Is the increase in eltrombopag dose cause of myocardial infarction?

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Introduction

Immune thrombocytopenia (ITP) is an acquired disorder caused by immune-mediated attack, enhanced clearance, and insufficient compensatory production of platelets. Historically, ITP treatment strategies have suppressed platelet destruction with glucocorticoids, intravenous immune globulin (IVIG), cytotoxic agents, and splenectomy (1). Eltrombopag is an oral non-peptide thrombopoietin receptor agonist (TPO-RA) approved for use in several countries for the treatment of ITP with insufficient response to corticosteroids, immunoglobulins, or splenectomy. In this study, we present a patient with ITP who developed recurrent myocardial infarction and intense thrombus in the stent after increasing the eltrombopag dose.

Case Report

A 52-year-old woman was admitted to our emergency room with chest pain. She had no traditional risk factors for coronary artery disease. We understood that the patient used eltrombopag as treatment for ITP; and 10 days ago, the dose of eltrombopag was increased from 50 mg/day to 75 mg/day owing to the platelet count being 9.000/mm^3. Electrocardiography demonstrated acute anterior ST elevation myocardial infarction (STEMI). Acetylsalicylic acid (ASA 300 mg) and clopidogrel (600 mg) were loaded, and coronary angiography was performed immediately. Angiography revealed 70% thrombotic occlusion in the proximal segment of the left anterior descending (LAD) artery. Unfractionated heparin (70 IU/kg) was administered, and a 3.0×24 mm drug-eluting stent was implanted (Fig. 1). Her presenting platelet count was found to be 530,000/mm^3. STEMI developed 10 days after the increase in eltrombopag dose. Therefore, drug-induced thrombosis was thought to be possible. Eltrombopag was discontinued with the recommendation of hematology. She was discharged on medical treatment (ASA 100 mg, clopidogrel 75 mg, atorvastatin 40 mg, metoprolol succinate 50 mg, ramipril 5 mg and pantoprazole).

Ten days later, the platelet count was 10,000/mm^3. ASA was discontinued, and IVIG treatment was started. Clopidogrel was continued. Despite IVIG, severe thrombocytopenia continued, and eltrombopag 50 mg/day was restarted. In the 10th month, eltrombopag dose was increased to 75 mg/day because the platelet count did not exceed 4000/mm^3. Notably, 10 days after the dose increase, she presented to the emergency department

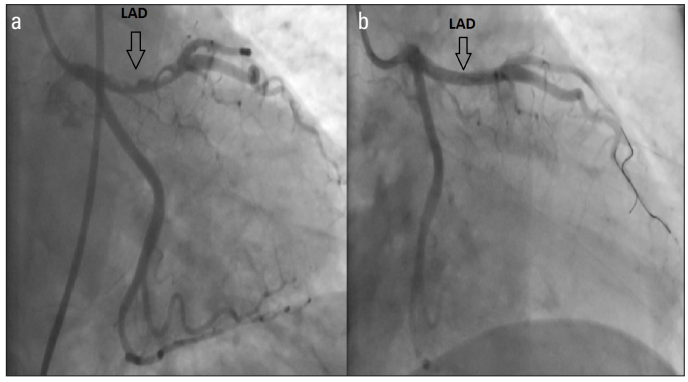

Figure 1. Coronary angiography images. (a) At presentation, acute anterior ST elevation. (b) After percutaneous coronary transluminal angioplasty was performed to the lesion in the proximal LAD
LAD - left anterior descending artery

