Perioperative Management of a Patient with Glanzmann's Thrombasthenia for Mitral Valve Repair Under Cardiopulmonary Bypass

Abstract

A 30-year-old male patient presented with Glanzmann's thrombasthenia and mitral valve prolapse. He was in acute decompensated congestive heart failure due to severe mitral and tricuspid regurgitation. After his cardiac failure had been stabilized, the patient was subjected to mitral and tricuspid valve repair. His transfusion requirements were guided by thrombelastography and his bleeding disorder was managed by infusing single donor plasmapheresed platelet transfusions in the perioperative period. The patient underwent surgery uneventfully.

Keywords: *Glanzmann's thrombasthenia, Mitral valve prolapse, Mitral valve repair*

Parimala Prasanna Simha,
Prasanna Simha Mohan Rao[1],
Deepak Arakalgud[1],
Rakesh Rajashekharappa[1],
Manjunath Narasimhaih

Departments of Anesthesiology and [1]Cardiovascular and Thoracic Surgery, Sri Jayadeva Institute of Cardiovascular Sciences, Bengaluru, Karnataka, India

Introduction

Glanzmann's thrombasthenia (GT) is a rare inherited autosomal recessive disorder with severe bleeding tendency. It is caused by abnormal platelet function with a normal platelet count. Patients present with gum bleeding and epistaxis. Hemarthrosis and serious gastrointestinal bleeding are rare. The bleeding associated with GT by itself is usually not life threatening but postoperative bleeding may be life threatening.[1] Bleeding in GT can be controlled by local hemostatic agents and antifibrinolytic drugs. However, platelet transfusions are required during major surgical procedures.[2] There are only a few case reports of patients undergoing open heart surgery. Valve replacement surgery has additional concerns about bleeding due to postoperative anticoagulation requirement. This case report describes the perioperative management of a patient with GT who was subjected to mitral and tricuspid valve repair.

Case Report

A 30-year-old male patient who worked as a laboratory technician was admitted to Intensive Care Unit (ICU) with congestive heart failure due to severe mitral and tricuspid valve regurgitation. He had progressive dyspnea on exertion for 3 months, pedal edema for 2½ months, and orthopnea and abdominal fullness for 10 days. History revealed multiple episodes of gum bleeding and epistaxis starting from childhood. Records showed that he was diagnosed with GT. The diagnosis of GT was made based on the results of prolonged bleeding time (>15 min), normal platelet count, and absence of aggregation of platelets with agonists such as adenosine diphosphate (ADP), collagen, arachidonic acid, and ristocetin. He required multiple blood transfusions in the last 5 years for correction of anemia consequent to multiple episodes of gastrointestinal bleeding and epistaxis.

On examination, he had pallor, bilateral pedal edema, and icterus. Jugular venous pressure was raised with prominent v waves. Pulse rate was 110 with sinus rhythm, blood pressure was 106/80 mmHg. Cardiac examination revealed pansystolic murmur of Grade IV/VI. On abdominal examination, there was minimal ascites with hepatomegaly. Transthoracic echocardiography showed mitral and tricuspid valve prolapse due to myxomatous degeneration, flail posterior mitral leaflet with ruptured chordae, severe mitral regurgitation (MR), severe tricuspid regurgitation, pulmonary hypertension, left ventricular dysfunction, and pericardial effusion.

Patient's hemoglobin was 7.3 g/dl, hematocrit 24.61%, and platelet count 1.05 lakhs/mm³. Peripheral blood

Address for correspondence:
Dr. Parimala Prasanna Simha,
No. 33, Shri Sampige Road, Malleswaram,
Bengaluru - 560 003, Karnataka, India.
E-mail: parimalapsimha@gmail.com

picture showed microcytic, hypochromic anemia. Serum total bilirubin was 3.5 mg/dl. Tests for D-dimer assay, abnormal hemoglobin, von Willebrand factor assay, total iron-binding capacity, osmotic fragility test, activated partial thromboplastin time, prothrombin time/international normalized ratio, and factor VIII plasma activity were within normal limits, whereas whole-blood platelet aggregation was done at low-shear stress-induced ADP; arachidonic acid and ristocetin showed no aggregation to all agonists. This confirmed the earlier diagnosis of GT. Preoperative baseline thrombelastogram (TEG) was done which showed a lower angle (17.3°, normal value 47–74) and a lower amplitude of 18.4 mm (normal 54–72), suggesting poor platelet function.

