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Is Liver Transplantation a Cure for Afibrinogenemia?

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Case Report

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Abstract

Background: Congenital afibrinogenemia is a rare coagulation disorder characterized by the absence of fibrinogen, leading to both bleeding and paradoxical thrombotic complications. Liver transplantation has been proposed as a potential curative approach, particularly in patients with concomitant severe liver disease. This report aims to present a case of afibrinogenemia undergoing liver transplantation and to discuss the associated clinical challenges.

Case description: A 43-year-old male with known congenital afibrinogenemia and chronic liver disease secondary to thrombosis underwent liver transplantation in 2019. He later presented with abdominal distension, pain, nausea, and vomiting. Imaging revealed portal vein thrombosis and stent occlusion. The patient developed decompensated liver disease characterized by ascites and grade 1 hepatic encephalopathy. Management included anticoagulation, antibiotics, and supportive therapy for encephalopathy and ascites. Due to vascular complications and clinical deterioration, he was referred to a specialized center for further interventional and transplant evaluation.

Conclusion: Liver transplantation may offer a therapeutic option for patients with afibrinogenemia and advanced liver disease; however, it does not fully eliminate the risk of thrombotic complications. The management of these patients remains complex, particularly regarding anticoagulation and long-term follow-up.

Clinical significance: This case highlights the persistent risk of thrombotic and hepatic complications after liver transplantation in patients with afibrinogenemia. It underscores the need for individualized management strategies and further research to establish optimal perioperative and postoperative protocols.

INTRODUCTION

Congenital afibrinogenemia is a rare disorder characterized by an undetectable level of fibrinogen (<0.1 g/L), resulting from compound heterozygous mutations in any of the three main genes coding for the fibrinogen protein, demonstrating autosomal recessive inheritance, even in homozygotes or multiple heterozygotes [1]. Fibrinogen, being the final molecule involved in the common pathway of the coagulation cascade, presents with a heterogeneous clinical presentation, including not only bleeding but also rarely thromboembolic events. Paradoxical thromboembolic events observed in patients with afibrinogenemia, though appearing multifactorial (genetic thrombophilia, use of fibrinogen replacement therapy, immobilization, pregnancy, or trauma) [2, 3], are fundamentally rooted in the concept that afibrinogenemia creates a prothrombotic background due to the antithrombin-like function of fibrinogen[2]. Despite the multifactorial nature of thrombotic or bleeding-related clinical scenarios in these patients, rare occurrences such as renal amyloidosis, variable severity of liver diseases, splenic rupture, bone cysts, impaired wound healing, and increased cardiovascular events have been reported in various case studies. In this particular case, a patient diagnosed with congenital afibrinogenemia

underwent liver transplantation due to chronic liver disease and was subsequently admitted to our clinic again with signs of decompensation.

CASE PRESENTATION

A 43-year-old white male with a known congenital afibrinogenemia, epilepsy, aneurysmal bone cyct and chronic liver disease due to thrombosis who underwent liver transplantation in 2019. He also has a history of tuberculosis. On October 11, 2023, he presented to the emergency department of a tertiary ED in his city with a 3-month history of abdominal distension, abdominal pain, nausea, and vomiting. At the time of admission, vital signs revealed only tachypnea. Physical examination showed widespread ascites in the abdomen.

A week before his current presentation, an abdominal CT angiography was performed due to similar complaints, and it reported "Heterogeneous contrast enhancement in the liver parenchyma with irregular contours. Occlusion of the splenic vein and portal vein stent is observed." The Doppler ultrasound performed in the emergency department showed a filling defect in the portal vein and a stent, consistent with subacute thrombosis. Due to this finding, the patient was hospitalized, and paracentesis for ascitic fluid sampling was planned.

However, the patient experienced a seizure after the procedure. Considering the possibility of requiring advanced life support due to the seizure, the patient was monitored in the intensive care unit. During this observation period, the patient received antibiotic therapy containing Ceftriaxone and Metronidazole for five days and anticoagulant treatment with Enoxaparin. Subsequently, the patient left the hospital of his own will and was admitted to our clinic’s ED on October 21, 2023.

His vital signs at admission showed a blood pressure of 80/50 mm Hg, a respiratory rate of 28/min, and other vitals within normal limits. The laboratory values at the time of admission are as follows: (Figure 1)

The patient was conscious, cooperative, and oriented, but speech and Movements were observed to be slowed. In the assessment of decompensation, the patient denied exposure to hepatotoxic substances and had no recent history of infections in the past 6 months. Although cyclosporine was prescribed as an immunosuppressive agent for the patient during transplantation, the patient reported insufficient medication adherence. Tense ascites was present on physical examination, and while no hepatomegaly was detected, a palpable spleen was detected below the costal margin. Asterixis was not present. While the patient exhibited cachexia in the extremities and temporal area, there were no signs of other peripheral presentations of cirrhosis.

The patient, initially evaluated as grade 1 HES, was started on rifaximin, lactulose, and L-ornithine L-aspartate for encephalopathy treatment. In the ascitic fluid sampling performed in the ward, the serum-

ascites albumin gradient was >1.1 (2.35), and the ascitic protein level was measured at -1.06 g/dL, consistent with portal hypertension. Ammonia level(Blood) was measured as 3.0 µg/dL. The hepatitis serology results were as follows; (Figure 2)

During hospitalization, intermittent paracentesis and intravenous diuretic treatment were applied for ascites palliation.

