Case Report

DOI: 10.5582/irdr.2018.01127

Anesthesia management of arthroscopic ankle arthrodesis for a hemophilia patient after living-donor liver transplantation

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Summary **Hemophilia is an X-linked recessive inherited coagulation disorder. We report the anesthesia management of a hemophilia patient who underwent arthroscopic ankle arthrodesis after living-donor liver transplantation due to cirrhosis. The 35-year-old male patient with hemophilia B was diagnosed with cirrhosis due to hepatitis C virus at the age of 23 years and underwent biologically-related partial liver transplantation at the age of 29 years. As a result, the activity of factor IX activity became normal and blood product treatment became unnecessary, but the patient required long-term immunosuppression. Perioperative coagulation factor activity monitoring was performed and an immunosuppressive drug that had been preoperatively administered were continued. General anesthesia was administered by inhalation. There was no significant fluctuation in perioperative factor IX activity. This case illustrates that even in patients with hemophilia B after living-donor liver transplantation undergoing an orthopedic surgical procedure, anesthesia management can safely be performed without perioperative coagulation factor replacement.**

Keywords: Hemophilia, living-donor liver transplantation, hemostatic management

1. Introduction

Hemophilia is an X-linked genetic bleeding disorder. Hemophilia A is caused by coagulation factor VIII abnormality, and hemophilia B is caused by factor IX abnormality (*1*). Careful perioperative hemostatic management is required for patients with hemophilia. Coagulation factor replacement therapy and hemostatic monitoring are usually recommended (*2*).

We report the experienced anesthesia management of an orthopedic surgery patient with hemophilia B who had undergone living-donor liver transplantation for cirrhosis due to the hepatitis C virus (HCV) infection. The patient's liver function was normal and his factor IX coagulation activity was high and more than 180%. He had been taking an immunosuppressive drug since the time of his liver transplantation. We performed hemostatic monitoring and perioperative management. The patient did not require coagulation factor replacement therapy. There were no complications such as postoperative bleeding and infection. We report the details of the case to augment the limited existing literature and describ the experience with anesthesia management in this setting.

2. Case Report

The patient was a 35-year-old male, 172 cm tall and 110 kg in weight. Hematoma first appeared at the age of 2 years old and severe hemophilia B (factor IX deficiency) was diagnosed at 5 years old, treated with blood preparation replacement therapy. Cirrhosis caused by hepatitis C virus infection and bulky splenomegaly were diagnosed at 23 years old with repeated variceal hemorrhage and refractory ascites. The patient received viral treatment with interferon and ribavirin, but no effect was found and the patient developed liver function. At the age of 29 years, he underwent living-donor transplantation from a healthy donor. Factor IX replacement therapy was used for hemostatic management during liver transplantation and the patient required coagulation factor replacement therapy until postoperative day 2. There were no major complications

Released online in J-STAGE as advance publication February 22, 2019.

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Table 1. Perioperative liver function and coagulation study

Items	5/12	6/17	6/23	6/29 (operation day)	6/30	7/2	7/6	7/13
AST (U/L)	27	24		68	32.7	24	29	29
ALT (U/L)	21	18		32	27	21	24	24
T-bil (mg/dL)	0.8	1.5			0.9	0.7	0.6	0.7
Plt ($\times 10^4$)	12.3	35.7		33.6	33.2	35.0	46.1	39.0
PT (sec.)	12.3		12.4	12.9	13.4	13.4	12.5	13.1
PT (%)	86		85	78	73	83	78	76
PT-INR	1.08		1.09	1.18	1.18	1.10	1.13	1.15
APTT (sec.)	24.7		26.9	25.8	25.8	26.6	26.3	26.6
Fib (mg/dL)	476		573	487	487	640	617	600
D-dimer	1.1							
Factor IX	181.3		151.5		167.7	178.9	172.1	1,635

AST, aspartate aminotransferase; ALT, alanine aminotransferase; T-bil, total bilirubin; Plt, platelet; PT, prothrombin time; INR, International normalized ratio; APTT, activated partial thromboplastin time; Fib, Fibrinogen.

during the perioperative period. Oral administration of immunosuppressive drugs was started, but no coagulation factor products were required.

However, the patient developed worsening arthropathy and had difficulty in walking at about 33 years of age. At 35 years old, he was referred to our hospital's department of joint surgery and arthroscopic ankle joint arthrodesis was scheduled. On perioperative examination, no abnormality was observed in blood biochemical examination and physiological testing. The preoperative factor IX activity was as high as 181.3%.

The patient took tacrolimus for immunosuppression, nifedipine for hypertension, uruso for hepatoprotection, furosemide and azosemide for edematous prevention. He was hospitalized 14 days before the operation for preoperative examination and rehabilitation. We planned general anesthesia by subconscious bronchoscopic endotracheal intubation because of obesity.

In the early morning of the operation day, nifedipine and tacrolimus was orally administered. The patient was sedated with fentanyl and midazolam and endotracheal intubation was performed with propofol under bronchoscopy. Anesthesia was maintained with desflurane and remifentanil. The surgery was completed without a change in circulatory dynamics in particular using a tourniquet. The operation time was 226 minutes, and the anesthesia time was 339 minutes, bleeding volume was 57 ml. We administered non-steroidal anti-inflammatory drugs for postoperative analgesia.

Table 1 shows the results of perioperative liver function and coagulation system testing. Both preoperatively and postoperatively, factor IX activity was more than 150%. Bleeding was not observed and blood product support was not required. After recovery without notable complications and rehabilitation, the patient left the hospital on the 32nd postoperative day. Routine postoperative follow-up at our hospital was scheduled.

