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We present the case of a 61-year-old patient with a history of essential thrombocythemia (ET) who was diagnosed as having aortic valve stenosis and dilatation of his ascending aorta. His aortic valve and ascending aorta were replaced under hypothermic circulatory arrest (HCA). No clear guideline exists for preoperative, perioperative, and postoperative management of cardiac surgery using HCA for ET patients. After performing risk assessment, we prescribed preoperative aspirin therapy and postoperative care was planned as usual for cardiovascular surgery in our establishment. Unexpectedly, activated clotting time did not exceed 400 seconds, but the course of treatment was otherwise uneventful.

Keywords: essential thrombocythemia, hypothermic circulatory arrest

Introduction

Essential thrombocythemia (ET) is a myeloproliferative disorder characterized by chronically abnormally high platelet count and risk of thrombotic and hemorrhagic events, which can complicate perioperative management of cardiovascular surgery. On the other hand, hypothermic circulatory arrest (HCA) is an effective brain protection technique, but its major cause for concern is hypothermia-induced coagulopathy. Few reports are available on cardiac surgery using HCA in ET patients. Here, we present the case of a patient with ET who underwent aortic valve and ascending aorta replacement under HCA.

Case Report

A 61-year-old Japanese male with symptomatic moderate-to-severe stenosis of his bicuspid aortic valve, and with significant dilatation of his ascending aorta, was referred to us about 6 months after initial diagnosis. He suffered recurrent chest pain and dyspnea on exertion. Echo-Doppler evaluation revealed his bicuspid aortic valve with severe calcification and decreased mobility of the leaflets, but no regurgitation. The peak pressure gradient across the aortic valve was 66 mmHg, his aortic valve area was 1.15 cm^2 (indexed AVA 0.61 cm^2/m^2), with a peak trans-aortic flow velocity of 4.1 m/s. Preoperative computed tomography demonstrated a fusiform aneurysm of his ascending aorta with a maximum diameter of 48 mm. The only notable anomaly in his previous medical history was essential ET, which was diagnosed by the absence of reactive conditions (blood loss, iron deficiency, infection, etc.) and other clonal disorders (myeloproliferative disease and myelodysplastic syndromes). This diagnosis was made by a specialist in the Japanese Society of Hematology. The patient had no definitive history of thromboembolic events although his baseline platelet count had ranged between 640 × 10^3/μL and 760 × 10^3/μL. Other laboratory results were

(a)

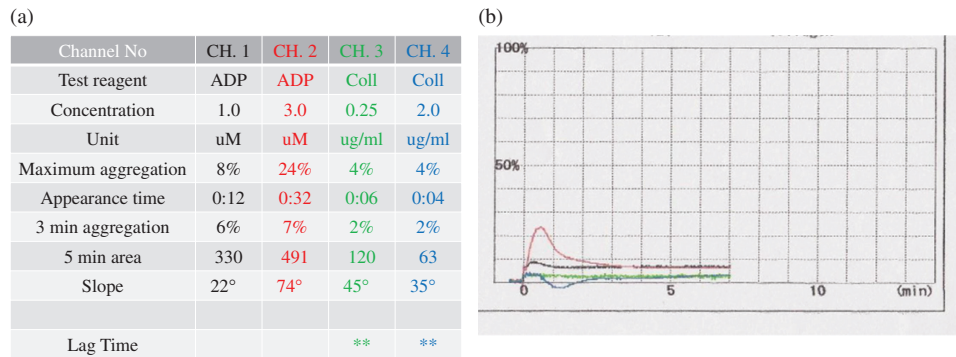| Channel No	CH. 1	CH. 2	CH. 3	CH. 4
Test reagent	ADP	ADP	Coll	Coll
Concentration	1.0	3.0	0.25	2.0
Unit	uM	uM	ug/ml	ug/ml
Maximum aggregation	8%	24%	4%	4%
Appearance time	0:12	0:32	0:06	0:04
3 min aggregation	6%	7%	2%	2%
5 min area	330	491	120	63
Slope	22°	74°	45°	35°
Lag Time			**	**

(b)

Fig. 1 The platelet aggregation test, with either ADP or collagen, showed reduced area under the curve. ADP: adenosine diphosphate

Item name	Result	Unit	Reference value	
J A K 2 Mutation	(+) ↑		(−)	

**Fig. 2** The JAK2 mutation was detected. JAK2: janus kinase 2

as follows: white blood cell count, 12900/μL; analysis of coagulation was normal (except for activated partial thromboplastin time at 42.5 seconds; von Willebrand factor antigen: 127%; von Willebrand factor activity 76%; cold agglutinin titer test: 1/16). The platelet aggregation test, with either adenosine diphosphate (ADP) or collagen, showed reduced area under the curve (**Fig. 1**). A bone marrow biopsy showed megakaryocytic hyperplasia with preserved maturation and no change in the erythrocyte and granulocyte series; neither fibrosis nor dysplastic change was observed. The janus kinase 2 (JAK2) mutation was detected (**Fig. 2**), and the test result for expression of breakpoint cluster region/abelson (BCR/ABL) was negative (**Fig. 3**). He had started on a low-dose aspirin therapy (100 mg/day) for this condition 6 months before presenting at our hospital, and it was continued preoperatively and postoperatively.

