

CASE REPORT

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Utility of thromboelastogram in cardiac surgery in Jacobsen syndrome associated with platelet dysfunction: a case report

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Abstract

Background: Jacobsen syndrome is a rare genetic disorder with multiple congenital anomalies and platelet abnormalities caused by chromosome 11 deletion.

Case presentation: A 7-month-old boy with thrombocytopenia underwent ventricular septal defect closure. At the beginning of surgery, the platelet count was $168 \times 10^3/\mu\text{L}$, and heparinized kaolin with heparinase reaction time (HKH-R), which represents clot formation time, was prolonged at 30.4 min. Platelet transfusion was continued, and at the end of surgery, the platelet count and HKH-R values improved to $215 \times 10^3/\mu\text{L}$ and 15 min, respectively.

Conclusions: As anesthetic management of patients with abnormal platelet function, the viscoelasticity test might be useful in evaluating hemostatic capacity.

Keywords: Chromosome 11, Hemostatic capacity, Jacobsen syndrome, Thrombocytopenia, Viscoelasticity

Background

Jacobsen syndrome (JS) is a group of rare genetic disorders associated with multiple congenital anomalies and mental retardation caused by the partial deletion of the long arm of chromosome 11 [1, 2]. These diseases are associated with hematopoietic disorders, such as thrombocytopenia and platelet dysfunction, which are present at birth [3, 4]. Abnormal bleeding such as cerebral hemorrhage has been reported to occur even when platelet counts are normal [5]. The perioperative use of thromboelastography (TEG), which measures blood viscoelasticity in real time using whole blood, helps in planning for blood product administration [6, 7]. However, no studies have investigated how abnormalities in platelet count and function affect TEG results in patients with JS.

Herein, we describe a case of intraoperative hemostatic control using comprehensive hemostatic assessment focusing on platelet function by TEG[®] 6s (Haemonetics,

Massachusetts, USA) [8] during the ventricular septal defect (VSD) closure in a JS patient who had abnormal platelet function despite a normal platelet count as well as coagulation function tests.

Written consent was obtained from the parent of the patient for publication of this case report.

Case presentation

A 1-day-old male infant was transferred to our hospital for heart murmur and progressive hypercapnia. He was born via spontaneous vaginal delivery at 36 weeks and 3 days of gestation with a birth weight of 2700 g. He had no remarkable family history, and the pregnancy course was uneventful. He was noted to have a high prominent forehead, low-set ears, a thin upper lip, and retrognathia. There were no abnormalities in the central nervous system, digestive system, and urinary system. On admission, the following thrombocytopenia and coagulation abnormalities were found. Platelet count was $39 \times 10^3/\mu\text{L}$, prothrombin time-international normalized ratio (PT-INR) was 1.65, activated partial thromboplastin time (APTT) was 48.8 s, and fibrinogen was 168 mg/dL.

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Aortic arch reconstruction and ductus arteriosus ligation were performed at 6 days of age. He developed intratracheal hemorrhage on postoperative day 4 and underwent emergency pericardial drainage for pericardial tamponade on postoperative day 11. He also had intraventricular hemorrhage and pancytopenia requiring regular transfusions of platelet concentrates (PCs) and red blood cells (RBCs). A bone marrow test was performed at 2 months of age to investigate the cause of pancytopenia. Genetic testing of bone marrow cells revealed a partial deletion of chromosome 11, leading to the diagnosis of JS. The levels of coagulation factors 8 and 9, von Willebrand, and proteins C and S were all within normal limits. Further close examinations of platelet function and morphology were performed in the fourth month of life after the diagnosis of JS was confirmed. A peripheral blood smear showed large platelets, and mean platelet volume (MPV) was 13 fL (normal: 7–11 fL). Platelet aggregation test showed no aberrant adenosine diphosphate (ADP) aggregation, but collagen aggregation was clearly decreased.

At 7 months of age (height 62.4 cm, weight 4998 g), VSD closure was planned for progressive pulmonary hypertension. Platelet count on readmission was $78 \times 10^3/\mu\text{L}$, and five PC units were transfused each of 5 days and 1 day before surgery. Immediately prior to VSD closure, platelet count was normal at $156 \times 10^3/\mu\text{L}$, and coagulation function tests were also normal with PT-INR 1.04, APTT 37.6 s, and fibrinogen was 159 mg/dL, slightly below normal. We planned to maintain

a platelet count $> 100 \times 10^3/\mu\text{L}$, also to monitor platelet function using TEG[®] 6s PlateletMapping[®] (Fig. 1).