Abdominal imaging showed that "The stent placed in the portal vein is patent on Doppler US, but the venous structure to which its distal end is attached is occluded." FibroScan results were CAP 171 dB/m, 7.3 kPa, S0, and F1.

The patient, who has no history of variceal bleeding but had esophageal varices in a pre-transplant endoscopy, has no varices. After evaluation by the Interventional Radiology department, a transfer decision was made to a center that could perform both transplantation and stenting procedures, and the patient was discharged.

DISCUSSION

Afibrinogenemia is a rare bleeding disorder with an estimated prevalence of 1:1,000,000 [4]. While it generally manifests with bleeding disorders, thrombotic complications such as ischemic foot lesions, ischemic stroke, renal and ovarian vein thrombosis, deep vein thrombosis, and pulmonary vein thrombosis have been reported in patients with afibrinogenemia following replacement therapy [5, 6]. In individuals with afibrinogenemia, concomitant hereditary thrombophilic disorders (e.g., protein C deficiency) have been observed, making this group at a higher risk of thrombosis after replacement therapy [7, 8]. Although the primary treatment in this patient group is provided through replacement, liver transplantation in individuals with severe liver disease creates a new opportunity for both the underlying fibrinogen deficiency and liver disease. However, there is currently no clear answer to the question of whether anticoagulant therapy should be administered during both the perioperative and postoperative periods in these patients. Even though replacement therapy and the inherent [9] prothrombotic risks of afibrinogenemia post-transplantation are eliminated, the risk of recurrence of this phenomenon post-transplantation, as observed in our case, is unknown due to limited cases and the unclear pathophysiology.

While patients diagnosed with afibrinogenemia initially receive a diagnosis with umbilical cord bleeding, they later experience mucosal, intracranial, skeletal, and intra-articular bleeding, as well as problems such as spontaneous miscarriages and/or spontaneous rupture of the spleen. After liver transplantation, patients face complications related to immunosuppression (hypertension, renal failure, infection, malignancy, various dermatological diseases), hepatobiliary (rejection, recurrence of underlying liver disease, and secondary biliary cirrhosis), and other additional problems. When this patient group is considered for liver transplantation, their INR values might be found to be higher than those with the same degree of liver disease due to underlying bleeding disorders, making them more advantageous for

transplantation. However, considering that transplantation is a decision that needs to be carefully considered on its own, this should be taken into account when deciding on transplantation [10].

CONCLUSION

In conclusion, liver transplantation may represent a potential therapeutic strategy for patients with congenital afibrinogenemia complicated by advanced liver disease; however, it cannot be considered a definitive cure for the underlying hematological disorder. Despite the restoration of hepatic synthesis function, the persistence or recurrence of thrombotic events, as observed in this case, suggests that the pathophysiology of thrombosis in afibrinogenemia extends beyond fibrinogen deficiency alone. The complexity of perioperative and postoperative management—particularly regarding anticoagulation strategies remains a major clinical challenge. Therefore, careful patient selection, close multidisciplinary follow-up, and individualized treatment planning are essential. Further studies with larger patient cohorts are required to clarify the long-term outcomes and to establish standardized management protocols.

Clinical Significance

This case provides important clinical insights into the management of patients with congenital afibrinogenemia undergoing liver transplantation and highlights several unresolved issues in current practice. It emphasizes that, although transplantation may correct the biochemical deficiency of fibrinogen, it does not fully mitigate the risk of thrombotic complications, which may persist due to multifactorial mechanisms. Additionally, the case underlines the importance of long-term monitoring for vascular complications, adherence to immunosuppressive therapy, and timely recognition of decompensation. From a clinical perspective, this report contributes to the limited body of literature on this rare condition and supports the need for developing evidence-based guidelines regarding perioperative anticoagulation, post-transplant surveillance, and risk stratification in this unique patient population.

ABBREVIATIONS

CAP: Controlled Attenuation Parameter

ED: Emergency Department

CT: Computed Tomography

Declarations

ETHICAL CONSIDERATIONS AND CONSENT FOR PUBLICATION

The patient's consent was obtained for this case presentation.

The manuscript does not report on or involve any personal data.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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Figures

Albumin - 2,72 g/dL	Bilirubin, total - 0,28 mg/dL	Hemoglobin - 9,3 gr/dL
ALT - 17 U/L	Prothrombin Time (INR) - 1,02 INR	WBC - 2,91 x10^3/µL,
AST - 21 U/L	Fibrinogen - 171,72 mg/dL	Platelet – 66 x10^3/µL
ALP - 110 U/L	aPTT - 25,6 sec,	
GGT - 56 U/L,	D dimer - 1,36 mg/L	

Figure 1

Legend not included with this version.

Anti-HAV IgM – Negative, Anti HBc Total – Positive, Anti-HCV –Positive, Anti-HAV Total - Positive mIU/mL, HBs Ag – Negative, copy/mL, HBV Viral load (Copy/ml) - Negative	Anti HBc IgM – Negative, Anti HBe – Positive, Anti HIV – Non-reactive, HBe Ag – Negative, HCV Viral load (copy/mL) – Negative

Figure 2

Legend not included with this version.