Severe thrombocytopenia in tetralogy of Fallot patients: A contraindication for corrective surgery?

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ABSTRACT

A 3-year-old boy with tetralogy of Fallot and recurrent cyanotic spells was found to have severe thrombocytopenia with platelet counts in the range of 11–30,000/mm^3. There was a hesitation to operate in view of the high bleeding risk due to profound thrombocytopenia. However, the total correction was done after excluding other causes of thrombocytopenia. His platelet count dramatically improved after the operation.

Keywords: Congenital heart disease, tetralogy of Fallot, thrombocytopenia

INTRODUCTION

Thrombocytopenia in cyanotic heart disease patients, although well known, is not adequately understood. The presence of thrombocytopenia *per se* poses a dilemma for performing any surgery. Institution of cardiopulmonary bypass (CPB) during the surgery further accentuates the challenge as thrombocytopenia is a known sequela of bypass.[1] Most surgeons will operate on patients with moderate thrombocytopenia in this setting. We present a patient of cyanotic congenital heart disease (CCHD) with severe thrombocytopenia (platelet count: 11–30,000/mm^3) who could be successfully operated. We review some of the concepts regarding thrombocytopenia in CCHD.

CASE REPORT

A 3-year-old boy presented with a history of recurrent cyanotic spells for the past 4 months. The child was found to have bluish discoloration of body in the 1st week of life, and during infancy, the child exhibited poor feeding, cyanosis, and generalized ill health. The cyanotic spells had increased in frequency and severity for 3 months before presentation. He was referred for surgery to our hospital in view of severe thrombocytopenia (platelet count – 20,000/mm^3) accompanying the heart disease.

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The child was brought to our emergency in a state of cyanotic spell which was managed with intravenous metoprolol, morphine, and intravenous fluids. Detailed examination after stabilization revealed a single second heart sound with ejection systolic murmur Grade III/VI in the left parasternal area. There was no hepatosplenomegaly. Chest X-ray, electrocardiography, and two-dimensional echo confirmed the diagnosis of tetralogy of Fallot.

Blood investigation revealed hemoglobin of 16.5 gm%, total leukocyte count of 5600/mm^3, and the platelet count of 22,000/mm^3. Prothrombin time (PT) and activated partial thromboplastin time (aPTT) were normal. Peripheral smear showed giant-sized platelets with no platelet clumping, thus ruling out pseudothrombocytopenia [Figure 1]. The giant-sized platelets suggested a young platelet population in the blood. Tests for tropical infections such as malaria, dengue, and chikungunya were negative. Liver function tests were normal. Thromboelastography could not be done due to non-availability. After 2 days of admission, his platelet count was found to be 11,000/mm^3. Despite medical management, the child continued

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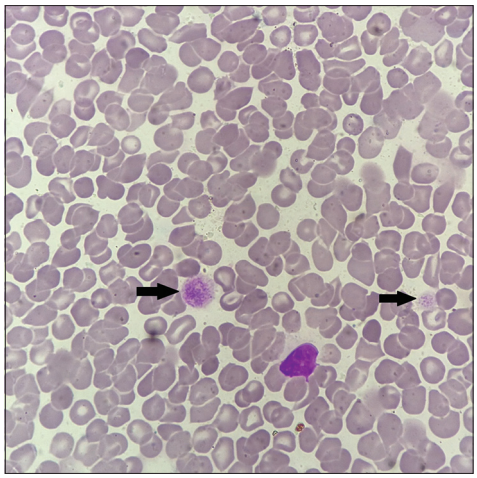

Figure 1: Peripheral blood smear showing giant platelets (arrows) (Jenner–Giemsa stain, ×1000)

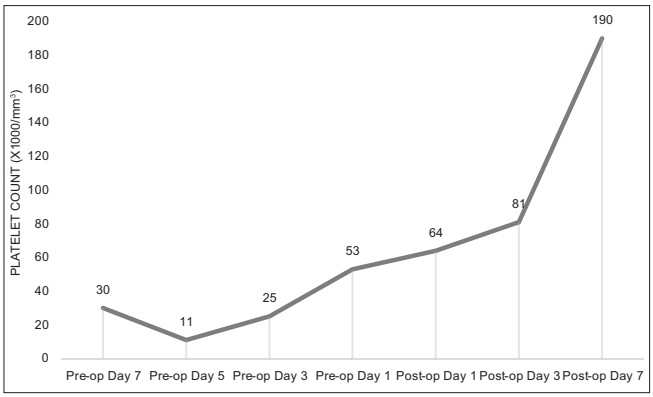

Figure 2: Perioperative changes in platelet count

to have recurrent spells during hospital stay. Hence, we decided to go for surgical correction despite the persistent severe thrombocytopenia based on our understanding that thrombocytopenia can be managed intraoperatively and it will improve after correction as no other cause was found.

With five units of random donor platelets (RDPs) transfused on the day before surgery, platelet count increased to 53,000/mm^3. During the surgery, coagulation management was done as per the unit protocol with activated clotting time monitoring. The patient was transfused one unit of RDP during surgery. He underwent trans-right atrium ventricular septal defect closure using Dacron patch and trans-right ventricular outflow tract infundibular resection with CPB time of 110 min. Following transfer to intensive care unit, he was transfused two units of RDP. The total chest drain over the ensuing 24 h was 40 ml. His postoperative course was uneventful with no excessive bleeding. On day 3, the platelet count was 81,000/mm^3 [Figure 2]. The child was discharged after 1 week of surgery with a platelet count of 1.9 lakhs/mm^3, and there were no giant-sized platelets in the peripheral smear as were seen previously.