Anesthesia was maintained with sevoflurane, fentanyl, and midazolam after uneventful induction with inhalational sevoflurane and tracheal intubation. The platelet count at the beginning of surgery was $168 \times 10^3/\mu\text{L}$. Although the platelet function showed a normal clot strength as indicated by the maximal amplitude for heparinized kaolin with heparinase (HKH-MA) of 53.1 mm (normal value: 53–68 mm), clot formation time by HKH reaction time (HKH-R) was prolonged to 30.4 min (normal value: 4.2–9.8 min) (TEG 1; Table 1, Fig. 2). After systemic heparinization, PCs were continuously administered during cardiopulmonary bypass (CPB) at 0.5 U/h. Although platelet count was fewer and HKH-R was longer than the normal range before CPB (TEG 2), both have improved after completion of CPB and surgery (TEGs 3 and 4, respectively). We administered 50 mL of RBCs and 150 mL of fresh frozen plasma (FFP) after CPB until the end of the surgery. Surgery and anesthesia lasted 5 h 8 min and 7 h 32 min, respectively. Intraoperative hemorrhage was approximately 66 mL, and 50 mL of RBCs, 150 mL of FFP, and 150 mL of PCs were transfused. Extubation was performed on postoperative day 1, and the patient was discharged on postoperative day 17. On postoperative day 22, the patient was readmitted to the hospital for subdural hematoma and underwent platelet transfusion.

