons to use cardiopulmonary bypass, heparin and anticoagulation in these patients. These concern increases particularly due to the use of warfarin following valve surgery [3]. In this text, we present three cases with essential thrombocytosis, mitral valve replacement was performed in one patient and coronary bypass grafting was performed in two patients.

### The presentation of the patients

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### Case 1

A 70-year-old female patient with chronic atrial fibrillation, severe mitral valvular stenosis and mitral valvular insufficiency admitted to our institution for mitral valve replacement. The patient had a blood thrombocyte count of  $1.100.000/\text{mm}^3$  and splenomegaly. The patient was being followed by an hematology clinic for two years and she had a history of cerebrovascular disease. The blood levels of uric acid and lactate dehydrogenase (LDH) were 12 mg/dl and 800 U/L respectively. The results of other blood tests including cardiac enzymes, troponins, hepatic and renal function tests and international normalized ratio (INR) were in normal ranges. Hydroxyurea therapy was administered for one week preoperatively after consultation of hematology clinic and blood thrombocyte count was lowered to  $350.000/\text{mm}^3$ . Because of not being suitable for mitral valve repair the patient underwent a mitral valve replacement after thrombocyte count reached to the reference range. Mitral valve replacement with a mechanic valve and radiofrequency ablation for chronic atrial fibrillation were applied. The patient who had 650 ml drainage postoperatively and no complications, was followed up with low molecular weight heparin (LMWH) in postoperative period. LMWH was stopped upon INR values reached 2.5 and the patient was discharged with warfarin, hydroxyurea and acetylsalicylic acid therapy on the 7th postoperative day. At 6-year follow-up, the patient showed no signs of thrombohaemorrhagic and microvascular complications.

### Case 2

A 66-year-old male patient who admitted with exertional chest pain had a history of smoking, diabetes mellitus, hypertension, hyperlipidemia and positive family history as coronary risk factors. Anterior and apical ischemia was detected in myocardial perfusion scintigraphy. Coronary angiography revealed a 90% stenosis at the left main, 80% stenosis at the circumflex coronary artery and total occlusion at the right coronary artery. On physical examination there was a splenomegaly. The patient had normal regular blood test values including inflammatory markers, however he had thrombocyte count of  $1.500.000/\text{mm}^3$ . After the diagnosis of essential thrombocytosis by the haematologist, hydroxyurea therapy was started preoperatively. Blood thrombocyte count of the patient decreased to  $400.000/\text{mm}^3$  following one week of medical therapy.

The patient underwent a successful three vessel coronary bypass grafting with cardiopulmonary bypass. The patient had a total drainage of 1000 ml in the first postoperative day. And after aprotinin administration in this patient postoperative course was uneventful. The patients postoperative medication was LMWH and acetylsalicylic acid and was discharged with oral hydroxyurea and acetylsalicylic acid therapies on his 8th postoperative day. At 6-month follow-up, the patient showed no signs of thrombo-haemorrhagic and microvascular complications or angina.

### Case 3

A 46-year-old male patient who had obesity and smoking as risk factors admitted to coronary angiography with unstable angina pectoris. Coronary angiography revealed 70% stenosis in the left anterior descending, 60% stenosis in the obtuse marginal branch of circumflex artery and 80% stenosis in the right coronary artery. The patient did not have diabetes mellitus, hypertension, hyperlipidemia or family history of a cardiac event.

The laboratory tests were in normal range except elevated serum LDH, uric acid and blood thrombocyte count was  $1.254.000/\text{mm}^3$ . With the diagnosis of essential thrombocytosis by the hematologist clinic, the patient administered hydroxyurea 100 mg/day for a week in order to reduce platelet count to  $500.000/\text{mm}^3$ . The patient underwent a successful three vessel on-pump coronary artery bypass grafting. There was a 750 ml drainage postoperatively. Postoperative thrombocyte levels of the patient was over  $1.000.000/\text{mm}^3$ . The platelet count was controlled using hydroxyurea 100 mg/day. The patient was discharged at 10<sup>th</sup> day after the surgery with a platelet count of  $300.000/\text{mm}^3$ . At one-year follow-up, the patient showed no signs of thrombo-haemorrhagic and microvascular complications or angina.

## Discussion

Essential thrombocytosis is a myeloproliferative disorder seen along with permanent and progressive elevation of blood thrombocyte count, thrombohaemorrhagic and microvascular complications.

It is typically characterized with megakaryocytic hyperplasia in bone marrow and splenomegaly [2-5].

