

## Shunt Operations Improved Thrombocytopenia in a Patient with Congenital Cyanotic Heart Disease

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**Cardiac and vascular intervention in thrombocytopenic congenitally cyanotic patients is more dangerous. Thrombocytopenia in these patients is related to immune thrombocytopenia, polycythemia, hyperviscosity, pseudothrombocytopenia, and drugs. Herein we report on a thrombocytopenic 8-year-old girl with tricuspid valve atresia and pulmonary valve stenosis admitted for catheterization. Thrombocytopenia (21,000/mm<sup>3</sup>) and shunt occlusion was noticed. Thrombocytopenia did not recover after intravenous immunoglobulin (IVIG) and phlebotomy therapies. During preparation for surgery, she suffered cardiopulmonary arrest. A Gore-tex graft was placed in the right pulmonary artery and truncus brachiocephalicus. After surgery, her platelet count spontaneously increased to within the normal range (178,000/mm<sup>3</sup> to 250,000/mm<sup>3</sup>). After resuscitation, she had right-sided hemiplegia sequelae, though there were no hemorrhagic findings on cranial magnetic resonance imaging (MRI) or computed tomography (CT) scans. Two months after surgery, the Blalock-Taussig (BT) shunt blood flow decreased, thrombocyte count dropped, and peripheral cyanosis reappeared. A Fontan operation was performed without hemorrhagic events, and after surgery the thrombocyte count reached 330,000/mm<sup>3</sup>. We suggest that if a patient with cyanotic heart disease has thrombocytopenia and there is no apparent cause, hypoxia-related thrombocytopenia must be considered. After reoxygenation by shunt or corrective surgeries, thrombocyte count and functions will recover. (Ann Thorac Cardiovasc Surg 2008; 14: 329–332)**

**Key words:** thrombocytopenia, cyanotic heart disease, pseudothrombocytopenia, Blalock-Taussig shunt

### Introduction

Cardiac and vascular intervention in thrombocytopenic congenitally cyanotic patients is more dangerous. Thrombocytopenia in these patients can be related to immune thrombocytopenia, polycythemia, hyperviscosity, pseudothrombocytopenia, and drugs. Patients with

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cyanotic heart disease are also exposed to several other complications, including hyperuricemia and blood clotting abnormalities, and they are open to complications from right-to-left shunts, including cerebral abscess, cerebral embolism, and endocarditis.<sup>1)</sup> However, thrombocytopenia is one of the most life-threatening conditions because it causes excessive intraoperative and postoperative bleeding, and it can sometimes cause resistance to medical therapy. In this study, we investigated a thrombocytopenic girl suffering from tricuspid valve atresia and pulmonary valve stenosis.

### Case Report

An 8-year-old girl who had undergone surgery to insert

**Table 1. Blood examination results**

	A	B	C	D	Normal range or -2 SD*
WBC ( $10^3/\mu\text{l}$ )	5.9	8.1	7.5	8.7	8.5 (4.5–13.5)
Platelets ( $10^3/\mu\text{l}$ )	21	250	108	331	$300 \pm 50$
Hemoglobin (g/dl)	18.4	16.0	13.2	10.8	13.5 (11.5)
Hematocrit (%)	64.1	55.8	43.4	35.6	40 (35)
MCH (pg)	19.0	17.8	19.7	21.4	29 (25)
MCHC (g/dl)	29.6	28.7	29.2	30.4	34 (31)
MCV (fL)	64.1	61.9	69.9	70.4	86 (77)
MPV (fL)	7.4	10.8	9.8	10.8	$8.9 \pm 1.5$

A, initial results (during admission to hospital); B, after Blalock-Taussig shunt operation; C, before Fontan operation; D, after Fontan operation; WBC, white blood cells; MCH, mean corpuscular hemoglobin; MCHC, MCH concentration; MCV, mean corpuscular volume, MPV, mean platelet volume.

\*Reference values for children 6–12 years of age.<sup>1)</sup>

a Blalock-Taussig (BT) shunt when she was 2 years old was admitted to our department for preoperative angiocardiology. She had tricuspid valve atresia, pulmonary valve stenosis, secundum type atrial septal defect, and a perimembranous outlet-type ventricular septal defect. On examination, we found central cyanosis and clubbing. On laboratory investigation, her thrombocyte count was  $21,000/\text{mm}^3$  (Table 1).<sup>1)</sup> On peripheral smear investigation, the platelets were giant, single, and rarely in double groups, and there were no hemolytic findings. Bleeding time (4 min), prothrombin time (PT) (15.5 sec), activated partial thromboplastin time (aPTT) (35.5 sec), international normalization ratio (INR) (1.30), and urine analysis were normal. On bone marrow examination, the megakaryocyte count and other cells were normal. Biochemical, viral (immunoglobulin M [IgM] titers for cytomegalovirus, Epstein-Barr virus [EBV], rubella, and parvovirus B19), and bacterial laboratory examinations were insignificant. She had no history of thrombocytopenia or abnormal bleeding, nor had she taken any relevant medications (such as aspirin, warfarin, and antibiotics). CD42b (glycoprotein Ib [GPIb]) and thrombocyte function test (with adenosine diphosphate [ADP], epinephrine, and ristocetin) findings were normal. Her platelet electron microscopy findings were normal. Phlebotomy was performed twice, producing suitable plasma for hyperviscosity, but there was no change in the platelet count. She was treated with immunoglobulin G (IgG) (0.5 g/kg/d) for 4 days, but response to the intravenous immunoglobulin (IVIG) therapy was not sufficient.

