Case Report

Acute Acquired Immune Thrombocytopenia After Cardiac Surgery: A Challenging Case

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ABSTRACT

Thrombocytopenia is a common condition that recognizes an infinite number of possible causes, especially in specific settings like the one covered in this case report: the postoperative period of cardiac surgery. We report a case of an old male with multiple comorbidities who underwent a coronary angioplasty procedure and aortic valve replacement. He showed severe thrombocytopenia in the postoperative days. Differential diagnosis required a big effort, also for the experts in the field. Our goal was to aggressively treat the patient with prednisolone, platelets, and intravenous immunoglobulins to maximize the prognosis. Our patient developed no complications and was discharged successfully.

Keywords: Acute Acquired Immune Thrombocytopenia, aggregometry, aortic valve replacement (AVR), cardiac surgery, intravenous immunoglobulins (IVIG), transcatheter aortic valve implantation (TAVI)

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INTRODUCTION

Immune thrombocytopenia (ITP), characterized by a platelet count of less than 100,000/μL, is a condition that causes autoimmune destruction of platelets, increasing the predilection for bleeding and post-cardiac surgical complications.[1,2] Reported incidences of ITP range from 2 to 5 per 100,000 individuals per year.[3] The disorder is caused by IgG autoantibodies and the clinical course of ITP may be different depending on whether it is a manifestation of primary immunodeficiency or associated with an underlying autoimmune condition, malignancy, or infection.[4] Another classification system subdivides the condition according to its duration.[5] Being a very heterogeneous syndrome with different pathological etiologies, its diagnosis remains one of exclusion, which also, therefore, entails the risk of misdiagnosis, even by experienced hematologists. There is scarce literature on the relevant treatment regimens for the perioperative management of patients with ITP. In this report, we describe the challenging case of a patient who developed ITP following aortic valve replacement (AVR) surgery and his treatment.

CASE REPORT

A 76-year-old man, who had been diagnosed 4 years previously with stage IV bilateral pulmonary neoplasia and has already undergone cycles of chemotherapy, was admitted to the emergency department with symptoms and signs of non-ST-segment elevation myocardial infarction. He underwent a percutaneous transluminal coronary angioplasty of the culprit vessel via placement of a drug-eluting stent (DES) in the circumflex coronary artery.

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Intraprocedural echocardiography indicated severe aortic stenosis and given the patient's oncological history, the heart team recommended an AVR using the transcatheter aortic valve implantation technique. A few days later, the patient underwent a transfemoral placement of a 29-mm Edwards Sapiens XT bioprosthesis. The procedure was complicated by the slippage of the valve in the aortic outflow tract, requiring an urgent AVR with the traditional surgical technique to place a 25-mm Edwards Magna. Despite mild post-operative thrombocytopenia, the patient underwent prophylaxis with acetylsalicylic acid (ASA) and enoxaparin according to the internal protocol. Transferred to the cardiothoracic ward, he developed mild respiratory insufficiency associated with fever and increased inflammatory indices, but negative culture tests. Empirical antibiotic therapy with Piperacillin Tazobactam was administered for 8 days—the time required for the patient's temperature curve and inflammatory indices to recede. The patient's hemoglobin levels and white blood cell counts from preoperative day 1 to postoperative day (POD) 19 are shown in Table 1. On POD 4, when the platelet count fell below 50,000/μL, we decided to suspend ASA and enoxaparin, despite the indication for dual antiplatelet therapy (DAPT) to protect the recent DES. On POD 8, with a platelet count of 37,000/μL, we started therapy with methylprednisolone 1 mg/kg. Specific blood tests were all negative, except for a slight reduction in IgG in the context of hypogammaglobulinemia with a normal Kappa/Lambda ratio and a mild leukocytosis that normalized immediately after antibiotic treatment. Despite the steroid therapy, the platelet count reached a nadir of 4,000/μL on POD 12. Clinically, the patient only showed purpura and no signs of bleeding. A total body computed tomography (CT) scan excluded thrombosis and/or any sites of hemorrhaging. Notwithstanding multiple apheresis platelet transfusions, the platelet count remained stable at 4,000/μL. On POD 13, given the persistence of diffuse petechiae and the lack of any response to steroid therapy, we treated the patient with a cycle of intravenous immunoglobulins (IVIG) 1 g/kg. The platelet count trend and time scale of the main therapies administered are shown in Figure 1. A peripheral blood smear confirmed thrombocytopenia and showed the presence of giant platelets without other abnormalities. Anti-Glycoprotein IIb/IIIa (GpIIb/IIIa) antibodies were detected in the patient's serum, whereas the heparin-induced anti-platelet factor 4 (anti-PF4) antibody test was negative, thus eliminating the possibility of heparin-induced thrombocytopenia (HIT). The preoperative multiplate electrode aggregometry performed to identify the safest surgical timing, given the ongoing DAPT (ASA and clopidogrel), showed a therapeutic response to the drugs with normal TRAP-test and RISTO-test values, excluding the possibility of a preexisting platelet deficit. Given the severe thrombocytopenia, postoperative aggregometry was not performed. Having excluded all other causes of thrombocytopenia, we diagnosed a case of ITP with multifactorial etiology—potentially related to an infectious disease or to the known pulmonary neoplasm, although an autoimmune component could not be excluded at that point. In the 24 h following IVIG infusion, with no consequent side effects, we saw an immediate recovery of the platelet count, which returned to the baseline value within 7 days without the need for further transfusions. Aggregometry, performed 7 days after IVIG therapy when the patient presented a platelet count of 179,000/μL, showed a normal response to platelet function tests; this allowed DAPT administration (ASA and clopidogrel) to be resumed. Following 7 days of DAPT, aggregometry showed an adequate therapeutic response, with an arachidonic acid induced aggregation (ASPI)-test value of 30 U and an ADP-test value of 35 U; the platelet count was 166,000/μL. The patient was discharged home in a stable condition.