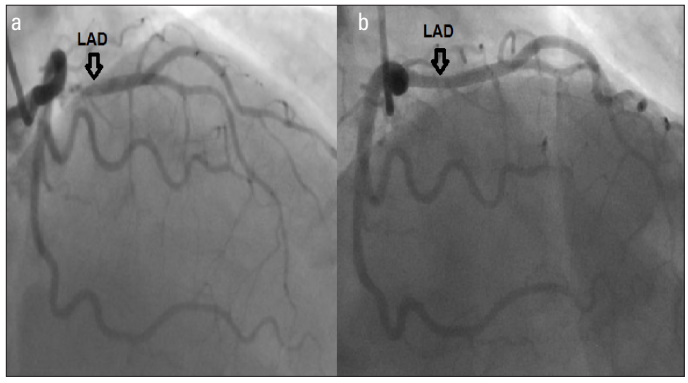

Figure 2. (a) Coronary angiography showed subtotal occlusion and intensive thrombosis at proximal portion of LAD in-stent. (b) Four days later, after abciximab infusion was administered, control coronary angiography revealed no thrombus and TIMI 3 flow
LAD - left anterior descending artery; TIMI 3 - thrombolysis in myocardial infarction 3

with chest pain. Angiography was performed again with the diagnosis of anterior STEMI. An intense thrombus appearance and subtotal occlusion in the LAD stent were seen on angiography. Platelet count was found to be 749,000/mm^3. It was decided to administer abciximab infusion (0.25 mg/kg IV bolus, then 0.125 mcg/kg/min intravenous infusion for 12 hours). Eltrombopag was ceased. Control angiography performed 4 days later showed that the thrombus had disappeared. Stent was not implanted (Fig. 2). No bleeding or ischemic event was observed during the 1-year follow-up.

Discussion

ITP is a disease that causes thrombocytopenia, and bleeding is common. Paradoxically, the risk of thromboembolism is also high. Increased risks of thromboembolic events are associated with larger platelets more adhesive to vascular surfaces, direct endothelial damage, and negative effects of therapy with steroids or intravenous immunoglobulin. More recent approaches have concentrated on enhancing platelet production with TPO-

Ras (1). TPO-RAs are thought to increase platelet adhesion by increasing the number of platelets and their functions (2). Bussel et al. (3) have reported an overall thromboembolic event rate of 4.5% in patients with ITP treated with eltrombopag. In addition, cases of myocardial infarction have been reported in patients treated with eltrombopag (4-6). In our patient, the rapid and excessive increase in thrombocyte count after the eltrombopag dose was increased to 75 mg/day may be responsible for the development of STEMI.

The aim of ITP treatment should be to reduce the risk of bleeding by keeping the platelet count in the range of 30,000/mm^3-50,000/mm^3 and to protect the patient from thrombosis by reducing the treatment when it exceeds 150,000/mm^3 (7). There is no established treatment protocol for patients with ITP and with STEMI. There are case reports of different treatments, such as stent implantation, thrombolytic therapy, and the use of potent P2Y12 inhibitors (8, 9). Management of the bleeding-thrombosis balance can be very challenging. It may be better to avoid stent implantation in patients with ITP because the response to dual antiplatelet therapy may differ from what is expected (9).

In our patient, we preferred to use glycoprotein 2B/3A (GP2B/3A) inhibitor with close follow-up for bleeding. We chose this treatment option instead of placing a new stent. The absence of thrombus in the control angiography suggested that the treatment was successful. However, it should not be forgotten that there are also drug-induced ITP in patients associated with GP2B/3A inhibitors in the literature (10). Therefore, when administering this treatment, the benefit-harm ratio should be well evaluated, and individual decision should be made.

Conclusion

In patients using eltrombopag, close monitoring of the platelet count, especially during dose increase, is important. Individualized treatment should be planned considering the balance of bleeding and ischemia in patients with ITP presenting with acute coronary syndrome.

Informed consent: Written informed consent was obtained from patient.

Video 1. Coronary angiography showing subtotal occlusion and intensive thrombosis at the proximal portion of LAD in-stent
LAD - left anterior descending artery

Video 2. Four days later, after abciximab infusion was administered, control coronary angiography revealed no thrombus and TIMI 3 flow
TIMI 3 - thrombolysis in myocardial infarction 3

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