Angiocardiology was performed under platelet transfusion support. Ascending aorta oxygen saturation

was 47%, and the BT shunt was not seen. For this reason a new BT shunt was advised, but the patient had a sudden cardiopulmonary arrest on the third day after angiocardiology when she was being prepared for surgery and had right-sided hemiplegia sequelae. After resuscitation, a Gore-tex graft was placed in the right pulmonary artery and truncus brachiocephalicus, with platelet support, without hemorrhagic complications. It is interesting that after the shunt operation her platelet count increased to within the normal range ( $178,000/\text{mm}^3$  to  $250,000/\text{mm}^3$ ) (Fig. 1). On cranial magnetic resonance imaging (MRI) and computed tomography (CT) scans, there were no hemorrhagic findings, but the gray matter was slightly atrophic. The patient was then discharged with aspirin (5 mg/kg/d) prophylaxis.

She was subsequently prepared for a Fontan operation. Angiocardiology was repeated before the surgery, and oxygen saturation measurements were inferior vena cava 49.9%, right atrium 54.9%, left atrium 70.6%, left ventricle 71.6%, and aortic artery 76%. Two months after the decision to operate, her thrombocyte count dropped to  $108,000/\text{mm}^3$  and Doppler echocardiography showed decreased BT blood flow. Peripheral cyanosis was evident, and a Fontan operation was performed, without hemorrhagic events, 4 months after the second BT shunt operation. After surgery, the patient's thrombocyte count reached  $330,000/\text{mm}^3$  and she was discharged. During the follow-up period, the hemiplegia started to disappear and she began attending school.

## Discussion

Increased platelet destruction, platelet distribution or

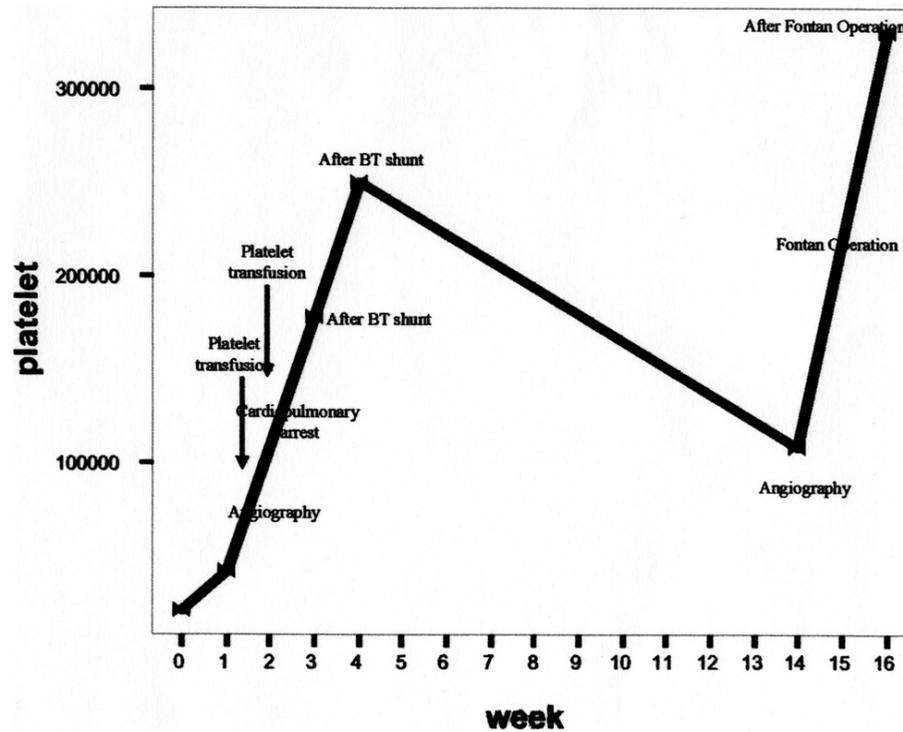


Fig. 1. Changes in platelet count.

