

Anticoagulation treatment of portal vein thrombosis in a patient with cirrhosis awaiting liver transplantation

A case report

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Abstract

Rationale: Portal vein thrombosis (PVT) is relatively common in patients with liver cirrhosis waiting for liver transplantation (LT). Anticoagulation is an important non-invasive treatment strategy for patients with cirrhosis and PVT.

Patient concerns: This is the case of a 51-year-old man who presented with cryptogenic liver cirrhosis associated with ascites. Computed tomography (CT) and Doppler ultrasonography (US) showed a partially obstructive thrombus of the portal vein (Yerdel Grade II).

Diagnosis: Portal vein thrombosis (Yerdel Grade II); liver cirrhosis.

Interventions: The PVT was completely recanalized after 4 months of treatment with the low molecular weight heparin (LMWH) medication enoxaparin but discontinuation of anticoagulants led to PVT recurrence. The patient's condition deteriorated, even though re-treating the anticoagulation with enoxaparin significantly reduced the PVT.

Outcomes: The thrombus was removed by a thrombectomy and LT was performed successfully without any vascular complications.

Lessons: Patients with cirrhosis and PVT who are waiting LT can be effectively treated with LMWH anticoagulants. Careful use of anticoagulation is generally safe. Early initiation of anticoagulation treatment may be associated with a high rate of portal vein recanalization.

Abbreviations: CT = computed tomography, DCD = donation after circulatory death, LMWH = low-molecular weight heparin, LT = liver transplantation, MELD = Model End-Stage Liver Disease, PV = portal vein, PVT = portal vein thrombosis, RCT = randomized controlled studies, SMV = superior mesenteric vein, US = ultrasonography.

Keywords: anticoagulation, liver cirrhosis, liver transplantation, portal vein thrombosis

1. Introduction

Portal vein thrombosis (PVT) is a relatively frequent complication of liver cirrhosis, and it is not uncommon in candidates for liver

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transplantation (LT).^[1] PVT is defined as thrombosis occurring within the trunk of the portal vein that can extend to the intrahepatic portal branches, superior mesenteric vein, or splenic vein. It is reported incidence has varied from 7.4% to 17.9% in patients with cirrhosis, and more PVT cases are incidentally diagnosed during LT.^[2–4] The specific pathogenesis of PVT in patients with liver cirrhosis is not fully understood. The widely accepted classification of PVT in LT is the system proposed by Yerdel et al^[5] and is based on operative findings, as shown in Table 1. PVT in cirrhosis is associated with negative outcomes following transplantation, especially early post-LT mortality.^[1] However, since the first successful LT in a patient with PVT was reported in 1985, PVT is no longer considered an absolute contraindication for LT.^[6]

Anticoagulation is an important noninvasive treatment strategy for patients with cirrhosis and PVT awaiting LT, and it has been shown to improve survival after LT.^[3] This case report highlights the safety and efficacy of anticoagulation therapy for PVT in candidates for LT. It also reviews the recent literature about the anticoagulation of PVT patients with cirrhosis in order to explore any possible practical guidelines for the clinical treatment.

2. Case report

A 51-year-old man presented with cryptogenic liver cirrhosis associated with ascites. Computed tomography (CT) and Doppler ultrasonography (US) showed a partially obstructive thrombus of the portal vein (PV) trunk and the splenoportal

Table 1**Classification of portal vein thrombosis findings during liver transplant procedure^[5].**

Yerdel grade	Description
Type I	Lumen occlusion < 50% PVT ± minimal or partial obstruction within SMV
Type II	Lumen occlusion > 50% PVT ± minimal or partial obstruction within SMV
Type III	Complete PV and proximal SMV thrombosis
Type IV	Complete PV and entire SMV thrombosis

PV=portal vein, PVT=portal vein thrombosis, SMV=superior mesenteric vein.