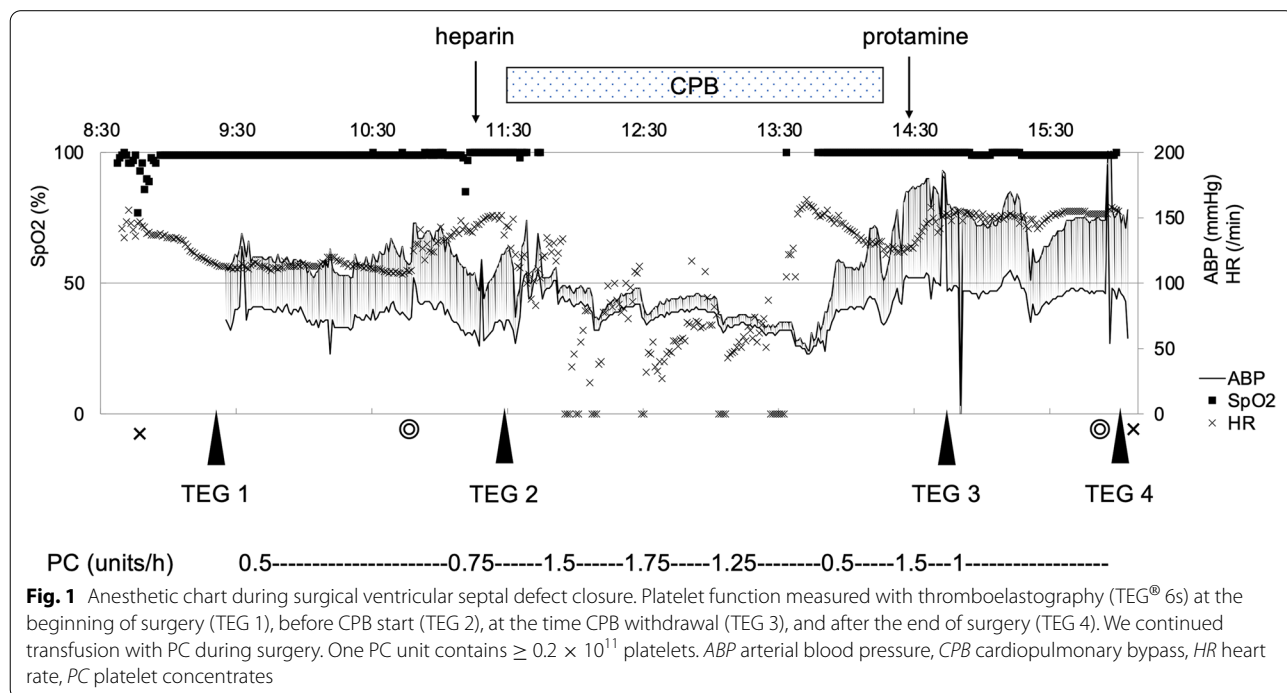


Table 1 Changes in platelet function measured with TEG® 6s during operation

Parameters	Measure point				Range
	TEG 1	TEG 2	TEG 3	TEG 4	
HKH-R (min)	30.4	15	10.8	15	4.2–9.8
HKH-K (s)	9.5	2.6	2.2	2.3	1.0–2.9
HKH-angle (degree)	42.9	60.5	65.5	65.3	57–75
HKH-MA (mm)	53.1	64.5	57.1	57	53–68
ActF-MA (mm)	6.1	9.6	2.3	3.4	2–19
ΔMA (mm)	47	54.9	54.8	53.6	
ADP-MA (mm)	54.4	56.3	31.3	44.6	45–69
ADP inhibition (%)	0	14.9	47.1	23.1	0–17
PLT (× 10 ³ /μL)	168	112	133	215	-
Hb (g/dL)	8.1	8.2	10.2	10.2	-

TEG1, TEG2, TEG3, and TEG4 represent preoperative, pre-cardiopulmonary, post-cardiopulmonary, and postoperative measurements, respectively. *Abbreviations:* TEG Thromboelastography, HKH Heparinized kaolin with heparinase, R Reaction time, K Coagulation time, angle α angle, ActF Activator F, MA Maximum amplitude, ADP Adenosine diphosphate, PLT Platelet, Hb Hemoglobin

Discussion

JS is a genetic disorder characterized by facial dysmorphism, cardiac disease, and thrombocytopenia. Its incidence is approximately 1 per 100,000 live births [9, 10]. Diagnosis is frequently based on clinical features and confirmed by karyotyping. Cardiac malformations are present in more than 50% of the patients diagnosed with JS, with two-thirds having VSDs or mitral or aortic

valve abnormalities [11]. In addition, platelet abnormalities are frequently observed in JS. The Paris-Trousseau platelet syndrome is present in 95% of patients with JS [3, 4]. Platelet abnormalities manifest as thrombocytopenia or pancytopenia during infancy, but our patient presented with thrombocytopenia from birth and continued to have bleeding events and pancytopenia after surgery leading to the diagnosis of JS. Brain hemorrhages are frequently accompanied in patients with JS as observed in our patient [5].

The TEG test uses whole blood and has been widely utilized in evaluating coagulation function within 10–15 min in the operating room [12]. Intraoperative TEG may help reduce perioperative blood loss, avoid blood transfusions, and determine the strategy of blood product and hemostatic agent administration [7, 13]. In TEG® 6s, the Global hemostasis® cartridge performs conventional coagulation tests, and the PlateletMapping® cartridge measures platelet function [8]. In the current case, we used Platelet-Mapping® to evaluate platelet function. The HKH in PlateletMapping® is the same as the CKH (citrate kaolin with heparinase) in Global hemostasis®. It contains heparinase that neutralizes heparin and measures thrombin formed by kaolin and clot strength formed by fibrin.

Platelet count was normalized preoperatively and managed intraoperatively to keep platelet count above 100 × 10³/μL with reference to platelet count and TEG® 6s. Before surgery, we detected the normal HKH-MA but prolonged HKH-R in our JS patient. This implies a normal

