

A Rare Case of Thrombotic Thrombocytopenic Purpura After Cardiac Surgery

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Abstract- Here we report a case of postoperative thrombocytopenia (TTP) in a 77-year-old case that has been undergoing mitral valve replacement with combined coronary artery bypass grafting. In the 5th days of operation, his platelet count was reduced and despite platelet transfusion, his platelet count reaches to a minimum level of 15000 $\mu\text{g}/\text{mL}$ on the 34th day of surgery. Despite platelet transfusion and plasmapheresis, platelet count continues to decrease and signs and symptoms of disseminated intravascular coagulation appeared by unexpectable renal and pulmonary bleeding. Finally high dose, steroid therapy was started and after some days, platelets count raised to 80000 $\mu\text{g}/\text{mL}$. DIC was recovered, but acute renal failure did not respond to medical and hemodialysis and the case expired with sudden cardiac arrest and ventricular fibrillation. We conclude that if the diagnosis of TTP was made earlier in the course of disease by consulting internist and steroids was instituted it might prevent ARF and its poor outcome.

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Introduction

In post cardiac surgery TTP, there was an autoimmune-mediated phase that related to antibodies against a cell protein i.e disintegrin and metalloproteinase with a thrombospondin type 1 (ADAMTS-13) (1,2). In our case, we did not have a laboratory facility for the detection of ADAMTS-13 activity or to anti ADAMTS-13 antibodies, but the exam showed a strong positive to the autoimmune target test. Since the case had low serum levels of complement C3 and C4 levels, we concluded that the surgical thrombocytopenia could not be interpreted by possible sepsis alone. Because of the progressive course of thrombocytopenia, renal failure and neurologic dysfunction and unresponsive to platelet infusion, negative sepsis workup, and negative response to a course of antibiotic therapy, a suspicion to postoperative TTP strongly considered. Since our treatment with steroids was too late and despite recovery of platelet counts, ARF was not recovered and lead to deadly outcome. However plasmapheresis was instituted on the 21th day of postoperative course, but, was not effective in raising platelet count, however it considered as a primary treatment for TTP subjects (3,4,5). We have performed this option because of the negative results.

methylprednisolone was started on the 30th day of operation and raised the platelet counts from 15000 to 45000 in a 3 day period. Kessler *et al.*, (6) confirmed that TTP is not only an exceptional postoperative syndrome, but also is an hematological emergency that if not properly managed, may lead to fatal outcomes. Some author recommended that with possible TTP diagnosis, preparation for urgent plasmapheresis could be prepared and then a high-dose steroids should be prescribed (7). Our patient did not respond to plasma exchange but responses to methylprednisolone therapy; The patient received a multiple antibiotic treatment in postoperative period for possible infection and managed for ARF even after the recovery of a thrombocytopenia, concomitantly the patient had shown the symptoms of central neurologic dysfunction and renal failure when he was expired from the ARF complication (8). In conclusion, we recognized that if the postoperative patient has prolonged thrombocytopenia that has not improved with routine management, postoperative TTP, even though it is a rare disorder, should be considered and ruled out.

Although thrombotic thrombocytopenic purpura (TTP) is a rare disease, when it develops in a post-cardiac surgery patient, it may have a fatal outcome. Since the frequency of early-onset thrombocytopenia in

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post-cardiac surgery patients is high, platelet concentrates are commonly transfused during postoperative management. However, when TTP is the likely diagnosis, platelet transfusion is not recommended. We experienced a postoperative TTP in a cardiac surgery patient and discovered the importance of identifying the etiology of postoperative thrombocytopenia. Here, we report the case with a brief review of the literature.

Case Report

A 77-year-old man was admitted for CAD and severe mitral valve regurgitation. In TEE, a severe mitral regurgitation and severe left ventricular dysfunction were detected. During the admission, he complained of mild dyspnea and chest pain that exaggerated with activity during the last month. After coronary angiography, it was planned that he should have a combined valve and CAD surgery. Mitral valve replacement with a biologic valve with three-vessel bypass grafting was done under cardiopulmonary bypass. Low cardiac output developed and with the combination of inotropic drugs and an intraaortic balloon pump was managed. On the 5th day of surgery, despite the prolonged tracheal intubation, finally he was extubated and had a good general condition but in laboratory analysis it was found to have a severe thrombocytopenia. Platelet concentrate was infused to decrease unexpected postsurgical bleeding and increase the platelet number. At ICU, TEE showed normal mitral valve function without any central or para-valvular regurgitation. Since from 9th postoperative day, he experienced a high fever 38°C and the laboratory exam revealed progressive reducing of platelet counts with signs of disseminated intravascular coagulopathy (DIC). Blood, tracheal and urine culture was negative. The sternotomy and saphenous harvesting sites was normal without any inflammation. Despite negative body cultures, he was treated with ceftazidime and vancomycin antibiotics for possible unknown sepsis. On the 10th day of surgery fresh frozen plasma and platelet transfusion for hematuria was ordered. Consciousness level was reduced and risk of aspiration urged us to reintubated the patient.