confluence (Yerdel Grade II), with a patent splenic vein. It also showed an enlarged spleen and ascites, and ruled out the presence of hepatic nodules that would suggest hepatocellular carcinoma. The patient's liver function and coagulation profile were within normal limits, the Child–Pugh class was A, the Model End-Stage Liver Disease (MELD) score was 9, and endoscopy demonstrated severe esophageal varices. Anticoagulant treatment with enoxaparin was administered subcutaneously (1 mg/kg, every 12 hours). After 4 months of treatment, CT showed that the PVT had completely disappeared and that the intra- and extrahepatic portal vein was patent (Fig. 1). Anticoagulant therapy was continued until the patient presented with a complaint of pain in the epigastric region 1 month later. Doppler US revealed calculus

of the common bile duct, and endoscopic examination showed no bleeding varices. At the patient's local hospital, anticoagulation treatment was discontinued in order to remove stones in the common bile duct with endoscopic retrograde cholangiopancreatography. Two weeks later, PVT was observed on US and CT, and anticoagulant treatment of enoxaparin was administered again. The PVT significantly decreased after 2 weeks of treatment (Fig. 2). However, the patient's condition was increasingly deteriorating; he had fatigue and increased ascites, his albumin was decreased, and his liver function and coagulation parameters were getting significantly worse. The Child–Pugh class was C and the MELD score was 23. Therefore, LT was indicated and ethical approval was obtained from the local ethics committee.

Orthotopic liver transplantation was performed 1 month later. During surgery, the thrombus was removed by simple thrombectomy and an end-to-end anastomosis was performed quickly between the donor and recipient portal veins. Good graft reperfusion was observed, without surgical or medical problems. Intraoperative Doppler US showed portal vein patency (Fig. 3). During the operation, blood loss was 1000 mL, and ascitic fluid volume was 6000 mL. A transfusion of 10 units of fresh frozen plasma (FFP) and 10 units of red blood cells was required. The overall operation time was 6 hours.

The patient's postoperative course was uneventful without any vascular complications. Subcutaneous enoxaparin was administered beginning on postoperative day 1 to prevent portal



Figure 1. (A) Computed tomography (CT) image of untreated portal vein thrombosis (PVT); (B) CT image of PVT after 4 months of anticoagulation treatment. CT = computed tomography, PVT = portal vein thrombosis.

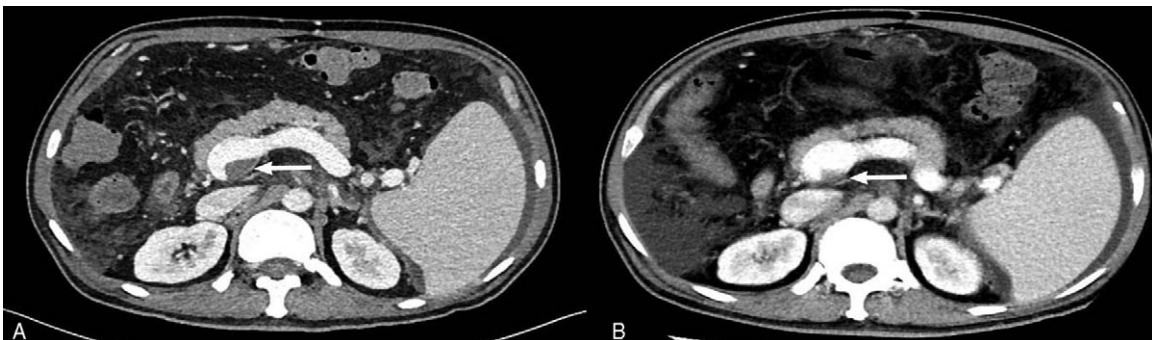


Figure 2. (A) Computed tomography (CT) image of recurrent portal vein thrombosis (PVT); (B) CT image of recurrent PVT after 2 weeks of anticoagulation treatment. CT = computed tomography, PVT = portal vein thrombosis.