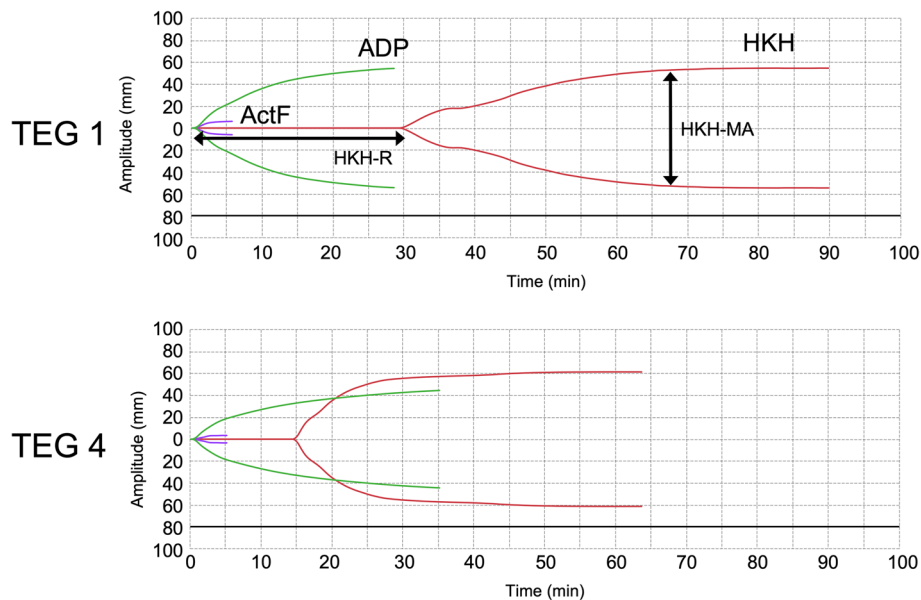


Fig. 2 Raw data of thromboelastography (TEG) before (TEG 1) and after surgery (TEG 4). The normal value of HKH-R is 4.2–9.8 min, and the normal value HKH-MA is 53–68 mm. The HKH-R was prolonged preoperatively (TEG 1) and shortened postoperatively (TEG 4) by continued intraoperative platelet transfusions. HKH heparinized kaolin with heparinase, ActF activator F, ADP adenosine diphosphate

maximum hemostatic capacity but a longer time to stop bleeding. This is consistent with the fact that JS is considered a granular release disorder because of the presence of giant granules in the smear [2, 4]. In general, HKH-R prolongation suggests a deficiency of coagulation factors. However, the maximal amplitude evaluated by activator F (ActF-MA), which reflects fibrinogen concentration, was within the normal range, and there were no coagulation factor abnormalities in the preoperative examination. Therefore, the prolonged HKH-R in this case may reflect abnormal platelet function such that only collagen aggregation is reduced while ADP aggregation is preserved.

Platelet transfusion was continued. HKH-R before the start and at the end of CPB improved to 15 min and 10.8 min, respectively. With this, we could perform anesthesia management and confirm that platelet transfusion improved the rate of platelet clot generation. Additionally, ActF-MA remained normal throughout the surgery. HKH-MA–ActF-MA, which indicates the clotting ability of platelets alone, also tended to improve throughout the surgery, suggesting the importance of platelet transfusion in this case.

The percent ADP inhibition increased to 47.1% after CPB withdrawal and improved thereafter (Table 1). Platelet count and ADP aggregation capacity have been reported to decrease after CPB to 57% and 10%, respectively [14]. The CPB time in our patient was approximately 2 h, but the increase in ADP inhibition may be due to CPB.

In conclusion, we presented a case of VSD closure in a JS patient with platelet abnormalities. As platelet count and platelet function need to be carefully monitored during the anesthetic management of patients with JS, a viscoelasticity test using TEG[®] 6s is a good tool to evaluate hemostatic capacity.

Abbreviations

ActF: Activator F; ActF-MA: Maximal amplitude evaluated by activator F; ADP: Adenosine diphosphate; APTT: Activated partial thromboplastin time; CKH: Citrated kaolin with heparinase; CPB: Cardiopulmonary bypass; FFP: Fresh frozen plasma; JS: Jacobsen syndrome; HKH: Heparinized kaolin with heparinase; HKH-MA: Maximal amplitude for heparinized kaolin with heparinase; HKH-R: Reaction time for heparinized kaolin with heparinase; MPV: Mean platelet volume; PC: Platelet concentrate; PT: Paris-Trousseau platelet syndrome; PT-INR: Prothrombin time-international normalized ratio; RBCs: Red blood cells; TEG: Thromboelastography; VSD: Ventricular septal defect.

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Authors' contributions

CT performed perioperative management, wrote the initial draft, and revised the manuscript. AH performed perioperative management, prepared the initial figures and table of the manuscript, and helped draft the manuscript. GY performed perioperative management and helped draft the manuscript. AM performed perioperative management and helped draft the manuscript. KT performed perioperative management and helped draft the manuscript. SK

supervised the perioperative management and helped draft, revise, and edit the manuscript. The authors read and approved the final manuscript.

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Availability of data and materials

The relevant data for this case report are unavailable for public access because of patient privacy concerns.

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Written consent was obtained from the parent of the patient for publication of this case report.

Competing interests

The authors declare that they have no competing interests.

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