pooling disorders, and decreased platelet production affect the platelet count of children. Cardiac and vascular intervention in thrombocytopenic patients is dangerous because of the increased risk of bleeding into a closed area. The most frequent cause of thrombocytopenia in children is immune thrombocytopenia.<sup>1)</sup> Thrombocytopenia in cyanotic congenital heart disease generally appears when the hematocrit level is more than 65% and the arterial oxygen saturation is less than 65%. This may be due to margination of platelets in the small blood vessels, which may occur in the presence of high hematocrit readings.<sup>1)</sup> There are many mechanisms involved in hypoxia-related thrombocytopenia, such as the influence of megakaryocyte differentiation, maturation and apoptosis via oxygen tension, and alteration of the physiological regulator (thrombopoietin).<sup>2-4)</sup> Prolonged hypoxia reduces the precursor cell commitment (colony-forming unit [CFU]-megakaryocyte; CFU-erythroid [CFU-E]; erythroid burst-forming units [BFU-E]; CFU-granulocyte-macrophage [CFU-GM]) to differentiate in the megakaryocyte series by enhancing demand for differentiation in the erythroid cell line in the marrow.<sup>5)</sup> Moreover, hypoxia significantly shortens

the survival of platelets in newborn and adult rabbit group studies.<sup>6)</sup> Hypoxia duration was considerable because it was demonstrated that a short severe hypoxia time was not associated with academia and did not produce thrombocytopenia, but it did significantly shorten platelet survival.<sup>6)</sup> The total circulating platelet count (TCPC) and total circulating platelet masses (TCPMs) showed biphasic responses to hypoxia on days 2-4; TCPC and TCPM were elevated, and then on days 6-14 of hypoxia they decreased.<sup>4)</sup> Also, it was demonstrated that megakaryocyte numbers decreased after 6-10 days of hypoxia and megakaryocyte size increased.<sup>4)</sup> Besides these theories, the effects of hypoxia on megakaryocyte deoxyribonucleic acid (DNA) content have been suspected but have not been demonstrated.<sup>4)</sup> The other causes of thrombocytopenia are pseudothrombocytopenia<sup>7)</sup> and heparin-induced thrombocytopenia,<sup>8)</sup> but these were evaluated by repeat peripheral smear examinations.

Further, monomeric Igs, corticosteroids, platelet transfusion, intravenous anti-D, and homologous blood transfusion are combined to minimize the risk of bleeding complications during the operative and post-

operative period for different types of thrombocytopenic patients.<sup>1)</sup>

Our patient's thrombocytopenia developed from severe hypoxia and severe cyanosis, and polycythemia and hyperviscosity were caused by occlusion of the former BT shunt. Moreover, our patient's cranial MRI and CT proved that the neurological situation was caused by sudden cardiovascular arrest and chronic hypoxia.

In conclusion, platelet transfusions and IVIG caused no improvement in our patient's thrombocyte count, which recovered only after the shunt operation. Our opinion is that if a patient has thrombocytopenia with no apparent cause, hypoxia-related thrombocytopenia must be considered, and for that reason a shunt operation must be performed.

## References

1. Lanzkowsky P. Disorders of platelets. Manual of Pediatric Hematology and Oncology. California: Academic Press, 2000; pp 233–85.
2. Mostafa SS, Miller WM, Papoutsakis ET. Oxygen tension influences the differentiation, maturation and apoptosis of human megakaryocytes. *Br J Haematol* 2000; **111**: 879–89.
3. Nakanishi K, Tajima F, Osada H, Kato T, Miyazaki H, et al. Thrombopoietin expression in normal and hypobaric hypoxia-induced thrombocytopenic rats. *Lab Invest* 1999; **79**: 679–88.
4. McDonald TP, Cottrell MB, Steward SA, Clift RE, Swearingen CJ, et al. Comparison of platelet production in two strains of mice with different modal megakaryocyte DNA ploidy after exposure to hypoxia. *Exp Hematol* 1992; **20**: 51–6.
5. Rolovi Z, Basara N, Biljanovi -Paunovi L, Stojanovi N, Suvajdzi N, et al. Megakaryocytopoiesis in experimentally induced chronic normobaric hypoxia. *Exp Hematol* 1990; **18**: 190–4.
6. Castle V, Coates G, Mitchell LG, O'Brodovich H, Andrew M. The effect of hypoxia on platelet survival and site of sequestration in the newborn rabbit. *Thromb Haemost* 1988; **59**: 45–8.
7. Shreiner DP, Bell WR. Pseudothrombocytopenia: manifestation of a new type of platelet agglutinin. *Blood* 1973; **42**: 541–9.
8. Menajovsky LB. Heparin-induced thrombocytopenia: clinical manifestations and management strategies. *Am J Med* 2005; **118** (Suppl 8A): 21–30S.