DISCUSSION

The prevalence and pathogenesis of thrombocytopenia in CCHD have not been well established. It is known that there is an inverse relationship between the magnitude of right-to-left shunt as judged by the hematocrit and systemic arterial saturation, with the platelet counts. Thrombocytopenia in CCHD appears to represent the far end of a continuum that begins with low normal platelet counts and ends with thrombocytopenia.[2]

Four mechanisms are potentially responsible for thrombocytopenia in CCHD: (1) decreased megakaryocyte production, (2) decreased platelet production from megakaryocytes, (3) increased platelet destruction, and (4) increased platelet activation. The pathogenesis of thrombocytopenia in CCHD is based on the right-to-left shunts that deliver large precursors of platelets from the systemic venous into the systemic arterial circulation, thus circumventing the lungs and reducing the number of platelets produced in the pulmonary bed. Shunted megakaryocytes release platelets at systemic impact sites, but the released platelets remain *in situ*, without contributing to platelet counts in the blood. Polycythemia, increased blood viscosity, and other rheological factors stimulate lysis and adenosine diphosphate (ADP) release, which may also cause thrombocyte aggregation and result in thrombocytopenia.[3]

Lill *et al.*[2] studied 105 patients with CCHD and attempted to determine the cause of thrombocytopenia in these patients. Platelet count <100,000/mm^3 was seen in 26 patients. Although megakaryocyte mass, as determined indirectly by thrombopoietin levels, was normal, the absolute number of reticulated platelets (young platelets) was significantly reduced, suggesting decreased platelet production. Normal PT, aPTT, and D-dimers excluded increased platelet destruction. Platelet activation was minimal or absent based on normal or only slightly elevated platelet factor 4 and β-thromboglobulin levels. They hypothesized that right-to-left shunts deliver megakaryocytes into the system circulation, bypassing the lungs where megakaryocytic cytoplasm is fragmented into platelets, thus reducing platelet production.

Ekert and Gilchrist[4] in a study of 17 children with CCHD found no correlation between the thrombocytopenia and the prolonged bleeding time. They postulated that whole-blood platelet counts in these children may not be a true reflection of their circulating platelet pool, as in the presence of a high hematocrit, there is margination of platelets in small blood vessels. Platelet survival time has also been shown to be reduced in these patients. Goldschmidt *et al.*[5] studied platelet survival time in 13 patients with CCHD and found it to be significantly reduced in comparison to controls (5.5 ± 0.96 days vs.

10.2 ± 0.69 days). They also found that patients with normal or decreased platelet count had an increased percentage of large platelets (platelet diameter ≥2.5 μm) in comparison to controls, suggesting a younger platelet population in the patients.

Horigome *et al.*[6] studied 19 patients of CCHD with polycythemia and found markedly increased platelet microparticle production (markers of platelet activation) at hematocrit values above 60%, while platelet aggregation response to ADP showed a significant negative correlation with hematocrit. They suggested that hyperviscosity-related microparticle production and platelet aggregation suppression may play a significant role in the pathogenesis of hemostatic defects in patients with CCHD.

Cui *et al.*[7] studied perioperative hemostatic changes by real-time thromboelastograph (TEG) monitoring in 36 infants with transposition of great arteries. They found that the clot strength at the baseline was obviously lower than the normal level, and the dysfunctional fibrinogen contributed most to the coagulation dysfunction. The platelet function was relatively normal, but had significant negative correlations with preoperational hematocrit.

TEG can monitor the real-time changes of hemostasis and reveal the individual contributions of platelets and fibrinogen to the clot strength and, thus, may be utilized as a point of care test during surgeries whenever available, to determine appropriate blood component transfusion.

Taken together, all these studies suggest that while thrombocytopenia in CCHD is common and can be from multiple mechanisms, its role in postoperative bleeding might have been overemphasized. The thrombocytopenia resolves after the corrective surgery as shown in this patient also.

In general, most cardiac surgeons will still operate even if the patient has mild-to-moderate thrombocytopenia (platelet count: 0.7–1.49 lakhs/mm^3). Most of the reports in the literature of cardiac surgical procedures in patients with low platelet counts have been in the setting of idiopathic thrombocytopenic purpura and heparin-induced thrombocytopenia in adults.[8,9] There are only few reports of surgery in CCHD with severe thrombocytopenia as in this patient. Olgar *et al.*[10] reported a case of thrombocytopenia (platelet count: 21,000/mm^3) in an 8-year-old girl with tricuspid atresia and pulmonary stenosis who underwent a shunt surgery with platelet support, after which the platelet count spontaneously increased to 1.78 lakhs/mm^3, and there were no hemorrhagic complications noted. The report is to document the fact that patients with CCHD and severe thrombocytopenia related to the CHD need not be denied corrective surgery. Perioperative hydration and platelet transfusion are helpful in the management of thrombocytopenia in CCHD patients, and the issue may not be as dangerous as is generally perceived.

CONCLUSION

Thrombocytopenia in children with CCHD occasionally is severe. Patients may undergo corrective surgery despite severe thrombocytopenia and the platelet counts improve after operation.

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.

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Conflicts of interest

There are no conflicts of interest.

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