Replacement Therapy for Hemophilia Patients Undergoing Cardiac Surgery: Report of Three Cases

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ABSTRACT

Hemophilia is an X-linked recessive inherited bleeding disorder. Despite the improved treatment in recent years with the advent of replacement therapies, the progression of atherosclerosis is not slowed down after the reduction of clotting factors in hemophilia. As life expectancy increases, more hemophilia patients will suffer from age-related cardiovascular diseases. Since cardiac surgery needs heparinization and cardiopulmonary bypass (CPB), it is extremely challenging to balance hemostasis and coagulation in patients with hemophilia. Here we report three cases of hemophilia patients who underwent cardiac surgery successfully.

Key words: Hemophilia; cardiac surgery; replacement therapy

INTRODUCTION

Hemophilia is an X-linked recessive inherited bleeding disorder. Despite the improved treatment in recent years with the advent of replacement therapies, the progression of atherosclerosis is not slowed down after the reduction of clotting factors in hemophilia. As life expectancy increases, more hemophilia patients will suffer from age-related cardiovascular diseases.

Since cardiac surgery needs heparinization and cardiopulmonary bypass (CPB), it is extremely challenging to balance hemostasis and coagulation in patients with hemophilia. Here we report three cases of hemophilia patients who underwent cardiac surgery successfully.

CASE DESCRIPTION

Case 1

A 57-year-old man was admitted with acute chest pain

and palpitations, which were not relieved by nitroglycerin. The patient had a previous history of hemophilia B and he had received multiple blood product replacement treatments since he was 7 years old. He underwent a successful right knee replacement surgery under recombinant factor IX (FIX) replacement therapy for hemophilic arthritis in 2017, followed by intermittent prothrombin complex concentrate (PCC) and recombinant FIX infusion therapy 20 - 30 times annually. One of his elder brothers died of hemophilia at an early age. Coronary angiography showed severe three-vessel disease. Since the patient could not tolerate dual antiplatelet therapy after percutaneous intervention (PCI) because of hemophilia, coronary artery bypass surgery was recommended, which was successfully performed under the recombinant nine-factor replacement therapy. PCC replacement therapy was offered five days after the operation. The patient was smoothly discharged on the 20th day after surgery.

Case 2

A 62-year-old man was diagnosed with dilated ascending aorta, which increased in diameter from 42mm to 61mm in 10 years. With a history of hemophilia B, the patient was admitted with an FIX activity of 2.2%. He has been treated with PCC intermittently and currently he has no joint deformities. Coronary CTA indicated multiple calcification and mild stenosis of the coronary arteries. Echocardiography revealed aortic valve malformation, combined with moderate stenosis and insufficiency. The patient underwent aortic root replacement. Hematologists participated in the establishment of alternative treatment plans before surgery. Due to economic consideration, PCC was used as an alternative treatment option. The drainage tube was removed on the 9th day after the operation and the patient was discharged from the hospital.

Case 3

A 49-year-old patient was diagnosed with hypertrophic cardiomyopathy (HCM), a hereditary heart muscle disease. Preoperative laboratory examination revealed an activated partial thromboplasting time (APTT) of 53.9 seconds and an FVIII activity of 9.6%. After consultation with a hematologist, a diagnosis of hemophilia A was made. He had never been treated by PCC or recombinant coagulation factors before admission. Echocardiography suggested obstructive hypertrophic cardiomyopathy associated with moderate mitral regurgitation. Marrow surgery was performed, followed by the use of FVIII replacement therapy until the 7th day after surgery. The drainage tube was removed on the 4th day after surgery.

The clinical presentation and pre-test and alternative schemes of all the three cases are summarized in

Table 1.