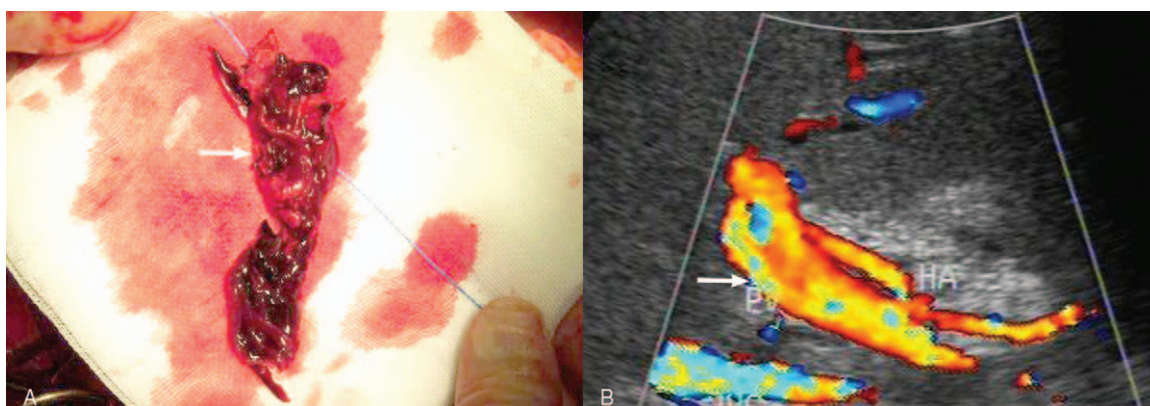


Figure 3. (A) Thrombus removed during the surgery; (B) intraoperative Doppler ultrasonography shows portal vein patency.

thrombosis. Laboratory investigation on day 7 showed excellent graft function and smooth portal blood flow, and there was no portal vein thrombosis observed on US. Three months after LT, the patient was in good clinical condition, and Doppler US scan showed no signs of thrombosis recurrence. The patient provided informed consent for the publication of his case.

3. Discussion

LT is a highly successful treatment for many patients with end-stage liver disease.^[7] The relatively high prevalence of PVT in candidates for transplantation may be related to the repeated detailed imaging while the patient on the LT waiting list. However, a significant proportion of PVT confirmed at LT is unrecognized preoperatively.^[8] In orthotopic LT, the incidence of PVT in cirrhosis ranges from 14% to 39%.^[9] The incidence of PVT in our center was 10.09% (253 diagnosed cases out of 2508 adult patients).^[6] Decreased portal venous flow velocity has been found to be an independent risk factor for the development of PVT.^[10] Other factors, such as focal inflammatory lesions (pancreatitis, duodenal ulcer, cholecystitis, appendicitis, etc.), injury to the portal venous system (splenectomy, gastrectomy, cholecystectomy, etc.), and large portal-collateral vessels, have been found to be associated with the development of PVT.^[11,12]

A meta-analysis conducted by Stine et al^[13] showed that PVT increases hepatic decompensation from ascites, but those results may not be generalized because of the small number of included studies. However, PVT may be a source of technical difficulties in the operation of LT, with increased operative times, higher blood transfusion requirements, and longer intensive care unit and hospital stays, which may negatively affect outcomes.^[1] When PVT is suspected, US is the first-line diagnostic approach because of its affordability, noninvasive nature, and repeatability. It has been shown that performing US every 3 months is the most sensitive for detecting PVT in patients with cirrhosis.^[14] CT is recommended for diagnosing PVT because it can better estimate the superior mesenteric vein, the state of the abdominal organs and the extent of thrombus.^[15] Some prophylactic strategies have been proposed in patients with advanced cirrhosis awaiting LT, such as the use of enoxaparin to prevent PVT. Villa et al. have shown that patients with cirrhosis treated with enoxaparin for 1 year were less likely to develop PVT than were controls, and their survival was also better during a 3-year follow-up.^[2] However, a meta-analysis demonstrated that prophylactic treatment with heparin does not decrease the risk of venous thromboembo-

lism.^[16] Multicenter randomized controlled trials are needed to provide sufficient data on the risks and benefits of anticoagulation for preventing PVT in patients with cirrhosis.

