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CASE REPORT

# Fulminant Hepatitis as the First Presentation of Wilson's Disease

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## ABSTRACT

Wilson's disease is rare, but it affects 6-12% of patients with an indication for urgent liver transplantation. The main manifestations, in addition to the liver, are neurological and psychiatric, with evolution with fulminant hepatitis without neuropsychiatric symptoms being rarer. Despite the urgency, the prognosis for post-transplant patients averages 85% 5-year survival. In this report, we present the case of a female patient, 18 years old, with the onset of abdominal pain, jaundice and choluria that progressed to fulminant hepatitis and the need for urgent liver transplantation. The patient evolved postoperatively with septic shock due to herpetic encephalitis, duodenal ulcer with active bleeding and hepatic artery pseudoaneurysm. Despite measures for stabilization and the request for a transplant again, the patient died.

Descriptors: Fulminant Hepatic Insufficiency; Liver Transplantation; Pseudoaneurysm.

## *Hepatite Fulminante como Primeira Apresentação da Doença de Wilson*

## RESUMO

A doença de Wilson é uma rara patologia, porém, que engloba 6–12% dos pacientes com indicação de transplante hepático de urgência. As principais manifestações, além de hepáticas, são as neurológicas e psiquiátricas, sendo mais raro a evolução com hepatite fulminante sem sintomas neuropsiquiátricos. Apesar da urgência, o prognóstico para os pacientes pós-transplante é, em média, 85% de sobrevivência em cinco anos. Neste relato, é apresentado o caso de uma paciente mulher, 18 anos de idade, com início de dor abdominal, icterícia e colúria com evolução para hepatite fulminante e necessidade de transplante hepático de urgência. A paciente evoluiu no pós-operatório com choque séptico devido encefalite herpética, úlcera duodenal com sangramento ativo e pseudoaneurisma de artéria hepática. Apesar das medidas para estabilização e solicitação, novamente, de um transplante, a paciente evoluiu para óbito.

Descritores: Insuficiência Hepática Fulminante; Transplante de Fígado; Pseudoaneurisma.

## INTRODUCTION

Wilson's disease is a genetic disorder of copper metabolism.[1] Acute liver failure is an uncommon disease presentation, occurring in only 5% of cases. On rare occasions, it may present with fulminant hepatitis (FH), whose prognosis is fatal without urgent transplantation.[1,2]

This report presents the case of an 18-year-old patient who presented with fulminant hepatitis as the first manifestation of Wilson's disease, requiring liver transplantation. However, due to postoperative complications, she died.

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## DESCRIPTION

Female patient, 18 years old, with a history of abdominal pain for ten days associated with jaundice and choluria for two days, with no other associated complaints. No comorbidities or use of previous medications. On physical examination, presence of diffuse abdominal pain, without signs of peritoneal irritation. In laboratory tests, hemoglobin of 5.3, hematocrit of 15.53, and leukocytosis of 29,650 with left shift (13% of rods), without platelet alteration. Liver function tests with increased GT gamma (257), TGO (225), bilirubin of 40.05 with a direct fraction of 15.28, and no changes in alkaline phosphatase or TGP. In addition, She had lactate dehydrogenase of 1823.7, CPK without alteration. Suspected hemolytic anemia, but investigation with direct and indirect Coombs was negative.

After hospital admission, the patient evolved with hemodynamic instability and respiratory failure, requiring orotracheal intubation (OTI) and vasoactive drug (VAD) 0.2 mcg/kg/min, associated with acute renal failure. When the patient was diagnosed with fulminant hepatitis, an investigation was carried out for yellow fever, dengue, leptospirosis, chikungunya, hepatitis A, B and C, all with negative serology, with suspicion of Wilson's disease. The patient was listed for liver transplantation, performed two days later with an expanded donor (80 years old). Intraoperatively, evidence of fibrotic liver with perfusion changes. She required a transfusion of 10 units of packed red blood cells, 2 liters of plasma and 2 platelet apheresis, ending the procedure with VAD at 0.6 mcg/kg/min.

In the postoperative period, she remained in an ICU, needing hemodialysis. Postoperative Doppler echocardiography showed pervious hepatic vessels with no change in flow. The anatomopathological analysis showed a picture of acute, chronic liver failure due to Wilson's disease (presence of copper deposits). After two weeks, she presented clinical improvement, and extubation was indicated. However, she had herpes in the eye and face, and treatment with Acyclovir was started. However, she developed septic shock in the following days due to herpetic encephalitis, again requiring VAD, 0.2 mcg/kg/min, and OTI.

An unsuccessful extubation attempt was made, and a tracheostomy was chosen. In the following days, the canalicular enzymes worsened, but the liver biopsy showed no signs of rejection. The patient showed gradual clinical and hemodynamic improvement. However, she had an episode of hematemesis due to the presence of a duodenal ulcer with active bleeding demonstrated by upper digestive endoscopy. She evolved with the need for sclerotherapy and coagulation with electrocautery.