Table 1: Hemoglobin (Hb) levels and white blood cell (WBC) counts from preoperative day to POD 19. Only the PODs for which the blood count was available are shown

	Hb (gr/dL)	WBC (×10^3/mmc)
POD -1	10.7	8.97
POD 0	9.0	9.87
POD 1	8.8	10.00
POD 2	9.5	9.70
POD 3	9.0	8.84
POD 5	8.1	6.32
POD 7	8.8	6.56
POD 10	8.4	6.96
POD 11	8.1	6.96
POD 13	8.5	6.52
POD 15	9.0	9.79
POD 17	10.0	11.93
POD 18	10.3	11.00
POD 19	9.8	9.26

POD: Postoperative day

DISCUSSION

Thrombocytopenia, a common perioperative issue in cardiac surgery, is associated with a wide variety of conditions. Its signs and symptoms are very variable, ranging from an uneventful course to life-threatening hemorrhage or thrombosis (as in the case of HIT). Most cardiac surgery patients reach their platelet count nadir on POD 2–3, the cause of which is due mainly to hemodilution and the destruction of platelets in the cardio-pulmonary bypass circuits. Owing to the stimulating action of thrombopoietin, platelet counts tend to recover to baseline values by POD 5. An autoimmune origin of thrombocytopenia, as in the case of HIT and ITP, does not usually manifest before the second postoperative week because

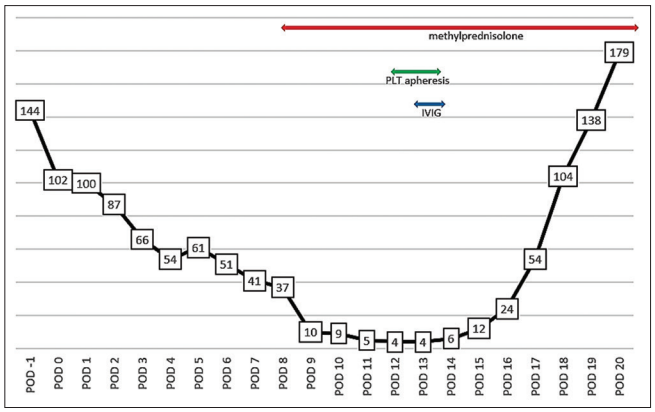

Figure 1: Platelet count trend and the therapies administered. PLT count is expressed as the absolute number × 10^3/μL. Methylprednisolone was administered from POD 8 to POD 20, apheresis platelets were administered on POD 12 and POD 13, while IVIG therapy was administered on POD 13 alone