In brain CT scan, except to brain edema no remarkable pathology was found. However consciousness recovered partially, but he did not obtain full criteria for extubation. In 2th weeks of surgery a tracheostomy performed. Since his thrombocytopenia did not improve with transfusion, he received an

intravenous immunoglobulin G and oral methylprednisolone 5 mg daily. Despite of all kinds of treatment, not only the platelet count increase, but it also even worsened, and it decreased to a 20.000 mm. The minimum platelet count observed on the 17th day of surgery. To verify the cause of this refractory thrombocytopenia and unresponsiveness to platelet infusion, a study of antiplatelet platelet and immunologic exam were done on 20th postoperative days. The results showed immune hemolysis (hemoglobin=7.6 g with thrombocytopenia L, platelet=12,000/ μ L, and presence of fragmented red blood cells or schistocytosis (2pluse). In a blood smear, direct and indirect Coombs tests were negative, decreased serum haptoglobin level (2.5 mg/dL), and despite discontinuation of oral warfarin international normalized ratio was remained in the upper normal level (INR 2), activated partial thromboplastin time (40 seconds) and serum fibrinogen level of 279 mg/dL, elevated serum D-dimer to 5 μ g/mL.

Increased serum bilirubin (total bilirubin 6 mg/dL, direct bilirubin 3 mg/dL), increased serum lactate dehydrogenase level to 580 mg/dL, normal levels of hepatic function tests (serum alanine aminotransferase (37 IU/L) and aspartate aminotransferase (45 IU/L). Renal function test showed a raised blood urea nitrogen (78 mg/dL), creatinine (3 mg/dL), hematuria (>20 red blood cell in a field), human immunodeficiency virus antibody was negative, and hepatitis B surface antibody was positive. The immunologic workup revealed decreased serum level of complement 3 and 4 levels (40/7 mg/dL subsequently; with normal range (800-200/11-50 mg/dL) and a positivity of autoimmune cytoplasmic antibody to level of 6. Antiplatelet serum antibody was strongly negative. For proper diagnosis of a postoperative thrombotic thrombocytopenic purpura (TTP), infusion of platelet transfusion was stopped and the dosage of steroids was raised to 65 mg/day. Despite increasing the platelet count level to 80000 with the increasing dosage of steroids, and maintenance of this count within a stable range in a 10 day period, renal failure became a deadly complication.

When the patient's thrombocytopenia, was recovered and renal and lung bleeding were stopped, the tapering of the dosage of steroids was started. The renal function was not recovered despite hemodialysis. The patient expired on postoperative day 34 after a long period of treatment for possible sepsis, but also management and monitoring for thrombocytopenia by plasmapheresis.

Discussion

Postsurgery TTP have been reported in a numerous surgical intervention, but most common of them is cardiac surgery that may be associated with extensive endothelial damage (9). TTP usually appeared after 6-9 days of surgery in most of the subjects. The true underlying cause is not clear today, but, it has been expected that endothelial injury during operation may cause, huge releasing of von Willebrand Factor (vWF) in an amount that overwhelmed the capacity of a cleaving enzyme that disintegrated the vWF. Despite the huge number of cardiac surgery in the world annually, only a handful of case reports has been described. This may partially be explained by the existence of numerous interrelating factors such as bleeding, cardiopulmonary bypass (CPB) induced hemodilution, sepsis, and heparin-induced thrombocytopenia. Another rare cause of TTP may be found in the rare subjects with genetically absence or low serum levels of disintegrating enzyme. TTP secondary to combine mitral valve replacement and CABG has rarely been described in the medical literature so far. Mild thrombocytopenia is a common issue in the post-cardiac surgery cases. With persistence of thrombocytopenia it is important to find its exact etiology to prevent unexpectable bleeding from surgical sites and others organ, but its exact pathology is difficult to find. However post cardiac surgery TTP is less common compared to heparin-induced thrombocytopenia, but it may accompany with high postoperative morbidity and mortality (10). A specific feature of surgical TTP is the presence of hemolytic anemia of microangiopathic type. The known pentad of high fever, Persistent thrombocytopenia, microangiopathic hemolytic anemia, renal failure, and central neurogenic symptoms is recognized in only a in 30% of subjects. However TTP following an endothelial injury has been diagnosed for more than 4 decades, but postoperative TTP has recently been presented as an exclusive clinical finding in the cardiac surgery field. In other hand, an unspecific clinical picture makes its clinical diagnosis a difficult clinical task (11). The disease to be considered in the differential diagnosis of postoperative thrombocytopenia may include TTP, hemolytic uremic syndrome, DIC, uncontrolled malignant hypertension, a syndrome contains three components of hemolytic anemia, elevated hepatic enzymes and thrombocytopenia syndrome, primary or drug-induced lupus erythematosus, TTP related to drugs, and disseminated cancer (12). In our case, the platelet count in the 5th day

of surgery reduced to $\frac{1}{4}$ preoperative level and this process was continued until the steroids started. This phenomenon was in contrast to CPB or heparin-induced thrombocytopenia that response to platelet infusion with discontinuation of heparin (13). As our case had experienced signs and symptoms of sepsis and DIC in the 7th postoperative day, the thrombocytopenia was diagnosed as one of the complication of CPB and heparin and its signs was treated by routine infusion of platelets concentrates for possible unexpectable bleeding episode through a surgical incision. However, in contrast to CPB or heparin-induced thrombocytopenia, in surgical TTP the decreasing platelet count has a progressive course and exaggerated with time and did not respond to platelet transfusion despite temporary improvement of DIC and bleeding episodes (14). Once we expected that the etiology of the thrombocytopenia may not only infection, but also had a postoperative TTP basis, platelet infusion, was stopped, and the laboratory exam for differential diagnosis was started. The sole Platelet infusion has been conventionally accompanied with poor outcomes (14-18).

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