Patient's congestive heart failure was treated with diuretics and dobutamine infusion at 5 μg/kg/min. Two units of compatible blood was transfused to correct anemia. Pulsed steroid therapy was instituted to allay risks of autoimmunity against platelets due to allotransfusions. Prophylactic oral antifibrinolytic tranexemic acid 500 mg was administered twice daily for a week. A unit of single donor (SD) plasmapheresed platelet concentrate was transfused the day before surgery.

General anesthesia was induced with fentanyl 150 μg, midazolam 3 mg, and propofol 40 mg. His trachea was intubated after muscle relaxation with rocuronium 50 mg. Anesthesia was maintained with O_2-air (50–50%) and sevoflurane. Central venous access was obtained through right internal jugular vein cannulation. To avoid nasal mucosal injury, temperature probe and Ryle's tube were put through oral cavity. Transesophageal echocardiography (TEE) probe was placed and preoperative findings confirmed [Figure 1]. The chest was opened by midline hemisternotomy. His baseline activated clotting time (ACT) was 126 s. After heparinization, ACT was 646 s. Cardiopulmonary bypass (CPB) was instituted. Retrograde autologous priming and vacuum assisted venous drainage were employed to minimize crystalloid prime volume. The heart was arrested with hypothermic hyperkalemic antegrade and retrograde cardioplegia with topical cooling. Mitral valve was repaired and a 28 mm Carpentier-Edwards (CE) annuloplasty ring was inserted. The tricuspid valve was repaired with 28 mm CE annuloplasty ring. The patient was weaned off CPB and when TEE was done to confirm the efficacy of repair, a periannular leak was noticed to be causing significant MR (Grade II) [Figure 2]. The patient was immediately put back on CPB and the defect was corrected. Total CPB time was 188 min and clamp time was 89 min. After second bypass, TEE showed no MR, with a depth of coaptation of 14 mm [Figure 3] and mild tricuspid regurgitation. TEE showed right ventricular dysfunction, so the patient was weaned from CPB with dopamine and dobutamine at 3 μg/kg/min and milrinone at 0.33 μg/kg/min. After achieving hemostasis, heparin was reversed with protamine. After protamine ACT was normalized to 132 s,
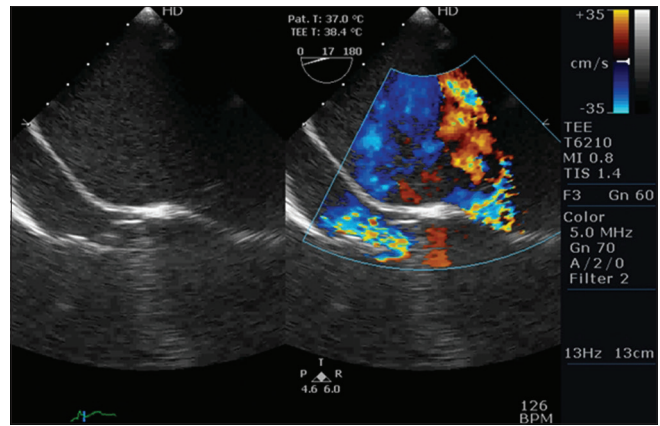

Figure 1: Midesophageal four chamber view showing giant left atrium, enlarged left ventricle, right atrium, and right ventricle with severe mitral regurgitation and tricuspid regurgitation
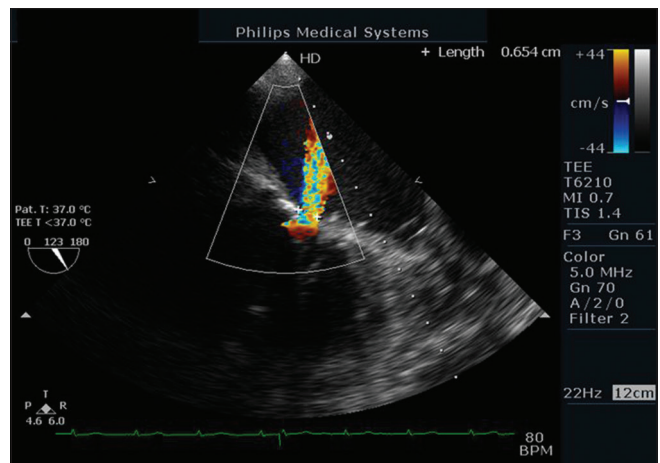