The operation was performed under general anesthesia, and the sternum was opened. After heparin sodium 300 IU per kg bodyweight had been given intravenously, the activated coagulation time (ACT) increased from 139 seconds to 352 seconds, but because ACT did not exceed 400 seconds, additional heparin sodium 5000 IU was added twice (for an eventual ACT of 363 seconds). Cardiopulmonary bypass (CPB) was initiated by ascending aorta blood delivery and superior and inferior vena cava blood removal. CPB was suspended at a tympanic temperature of 25°C, when the aorta was opened. The myocardium was protected by retrograde cardioplegia. Replacement of the ascending aorta was performed using an open distal anastomosis technique under circulatory arrest only. After completion of the distal repair, the vascular prosthesis (J Graft SHIELD NEO, Japan Lifeline, Tokyo, Japan) was clamped, then antegrade systemic circulation was restarted through the side branch of the prosthesis, and rewarming was begun. After confirmation that the aortic valve was bicuspid, that valve was resected and replaced with a bioprosthetic valve (Carpentier-Edwards Perimount (CEP) Magna Ease, Edwards Lifesciences, Irvine, CA, USA) in a supra-annular position. The proximal anastomosis was performed about 1 cm above the sinotubular junction. After that, coronary circulation was restarted. No clots were seen in the circuit, and weaning from CPB was trouble-free. Protamine sulfate 310 mg was administered intravenously to neutralize the heparin, and the ACT returned to 149 seconds. The CPB time was 103 minutes, the cross clamp time was 74 minutes, and the HCA time was 16 minutes (**Fig. 4**). Intraoperative blood transfusion was not required.

The patient was extubated 14 hours later, and he left intensive care unit on postoperative day 1. Aspirin 100 mg per day, and warfarin controlled from prothrombin time-international normalized ratio (PT-INR) 1.6 to 2.6, were started on postoperative day 1. Postoperative recovery was uneventful. He was discharged on postoperative day 17. Platelet counts during hospitalization were under 700×10^3/μL. No thrombotic or bleeding episodes occurred through postoperative day 749.

(a) BCR/ABL - Mononuclear cell
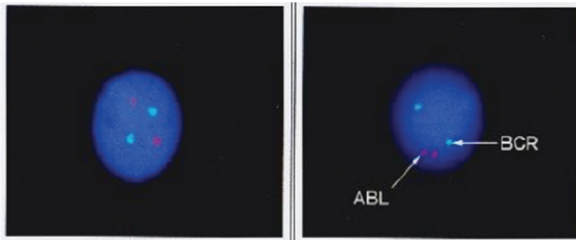
(b) BCR/ABL – Neutrophil cell
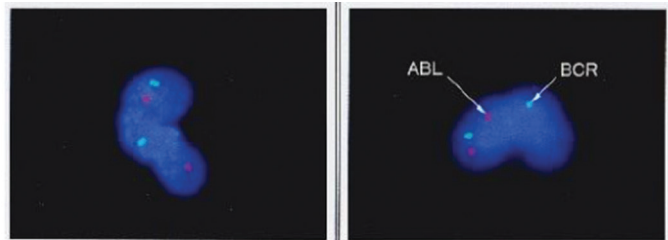
BCR/ABL - Mononuclear cell fusion signal