3. Discussion

Hemophilia is an X-linked recessive inheritance-related coagulation disorder. Affected individuals have a deficiency or activity reduction of factor VIII or factor IX. Hemophilia A is attributed to factor VIII deficiency, and hemophilia B to abnormalities of IX (*1*). In Japan, the Nationwide Survey on Coagulation Disorders 2017 reported 5,326 patients with hemophilia A and 1,129 patients with hemophilia B (*1*). Individuals with hemophilia may develop arthropathy causing remarkable physical function deterioration due to severe deformation and contracture involving multiple joints due to repetitive intra-articular bleeding. Therefore, surgical treatment such as artificial joint replacement or arthroscope synovial resection may be complicated by post-operative bleeding and viral infection (*2-4*).

HCV infection in hemophilia patients is due to the administration of non-heated concentrate formulations used before 1986. Individuals who used unheated preparations before the current heated formulations were approved have a nearly 100% rate of infection (*5*). Also, many patients are coinfected with human immunodeficiency virus. It has been reported that the progression to chronic liver disease is faster in individuals with concomitant HCV and human immunodeficiency viral infection (*6,7*). Interferon and antiviral drugs have been used to treat HCV, but they do not completely cure the infection and many patients progress to cirrhosis and liver cancer.

Living-donor liver transplantation may be performed for these patients. If the donor does not have hemophilia, the transplanted liver will produce the coagulation factor previously deficient in the recipient with hemophilia, and the recipient may no longer need treatment with coagulation factor preparations. However, it has been reported that coagulation factor production may be insufficient when the liver donor is deceased or is a hemophilia carrier (*8*). In our case, as in others, immunosuppressive treatment was continued during the perioperative period. Tacrolimus, which is commonly used in this setting, mainly suppresses interleukin-2 cytokine production from T-helper cells (*9*). The Nationwide Survey on Coagulation Disorders

Table 2. Stage of hepatic disease in individuals with hemophilia

Items	Hepatitis	Cirrhosis	Liver cancer	Hepatic failure	Liver transplantation
Hemophilia A	1,029	92	56	1	8
Hemophilia B	224	54	17	0	3
Total	1,253	146	73	1	11

The original source of data is Project entrusted by Ministry of Health, Labor and Welfare. Nationwide Survey on Coagulation Disorders 2017. Published by Japan Foundation for AIDS Prevention (*1*).

Table 3. The characteristics of 184 hemophilic patients who underwent surgery in our hospital (2006-2015)

Characteristics	Cases (%)
Hemophilia cases underwent surgery	
THA or re THA	23 (12.5)
TKA or re TKA	82 (44.6)
TEA	2 (1.1)
TAA	1 (0.5)
Arthroscopic surgery	34 (18.5)
Other	42 (22.8)
Age median (range) years	41 (13-72)
Sex	
Male	182 (98.9)
Female	2 (1.1)
Diagnosis	
Hemophilia A	142 (77.2)
Hemophilia B	40 (21.7)
Factor VII deficiency	1 (0.5)
Von Willebrand disease	1 (0.5)
Infections disease	
HCV(-) HIV(-)	27 (14.7)
HCV(+) HIV(-)	109 (59.2)
HCV(-) HIV(+)	1 (0.5)
HCV(+) HIV(+)	47 (25.5)
Preoperative infection	
-	174 (94.6)
+	10 (5.4)

THA or re THA, Total Knee Arthroplasty or re Total Knee Arthroplasty; TKA or re TKA, Total Knee Arthroplasty or re Total Knee Arthroplasty; TEA, Total Elbow Arthroplasty; TAA, Total Ankle Arthroplasty.

2017 in Japan shows the stage of the liver disease in individuals with blood coagulation disorder (Table 2). 11 cases of liver transplantation were reported.

Most patients with hemophilia require perioperative hemostatic management with supplementation of the deficient coagulation factor according to the extent of surgery and related treatments; in these patients, we apply the hemostatic treatment guidelines for patients with congenital hemophilia by The Japanese society on Thrombosis and Hemostasis (*10*). For arthroscopic surgery, the clotting factor target peak level should be maintained at 100% or more, and additional infusion should generally be continued intravenously to maintain a minimum factor level of at least 80% (*1*). Our hospital has handled a large number of hemophilia cases; from 2006 to 2015, 184 patients with hemophilia underwent surgery at our facility (Table 3) (*11*).

In this case, liver function was normal because the patient, who had developed hepatic failure due to complications of HCV infection, received a segmental liver transplant from a living-donor who did not have hemophilia. The transplanted liver generated sufficient coagulation factors and normalized the recipient's hemostatic function. However, hemophilic arthropathy progressed and made walking difficult without a cane. For this reason, arthroscopic arthrodesis was scheduled. On preoperative examination, the patient's factor IX activity was 180%. Perioperative hemostasis monitoring was performed but coagulation factor replacement therapy was not needed. We did not observe problems during the operation. Neither bleeding nor infection occurred during the perioperative period, and liver function remained normal.

This is the first report of orthopedic surgery in our knowledge, but there have been no previous reports of anesthesia experiences for patients with hemophilia and cirrhosis who have undergone partial living-donor liver transplantation. In this patient with hemophilia B status-post living-donor liver transplantation, we were able to safely perform anesthesia management for the elective orthopedic surgery without coagulation factor supplementation (*12*).

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(Received November 28, 2018; Revised January 30, 2019; Accepted February 4, 2019)