The worldwide incidence of this disease is 1.5/100,000 per year [4, 5]. Causes for mortality and morbidity in essential thrombocytosis are thrombosis, bleeding and progression to myelofibrosis or acute leukemia [5]. Only 9.4% myocardial infarction and 9-22% vascular events were reported in patients with essential thrombocytosis [1, 4]. Except a history of thrombosis, risk factors for cardiovascular disease including smoking, hypertension, hyperlipidemia and diabetes are risk factors for thrombosis as well [1, 4]. There are non-endothelial contact, heparin, platelet activating factors and hypercoagulopathy induced by increased thrombin with cardiopulmonary bypass during cardiac surgery. There is a tendency of bleeding due to hemodilution, heparinization, platelet dysfunction and hypothermia as well [6]. Increase in thrombocyte aggregation, platelet dysfunction and von Willebrand factor deficiency were shown in patients with essential thrombocytosis [2, 5]. Therefore, these type of patients who undergo cardiac surgery are at risk of bleeding and thrombosis [1, 6]. Bleeding, thrombosis and neutralization of heparin with protamin become more complex and major bleeding may result in fatality. In general, patients under 40-years of age without any thrombo-haemorrhagic disease are accepted as low-risk group and aspirin therapy is suggested for the treatment of essential thrombocytosis [1, 2, 5]. However, thrombocyte reduction therapy is suggested before surgery to take myeloproliferation under control and reduce the risk of bleeding in patients with extreme thrombocytosis [2]. Drugs such as hydroxycarbamide, anagrelide, interferon- $\alpha$  and hydroxyurea are suggested to reduce thrombocyte count to normal range in the preoperative period [2, 5]. Reduction of platelet count to normal levels would also lower the risks of thrombocyte aggregation and microemboli during cardiopulmonary bypass [4, 7].

Our patients underwent cardiac surgery with reduction of thrombocyte count to normal levels and there were no complications afterwards. Hydroxyurea was started in our patients for thrombocyte reduction therapy and the reference levels were reached after approximately one week treatment. Preoperative usage of hydroxyurea that lowered the thrombocyte count seems likely to influence postoperative outcomes positively which should be examined in further studies. Immune suppression with these drugs has been worrisome regarding postoperative infections. Although hydroxyurea is cytotoxic, it is also shown for this drug has no a negative effect on antimicrobial

functions of the leukocytes [8]. Postoperative bleeding occurred in one of our patients for whom complete neutralization of heparin couldn't be obtained even with full dose of protamin. 1000 ml of drainage occurred in this patient in the first postoperative day. This patient was given aprotinin, which significantly reduced the bleeding. Aprotinin was reported to provide significant reduction in postoperative bleeding in patients with thrombocyte dysfunction [9]. Off-pump operations are recommended for hematologic diseases to avoid adverse effects of cardiopulmonary bypass and surgical complications of extreme bleeding or thrombosis [5]. Risk factors evaluation should be made individually for thrombohaemorrhagic complications under cardiopulmonary bypass. Smoking, obesity, hypertension and high blood thrombocyte count are shown as risks for thrombohaemorrhagic complications [2]. Risk of bleeding and thrombosis are higher particularly for patients over 60 years of age and in patients with thrombocyte counts over  $1.500.000/\text{mm}^3$  [1, 2, 5, 8]. Our patients were also at high risk; thrombocyte levels were reduced to reference range preoperatively with hydroxyurea and aspirin therapies regarding recommendations of the hematologist and postoperative changes in life style (such as weight loss for obese patients, to give up smoking for smokers etc.) were suggested. Catastrophic hemorrhagic complications may occur during warfarin therapy particularly in patients at high risk group who have essential thrombocytosis, where a much aggressive therapy (such as chemotherapy or bone marrow transplantation) may be necessary.

Nevertheless, therapeutic attempts to stop bleeding may result in valve thrombosis [2]. For this reason, bioprosthetic valves should be preferred to avoid a lifetime warfarin therapy. However, metallic valves may be chosen for young patients with low risk of essential thrombocytosis [2]. For our mechanic valve replaced patient, necessity of warfarin usage due to chronic atrial fibrillation and history of a thromboembolic event made us prefer a mechanical valve.

## Conclusion

In conclusion, special attention is necessary in patients with essential thrombocytosis undergoing open cardiac surgery to go on with the precise balance

between the risk of bleeding and tendency of thrombosis. Preoperative usage of hydroxiurea reduces the thrombocyte count and seems likely to influence postoperative outcomes positively. There are open cardiac surgical operations of patients with essential thrombocytosis in current literature. However, there is not yet sufficient data for optimal therapy for these patients, requires further studies in large patient populations.

#### *Informed consent*

Written informed consent was obtained from the patients for the publication of this case report.

#### *Conflict of interest*

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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