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CASE REPORT

Management of immune thrombocytic purpura and acute coronary syndrome: A double-edged sword!

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Abstract Treating patients known to have immune thrombocytopenic purpura (ITP) presenting with acute coronary syndrome (ACS) pose challenges, especially if they undergo percutaneous coronary intervention and stenting, as they require certain period of dual anti-platelet medication based up on the type of stent been deployed. Co-existence of therapies to increase platelet number as well as anti-platelet efficacy at the same time appears contradictory; imbalance in antagonistic treatment approach of increasing platelet number to treat ITP and inhibiting their activity to treat ACS can result in life threatening complications.

1. Introduction

Immune thrombocytopenic purpura (ITP), characterized by immune-mediated premature platelet destruction, results in thrombocytopenia and bleeding complications.[1] Those presenting with the adult-onset, chronic form of ITP, which is refractory to conventional treatment, have a higher mortality rate, due to bleeding complications.[2] Anti-platelet medications are the most commonly used treatment in patients with acute coronary syndrome (ACS) and have been demonstrated to reduce secondary thrombotic events and improve clinical outcomes.[3,4] Treating patients known to have ITP who present with ACS poses a major challenge, especially if they undergo percutaneous coronary intervention (PCI) and stenting, as they require a certain period of dual anti-platelet medication (DAPT)

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based on the type of stent. Imbalance in the antagonistic treatment approach of increasing platelet numbers to treat ITP and inhibiting their activity to treat ACS can result in life-threatening complications.

2. Case

A 42-year-old female presented with new-onset central, squeezing chest pain and elevated troponin (troponin-I −0.35 ng/ml, normal<0.03 ng/ml). Electrocardiogram demonstrated dynamic 'T' wave inversion in leads V_{1-4}. Trans-thoracic echocardiogram demonstrated mid and apical anterior wall hypokinesia. She was known to have ITP since 20 years of age. Over the years her treatment-regimen required multiple changes to maintain a platelet count of more than 30,000/μL, as drops in platelet counts below 25,000/μL resulted in bleeding complications, mainly petechia or menorrhagia. At the time of her presentation with ACS she was managed with prednisolone and azathioprine. Previously, she required treatment with intra-venous immunoglobulin (IVIg) infusion to treat ITP; and once, three days after IVIg infusion, she suffered with deep vein thrombosis (DVT). There was no apparent reason for her to have limited mobility and thrombophilia screen was negative. DVT was suspected to be due to IVIg treatment. From a cardiovascular risk factors point of view, she was also diagnosed with impaired glucose tolerance for nearly 10 years.

At the time of admission her platelet count was 35,000/μl. As there were concerns with DAPT and heparin use, she was treated with IVIg (1 gm/kg), in addition to routine use of prednisolone and azathioprine. Forty-eight hours later her platelet count increased to 85,000/μl and she was taken to the cardiac catheterization laboratory. Coronary angiography (CAG) demonstrated a moderate lesion in the proximal-mid part of the left anterior descending (LAD) artery (Fig. 1A). In view of a prognostically significant lesion, PCI was performed using 3.0×23 mm Genous stent® (OrbusNeich, Ft. Lauderdale, FL, USA), (which is coated with anti-$CD34^+$ antibody that helps cover stent struts with endothelial progenitor cells, promoting earlier strut coverage and reduced risk of thrombosis), and eventually required a short duration of DAPT use, up to 1 week.[5,6] PCI was successfully completed and good final results were achieved (Fig. 1C).

She was discharged home 48 hours post PCI with advice for long-term aspirin use and clopidogrel for 28 days. She represented back to hospital on the night of her discharge with anterior ST elevation myocardial infarction (STEMI). Primary-PCI call was activated; CAG demonstrated her to have in-stent thrombosis (ST) (Fig. 1D). She was treated with thrombus aspiration and further stenting with two 3.5×13 mm Genous® stents (Fig. 1E and F). Platelet count on the day of stent thrombosis was 135,000/μl, and this time her clopidogrel was changed for ticagrelor.

As we wanted to minimize the duration of DAPT, the patient was brought back to the catheterization laboratory for repeat CAG, and optical coherence tomography (OCT), six weeks from her re-do PCI. The OCT examination suggested satisfactory stent strut coverage; and therefore, she was advised to stop ticagrelor (Fig. 1G–J). However, despite the apparent stent strut coverage, the patient was readmitted with further chest pain and troponin rise (1.76 μg/μl) seven days later, and the CAG demonstrated patent stents and no further intervention was required. Ultimately, ticagrelor was recommended for 12-months with long-term aspirin. During this 12-month period, while she was on DAPT, her platelet count was carefully managed with the use of prednisolone, azathioprine and romiplostim. At 12-months the ticagrelor was stopped and she has remained asymptomatic for more than 2 years.

3. Discussion

There is a lack of "evidence based treatment" for patients known to have ITP and presenting with ACS. Inhibiting platelet-aggregation, especially when the platelet count is very low, is a challenging situation for the treating clinician. This case raises many questions, including (1) What should be the ideal minimum platelet count when treating such patients with DAPT for ACS/post-PCI? (2) What are the ideal anti-platelet therapies to be used in such patients? (3) What was the mechanism of ST in this patient? And most importantly: (4) How do we avoid bleeding/thrombotic complications, while maintaining adequate platelet count and continuing with DAPT?

While treating patients with ITP, platelet counts are aimed to be maintained between 30 and 50,000/μL.[1] There is no consensus on minimum acceptable platelet count level while treating ITP patients presenting with ACS. Thrombotic events are reported in patients not only with thrombocytosis[7] but also with thrombocytopenia associated with various conditions.[8] One should not be preoccupied with platelet count alone, as platelet functions are not affected merely by a change in their numbers; but at the same time it is equally difficult to commence DAPT, when platelet count is very low, as bleeding can result in fatal consequences. Identifiable markers to assess platelet activity in such patients are lacking, and platelet function assays have not even been validated for use in patients with thrombocytopenia. Evidence-based DAPT combination in treating patients with ITP is unknown.

Multiple factors may have played a role leading to ST in this patient and can be divided into factors related to ITP or PCI. Use of IVIg has been associated with arterial/venous thrombotic events, mainly at the time of infusion or up to 8 days after the infusion.[9] In our patient, the thrombotic event occurred four days after IVIg infusion, and the platelet count was the highest ever noted since she had been undergoing treatment for ITP. Our patient also suffered with DVT many years ago after IVIg treatment, and her platelet counts were reportedly more than 100,000/μl at that time. We were not aware of her history of DVT with IVIg use, as the patient was treated in another hospital at that time and she did not provide this information in her history. Should we have known of this complication, we would have avoided IVIg use, or may have kept the dose very low. Thrombotic events in the form of ACS or stroke have been reported in patients treated with IVIg, especially with incremental platelet count and the presence of underlying coronary artery disease. Based upon aggregometry studies, the platelet agonist properties of IVIg have been

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