the production of the antibodies responsible for platelet loss usually requires at least 5 days.[6] Our patient presented mild early thrombocytopenia secondary to perioperative dilution and consumption by the valve prosthesis. The presence of severe thrombocytopenia from POD 5 required a differential diagnosis, mainly between HIT and an immune-mediated disorder. Once HIT had been ruled out, due to anti-PF4 antibody negativity, we focused on the possibility of ITP. The platelet count is the most important marker of the degree of ITP and it inversely relates to bleeding morbidity, but it is only one of the numerous factors that influence a patient's bleeding risk. Patients with severe bleeding signs almost invariably have severe thrombocytopenia, but most patients with severe thrombocytopenia do not have bleeding complications.[7] Our patient presented diffuse purpura, stable hemoglobin values, and no symptoms/signs of bleeding or thrombosis, as confirmed by the total body CT scan performed on POD 12 when his platelet count had dropped to 4,000/μL. In this case, the presence of anti-glycoprotein antibodies was only confirmed after IVIG therapy had been administered and the therapeutic response had already become evident. In this patient, the thrombocytopenia may have had a multifactorial origin: the patient's history of neoplasm, the administration of antiplatelet drugs and heparin during the hemodynamic and surgical procedure, the postoperative infectious disease, and antibiotic administration may have all contributed to the condition. The American Society of Hematology and the International Society of Thrombosis and Hemostasis have published guidelines about the treatment of patients with ITP: first-line treatment focuses on inhibiting autoantibody production and platelet degradation, whereas second-line treatments include immunosuppressive drugs and splenectomy, and third-line treatments aim to stimulate platelet production by megakaryocytes. Each treatment aims at achieving one of the following three main objectives: (1) a rapid but transient rise in the platelet count; (2) maintenance of a stable hemostatic platelet count; (3) ITP remission. Traditional first-line treatments with corticosteroids plus IVIG or Rh(D) immunoglobulin (RhIg) are directed at the first goal of rapidly increasing the platelet count.[8] Immunoglobulins act by binding and saturating Fc receptors of the reticuloendothelial system, thereby reducing the destruction of antibody-covered neutrophils, red blood cells, or platelets, explaining their use in conditions like ITP.[9] IVIG is a blood product enriched with IgG antibodies obtained via the collection and pooling of human plasma from several thousand donors. Treatment with IVIG is generally recommended for ITP patients as an emergency rescue treatment in the case of critical bleeding, as well as for those who do not respond to or cannot tolerate glucocorticoids. According to the American Society of Hematology (ASH) guidelines 2011, IVIG treatment can be used in association with corticosteroids when a more rapid increase in platelet count is required (grade 2B), but this approach is not addressed in the 2019 ASH guideline on ITP.[3] Several clinical trials have shown that IVIG (up to 1 g/kg) is an effective treatment in 70% to 80% of patients with ITP.[10,11] Although IVIG treatment has a good record of low toxicity in adult patients, most products contain anti-A and anti-B iso-agglutinins, which can cause hemolysis in non-blood group 0 patients, sometimes life-threatening, with blood group AB patients being at the highest risk for a severe hemolytic episode. In ITP, bleeding events are often unpredictable, and even in the setting of severe thrombocytopenia, the patient may not exhibit bleeding beyond bruising and petechiae. However, more serious mucosal bleeding may occur, as well as menorrhagia, epistaxis, gastrointestinal hemorrhage, hematuria, or, rarely, intracranial hemorrhage. In addition to bleeding, ITP has a significant impact on health-related quality of life.[3] The clinical picture and severity of thrombocytopenia should guide toward the most appropriate treatment on a case-by-case basis. Our patient only showed diffuse purpura, but he was also a postoperative patient with a platelet count of 4,000/μL, thus at a high risk of bleeding complications. Thus, despite the lack of any severe hemorrhage, he was treated with platelet transfusions and high doses of glucocorticoids. The treatments were ineffective, and after 4 days of no response, we decided to combine a cycle of IVIG following the ASH guidelines 2011 for the treatment of acquired ITP, which indicate this strategy as the most effective when a rapid response in terms of an increased platelet count is needed. Treatment with IVIG induces platelet count recovery within 48 h, demonstrating its therapeutic advantage when a rapid increase in the number of platelets is required, such as in patients at a high risk of critical bleeding. This case report highlights the importance

of being aware of all possible etiological factors for the cause of thrombocytopenia in this clinical setting.

Contribution

The idea for the manuscript and collected data. EA, IV, and UL were responsible for the care of the patient. EA and IR wrote the first draft of the manuscript. IV, LV, TB, FB, and UL gave a significant intellectual contribution. All authors critically reviewed the manuscript and approved the final version for submission.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Patient consent for publication

Consent not obtained; patient deceased.

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Conflicts of interest

There are no conflicts of interest.

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