Table 1. Clinical presentation and pre-test and alternative schemes

Characteristics		Case 1		Case 2		Case 3	
Age/sex		57 years/M		62 years/M		49 years/M	
Weight (kg)		65		68		70	
Diagnosis		CAD		AA		HOCM	
Type of hemophilia		B		B		A	
Pre-test							
Drugs		FIX		PCC		FVIII	
Dosage		1000IU		30IU/Kg		3500IU	
Factor activity APTT (s)		FIX (%)	APTT	FIX (%)	APTT	FVIII (%)	APTT
0		3.6	47.3	2.2	44.4	10.6	43.5
15min		14.9	-	35.4	33.1	25.8	-
2h		-	-	31.7	29.6	104.2	-
4h		11.2	-	28.1	29.5	94.9	-
8h		9.1	-	27.8	29.3	79.7	-
12h		8.6	-	20.5	30.9	67.6	30.3
24h		11.5	37.5	-	31.9	57.0	31.8
Replacement therapy							
Drugs		FIX		PCC		FVIII	
Dosage		Preoperative	6000 IU	Preoperative	4200 IU	Preoperative	2800 IU
		12h	1500 IU	12h	2200 IU	12h	2800 IU
		D1-D2	3000 IU	D1	2200 IU	D1-D2	2800 IU
		D3-D4	2000 IU	D2-D3	2000 IU	D3-D4	1000 IU
		D5	change to PCC	D4-D6	1400 IU	D5-D7	1000 IU
					D7-D14	800 IU	

Continued Table 1. Clinical presentation and pre-test and alternative schemes

Characteristics	Case 1	Case 2	Case 3
ACT (s)			
Before CPB	596	530	585
Postoperation	104	95	108
Time of CPB (min)	92	171	79
Bleeding (mL)	300	500	500

CAD: coronary artery disease; AA: aortic aneurysm; HOCM: hypertrophic cardiomyopathy; FIX: recombinant coagulation factor IX; PCC: prothrombin complex concentrate; FVIII: plasma-derived coagulation factor VIII; APTT: activated partial thromboplastin time; ACT: activated blood clotting time; CPB: cardiopulmonary bypass.

DISCUSSION

Hemophilia accompanied by various heart diseases will not be rare in the near future. A perioperative management protocol for these patients is urgently needed, especially when there is no internationally-recognized consensus.^[1] Although there are only a few patients with hemophilia need to receive cardiac surgery, recent research has demonstrated the effectiveness and safety of replacement therapy^[1,2,3].

In our current series, all patients were consulted by hematologists before the operation, and the perioperative alternative treatment option was determined by the results of a coagulation factor pre-test. The concentrations of plasma coagulation factors and antibodies were monitored during the perioperative period. The ideal concentrations of coagulation factors in the perioperative period were set in advance according to the size of the operation. According to literature, factor replacement therapy used before and on the first day after surgery is highly effective in maintaining the coagulation deficient factor levels greater than 80% of normal.^[2] Typically, the concentrations of coagulation factors are maintained at about 100% on the day of cardiac surgery, about 80% at 1 - 3 days after the operation, about 60% at 4 - 6 days after the operation, and about 40% at 7 - 10 days after the operation. Sometimes, the concentrations of postoperative coagulation factors are appropriately reduced or increased, and the doses of coagulation factors are adjusted according to

wound drainage, surgical area swelling, and hemoglobin level, and blood transfusion and/or antifibrinolytic drugs such as tranexamic acid can be given if necessary.

CONCLUSION

To conclude, for hemophilia patients undergoing cardiac surgery, multidisciplinary collaboration, close monitoring of coagulation indicators during hospitalization, and the presence of inhibitors in patients after discharge are particularly important. A professional team composed of hematologists, cardiac surgeons, anesthesiologists, extracorporeal circulatory physicians, and nurses is needed to jointly establish a complete management system.

Conflict of interests

The authors disclosed no conflicting interest.

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病例报道

心脏手术中血友病患者的替代疗法：3 例报告

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摘要

血友病是一种 X 连锁隐性遗传性出血性疾病。近年来随着长效凝血因子及非因子治疗的问世，血友病的诊疗越来越多样化，使得血友病患者的预期寿命得到延长。但血友病患者血液中的凝血因子减少并不会减慢动脉粥样硬化的进展。随着预期寿命的增加，越来越多的血友病患者将患上与年龄相关的心血管疾病，并且将需要外科手术干预。由于心脏手术需要肝素化和体外循环，血友病患者的止血和凝血平衡极具挑战性。本文报告了三例成功接受心脏手术的血友病患者。

关键词：血友病，心脏手术，替代疗法

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