Figure 2: Transesophageal echocardiography after first cardiopulmonary bypass: Midesophageal long axis view showing significant mitral regurgitation (jet vena contracta = 6 mm)
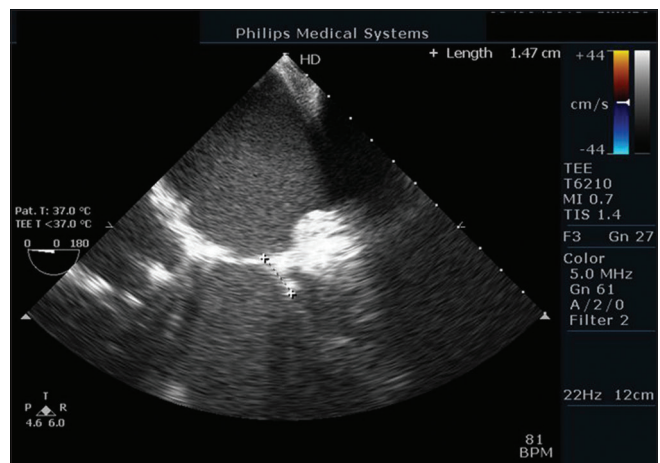

Figure 3: Transesophageal echocardiography after second cardiopulmonary bypass run showing good depth of coaptation (14 mm)

the patient was transfused with one unit of SD platelets. Mediastinal drains were placed. A vacuum suction drain was left in place but kept clamped. Chest was closed in

layers and patient shifted to the postoperative ICU. The patient remained hemodynamically stable postoperatively, with mediastinal drainage of 240 ml in the first 24 h. He received one unit of whole blood transfusion as Hb was 7.6 g/dl. The TEG showed a normal angle of progression (40.7°) and maximal amplitude of 52.9 mm mandating no further administration of platelet concentrates. Tracheal extubation was done next day morning and all the inotropes were weaned off. A unit of SD platelet concentrate was administered prophylactically and under its cover mediastinal drains were removed after ensuring that there was no active bleeding. The vacuum suction drain was left open to actively drain any residual bleeding from the chest. Opiates were given for postoperative analgesia. Drugs causing platelet dysfunction such as nonsteroidal anti-inflammatory agents and aspirin were avoided in the perioperative period. The patient was allowed orally and mobilized by evening after ensuring no further bleeding. Serous drainage of 100 ml was noted over the next 24 h from the vacuum drain and was subsequently removed as there was no further drainage. He was administered two doses of recombinant erythropoietin on alternate days to boost up RBC production. He was discharged on the 4th postoperative day with hematinics, ramipril 1.25 mg once daily, and furosemide once daily. Amiadarone 200 mg once daily was administered for 3 months prophylactically after electrocautery maze procedure even though he was in sinus rhythm. After 1½ years after surgery, the patient was admitted in medical ICU for gastrointestinal bleeding. At that time, echocardiogram showed no MR and moderate tricuspid regurgitation with right ventricular dysfunction. He succumbed to gastrointestinal bleeding 2 years after the open heart surgery.

Discussion

GT is the most frequent inherited disorder of platelet receptor integrin complex glycoprotein (GP) IIb and IIIa. Platelet membrane GPIIb/IIIa acts as fibrinogen receptor that mediates the incorporation of platelets into an aggregate or thrombus at the site of vessel injury. Eduard Glanzmann, a Swiss pediatrician, first described this disease in 1918 as "hereditary hemorrhagic thrombasthenia." GT has an incidence of 1/1,000,000, but is more common in populations of Northern Iran, Iraqi Jews, and southern India where consanguinity is common.[1] GT patients usually present with mucocutaneous bleeding such as purpura (86%), epistaxis (73%), menorrhagia (98%), or gingival bleeding (55%).[1] It is marked by prolonged bleeding time, normal platelet count, abnormal clot retraction, and absent platelet clumps on direct smear. There are three types of GT. Those patients with absent platelet aggregation and absent clot retraction are termed as having Type I disease; those with absent aggregation but residual clot retraction, Type II disease and Type III disease with abnormal aggregation and variably affected clot retraction.