	Negative	Positive
Number of measurements	200	0
Detection rate	100.0%	0.0%

BCR/ABL – Neutrophil cell fusion signal

	Negative	Positive
Number of measurements	200	0
Detection rate	100.0%	0.0%

Fig. 3 The test result for expression of BCR/ABL was negative. Mononuclear cell's BCR/ABL was negative, and neutrophil cell's BCR/ABL was also negative. BCR/ABL: breakpoint cluster region/abelson
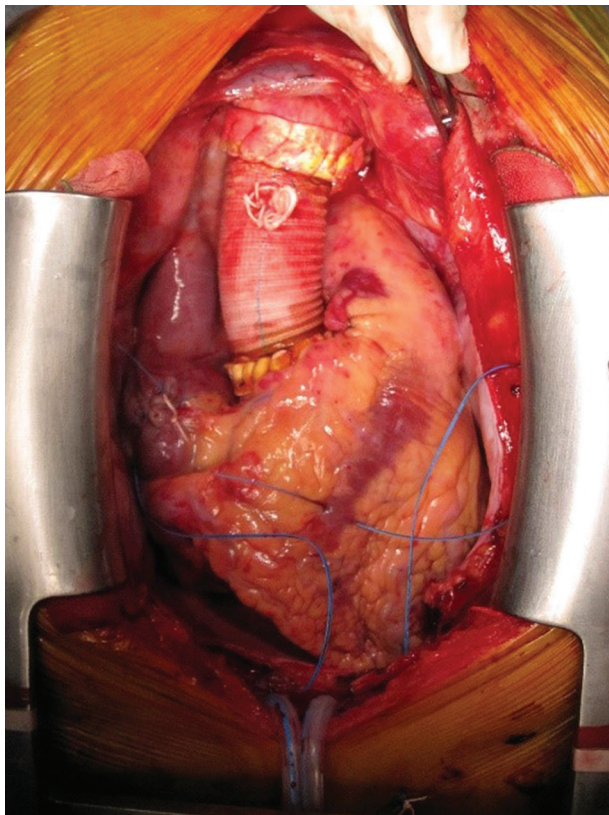

Fig. 4 After aortic valve replacement (CEP Magna Ease 27 mm) and ascending aorta replacement (J Graft SHIELD NEO 30 mm). CEP: Carpentier-Edwards Perimount

Discussion and Conclusion

We are unaware of any clear guideline for preoperative, perioperative, and postoperative management of cardiac surgery for patients with ET. ET is classified into two groups according to risk of thrombosis: high risk (age ≥60 years, or history of thrombosis, or platelet count ≥1500 × 10³/μL) and low risk (age < 60 years, no history of thrombosis, and platelet count <1500 × 10³/μL).[1] ET may also be classified into three groups according to life expectancy: high risk (age ≥60 years and WBC count ≥15000/μL), intermediate risk (age ≥60 years or white blood cell [WBC] count ≥15000/μL), and low risk (age < 60 years WBC count <1500 × 103/μL).[2] The reference indicates that cytoreductive therapy is not needed in low-risk ET patients, while recommending the use of low-dose aspirin in the presence of vasomotor symptoms or general indications for aspirin use.[3] Meanwhile, high-risk ET patients should be treated with cytoreductive therapy and low-dose aspirin.[4] We founds 12 published case reports describing patients with ET undergoing cardiovascular procedures requiring CPB.[5–16] Of these 12 patients, 3 patients reportedly suffered major complications postoperatively, and all three had preoperative platelet counts greater than 800 × 10³/μL. These three patients were classified as "high risk" for thrombosis and "intermediate risk" for life expectancy, and baseline platelet counts had ranged between 640 × 10³/μL and 760 × 10³/μL. Because of them, we treated this case with only aspirin in the preoperative period.

Because this case involved cardiac surgery with both CPB and HCA, some risk of adverse events in the hemostatic and coagulation system had been expected. Few English-language reports have been published on cardiac surgery using HCA in ET patients. Because this case had been categorized as high risk for thrombosis but intermediate risk for life expectancy, with platelet count

stable at less than $800 \times 10^3/\mu L$, perioperative and postoperative management was planned as usual for cardiovascular surgical cases in our hospital. Postoperatively, this case was treated with aspirin for oral antiplatelet therapy and warfarin as an oral anticoagulant. Warfarin was ended 3 months after surgery, and aspirin was continued. The postoperative course was smooth, the duration of hospitalization was 17 days, and no thrombotic or bleeding episodes have occurred through postoperative day 739.

After heparin administration at the start of CPB, the failure to extend ACT past the threshold of 400 seconds was unanticipated although such heparin resistance is not unprecedented.[4] We decided to pursue operation with CPB if the ACT could be extended beyond 350 seconds, so the patient was given 31000IU of heparin sodium in total. The results were good, the reservoir did not need to be changed and no clots were seen during CPB. The operation was performed with no undue difficulty. This case happened to be a successful case, but accumulation of data from far more cases will be needed before conclusions can be drawn.

In conclusion, we performed aortic valve replacement with a bioprosthetic valve and ascending aorta replacement using HCA in this patient with ET. As hoped, our standard surgical technique, with careful preoperative and postoperative management produced an uneventful result, but we suspect that treatment interventions based on thrombosis risk and life expectancy risk deserve further consideration.

Disclosure Statement

All authors have no conflict of interest.

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