After this episode, the need for VAD returned to 0.3 mcg/kg/min. After two weeks, she started again with jaundice and fever, with USG Doppler showing evidence of hepatic artery pseudoaneurysm associated with duodenal ulcer, and embolization was chosen. The patient did not show signs of improvement, with a new USG after four days still demonstrating the presence of the pseudoaneurysm. Therefore, she proceeded with a new embolization. In the following weeks, the patient's general condition worsened, with the need for transcutaneous biliary drainage. However, she developed refractory shock one day after being listed again, dying four months after her initial hospitalization.

## DISCUSSION

Wilson's disease is rare and usually presents between the 2nd and 3rd decades of life. The main manifestations are neurological, psychiatric and/or hepatic, and presentation with fulminant hepatitis without neuropsychiatric symptoms occurs in only 5% of cases.[2] The mechanism by which FH is triggered is unknown, and, in addition to liver involvement, it results in intravascular hemolysis and renal failure, as seen in this case.[2]

Typically, these cases begin with nonspecific symptoms, such as abdominal pain, fatigue, and rapid progression to jaundice.[3] They present high bilirubin values and a negative Coombs test, with the Kayser-Fleicher ring, a pathognomonic sign, found in less than 50% of patients[3] and not visualized in this patient on bedside examination with direct binocular ophthalmoscopy. Examination with a biomicroscope was not performed due to the patient's condition.

Despite being a rare disease, 6–12% of patients with an indication for urgent liver transplantation due to fulminant hepatitis have Wilson's disease. The prognosis for these patients after liver transplantation is excellent, with an average five-year survival rate of 85%.[2,3] The unfavorable evolution of this case was due to associated complications, mainly the pseudoaneurysm and late thrombosis of the hepatic artery. Pseudoaneurysm accounts for 6 to 10% of vascular complications after transplantation.[4] It can present itself through symptoms such as hemobilia, fever, liver dysfunction and gastrointestinal bleeding, alterations evidenced in this case. At present, it is an indication for urgent treatment to avoid the loss of the transplanted organ, which ends up occurring in 1–2% of cases.[4]

In addition, the patient also developed late thrombosis of the hepatic artery, the most frequent and severe vascular complication of liver transplantation, with an incidence of 2–9% in adults and a mortality rate of 11–35%, being the main cause of primary dysfunction and graft loss. Factors associated with its incidence include the technique used in the anastomosis, dissection of the artery wall, the donor's advanced age (> 60 years), state of hypercoagulability in the recipient, and cases of rejection or infection by cytomegalovirus. In this case, the patient had more than one risk factor for this complication, involving her donor's advanced age, 80 years, and the dissection and pseudoaneurysm of the hepatic artery a few days before. Regarding management in the case of thrombosis, there is currently no consensus on a single, more effective treatment, including an assessment of the time of evolution and the patient's condition. Early diagnosis, immediate revascularization and retransplantation are associated with a greater chance of a positive outcome for the patient. Retransplantation is the treatment of choice for most groups studied in the literature, offering the best survival results. The endovascular treatment option is viable in this situation but unavailable in the mentioned service. There is no established protocol or specific guidelines for the use of thrombolytics in these cases. Although open surgical revascularization is an option, there is a higher risk of complications, and the success rate is low (10.5%), maintaining the need for retransplantation. Due to evidence of late thrombosis and the patient's clinical conditions, a new liver transplant was chosen.[5-7]

In the case of hepatic artery pseudoaneurysm, its treatment may include a new surgical approach or interventional radiology. According to studies, performing a new procedure involves a high rate of morbidity and mortality, ranging from 28% to 85% in studies. In this case, the treatment of choice was embolization, requiring two embolizations in the management period. Due to the high mortality of both complications, the patient died before being able to perform a new transplant.[6,7]

Therefore, Wilson's disease should be suspected in young patients with fulminant hepatitis of unknown etiology. Despite being serious, the patient's prognosis after urgent liver transplantation is favorable. However, attention should be paid to possible post-transplantation complications, such as pseudoaneurysm and thrombosis of the hepatic artery, which, despite low incidence, can progress to a fatal outcome even with adequate treatment, as seen in this case.

## CONFLICT OF INTEREST

Nothing to declare.

## AUTHORS' CONTRIBUTION

**Substantive scientific and intellectual contributions to the study:** Garcia RFL, Lemos R, Haritsch F, Lima AC, Garcia CE; **Conception and design:** Lemos R, Haritsch F, Lima AC, Garcia CE; **Technical procedures:** Frainer DA, Welter CS; **Analysis and data interpretation:** Frainer DA, Welter CS; **Article writing:** Frainer DA, Welter CS, Theis C; **Critical revision:** Frainer DA, Welter CS, Theis C; **Final approval:** Garcia RFL, Lemos R, Haritsch F, Lima AC, Garcia CE.

## DATA AVAILABILITY STATEMENT

All datasets were generated or analyzed in the current study.

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