There are few studies that have analyzed the safety and efficacy of anticoagulants in patients with liver cirrhosis and PVT.^[17] Loffredo et al^[18] conducted a systematic review and meta-analysis that assessed the effects of anticoagulants in patients with cirrhosis and PVT. Eight studies were included, 353 patients received about 6 months of anticoagulant treatment with low-molecular weight heparin (LMWH) or vitamin K antagonists, and received about 2 years of follow-up. Recanalization of PVT was significantly lower in patients untreated with anticoagulants than treated patients (42% vs 71%). The rate of PVT progression was significantly higher in untreated patients than treated ones (33% vs 9%). The incidence of major or minor bleeding in patients treated with anticoagulants was not higher than controls (11% in both groups). The rate of variceal bleedings was significantly higher in untreated patients than patients treated with anticoagulants (12% vs 2%). It also showed that LMWH, but not warfarin, was significantly associated with complete PVT recanalization, and was associated with a significantly lower rate of variceal bleeding.^[18]

During transplantation, different approaches have been recommended to reestablish portal vein patency, and the approach depends on the degree and extent of PVT.^[6] Portal vein thrombectomy and direct anastomosis of the recipient and donor portal veins can be used for grades I and II PVT, and it can be performed successfully in most patients with PVT undergoing LT. A jump graft can be used for grades II or III PVT and can be achieved by making an anastomosis between the graft portal vein and the recipient superior mesenteric vein (SMV) using a segment of the donor iliac vein. Arterialization of the portal vein can be used for grades III and IV PVT and can be performed by anastomosing the graft portal vein to the recipient arterial inflow. The technique of portocaval hemitransposition is suitable for grades II and IV PVT and is performed by making an end-to-side anastomosis of the graft portal vein to the suprarenal inferior vena cava of the recipient. It has been shown that postoperative survival may depend on the grade of PVT and the type of surgery performed.^[19] The survival rates of patients with grades I to III PVT are similar, and the mortality of patients with grade IV PVT is higher.^[20] Anticoagulation treatment can recanalize PVT or slow its progression, prolonging the patient's stay on the waiting list for LT, reducing the risk of surgery, and improving postoperative survival.

In the present case, 4 months of anticoagulant treatment with enoxaparin almost resulted in complete PVT recanalization based on CT results. The interruption of anticoagulation treatment is believed to have led to the recurrence of PVT. The images of PVT on CT showed that the PVT was de novo rather than progression. Although furosemide and albumin were administered to control ascites and the PVT was significantly decreased after 2 weeks of treatment with enoxaparin, the patient's condition continued to deteriorate. We therefore decided to perform LT, and the PVT was removed by simple thrombectomy. With the continuation of anticoagulant treatment, postoperative PVT did not recur. The patient continues to be in good condition.

4. Conclusions

Patients with cirrhosis and PVT on the waiting list for LT can be treated effectively with LMWH anticoagulants. Careful use of anticoagulation therapy is generally safe. Early initiation of anticoagulation treatment may be associated with a higher rate of portal vein recanalization. Long-term use of anticoagulation therapy might prevent the recurrence of thrombosis. Thus, it could extend patients' stay on the waiting list and reduce the need for LT. However, at present, there is no consensus about anticoagulation therapy, initiation of when to begin treatment with medicine, or the duration of treatment and monitoring. Thus, randomized clinical trials are required to verify the reasonable use of anticoagulation therapy and to harmonize adverse events in accordance with the desired efficacy of anticoagulation therapy in this group of patients.

Author contributions

JW designed the report, JSC wrote the manuscript; YMZ and JW performed the operation; JW collected the clinical data.

Resources: Jian Wang.

Supervision: Ya-Min Zhang.

Validation: Ya-Min Zhang.

Visualization: Ya-Min Zhang.

Writing – original draft: Jia-Sui Chai.

Writing – review & editing: Jian Wang.

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