In Type I disease which is the most severe form, GPIIb/IIIa levels are <5%, Type II has 5–15% levels and Type III are heterozygous carriers with normal levels of dysfunctional GPIIb/IIIa levels. In GT, aggregation response is lacking to all platelet agonists such as ADP, collagen, arachidonic acid, and ristocetin. Platelet adhesion in GT is normal. There are other causes of thrombasthenia Bernard–Soulier syndrome is a disorder of platelet adhesion. There is deficiency of GPIb the receptor for von Willebrand factor. In this syndrome, there is abnormal ristocetin-induced platelet agglutination and platelets are large. Congenital afibrinogenemia and von Willebrand disease patients have abnormal coagulation parameters in addition to platelet dysfunction. Acquired thrombasthenia is seen in patients with acute promyelocytic leukemia. Patients with acquired autoantibodies that block aggregation are often thrombocytopenic.[2]

There are three types of mitral valve prolapse (MVP), namely, primary, secondary, and functional. There is an increased incidence of primary MVP in patients with various coagulopathies such as von Willebrand's disease and in patients with skeletal abnormalities.[3] This may be due to defective embryogenesis of cell lines of mesenchymal origin.[3] Secondary MVP is seen in the presence of a known connective tissue disorder and causes of functional MVP are a dilated mitral annulus and ischemic papillary muscle dysfunction.

Cardiac surgery with CPB is associated with increased propensity to bleeding due to the nonphysiological conditions and shear stresses that the blood is exposed to. It leads to impaired primary hemostasis through platelet dysfunction. Large doses of heparin are required for anticoagulation and CPB activates fibrinolysis. There are only a few cases of GT patients who have undergone cardiac surgery. One patient operated for ventricular septal defect (VSD) closure and tricuspid valve replacement with bioprosthetic valve was subjected to preoperative hematologic workup to rule out antiplatelet antibodies and to match donor platelets for compatibility. Verify Now^R IIb/IIIa assay system that is used to assess levels of functioning platelets in patients treated with GPIIb/IIIa inhibitors such as abciximab or eptifibatide, was used perioperatively to monitor levels of properly functioning platelets.[4] Garcia-Villarreal *et al.* have reported a case of redo MVR with a bioprosthetic valve for warfarin-related catastrophic bleeding after mitral valve replacement in their patient with GT.[5] Another 8-year-old male child with GT underwent successful VSD repair. Before the operation, he received 6 units of platelets and intravenous desmopressin at 0.3 µg/kg every 2 h for 4 doses.[6] Casati *et al*, reported a heterozygous carrier of GT who was free from spontaneous bleeding but had experienced excessive bleeding requiring platelet transfusions after abciximab infusion during percutaneous coronary intervention. Later the patient was subjected to coronary artery byass grafting under

cardiopulmonary bypass. There was excessive bleeding post operatively that was controlled with tranexamic acid infusion and autologous blood transfusion.[7]

Platelet transfusion is the standard treatment during the perioperative period in patients with platelet disorders. However, repeated platelet transfusions in patients with hereditary thrombasthenia may result in alloimmunization to human leukocyte antigens (HLA) and/or platelet membrane GPIIb/IIIa, rendering future transfusions ineffective. A 77-year-old female patient underwent emergency coronary artery bypass grafting complicated by cardiac tamponade on the 2nd postoperative day. She was found to be HLA-sensitized due to previous platelet transfusions during appendicectomy, renal surgery, and hysterectomy.[8] There have been reports of successful platelet transfusions following removal of platelet antibodies by plasmapheresis or immunoadsorption. Recombinant FVIIa (rFVIIa) is an attractive alternative to platelet transfusions for the treatment of dysfunctional platelet-related bleeding. However, there is one case report of serious side effect with rFVIIa in a GT patient. Bilateral deep vein thrombosis and pulmonary embolism was observed 6 days after discontinuation of high-dose rFVIIa administered by continuous infusion for 15 days to cover a bowel resection surgery in a 72-year-old woman with GT.[9]

Conclusions

Repair of the mitral valve was done in our patient with GT because of additional concern about postoperative bleeding when anticoagulation is required after valve replacement surgery. Although no specific treatment or guidelines have been laid out, prophylactic and therapeutic platelet transfusions have been found to be supportive. Recombinant factor VIIa has been proposed for postoperative bleeding in patients of GT who have developed antiplatelet antibodies.[10] Our patient was managed with SD platelets with TEG guidance without the requirement of factor VIIa. The successful management of our case suggests that proper application of a comprehensive transfusion protocol may prevent excessive bleeding in GT.

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.

Conflicts of interest

There are no conflicts of interest.

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