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LETTER TO THE EDITORS

# A heartbreaking case of Wilson's disease: Takotsubo cardiomyopathy complicating fulminant hepatic failure

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Dear Sirs,

Wilson's disease is an inherited metabolic disorder, associated with decreased copper excretion and its accumulation within different tissues, mainly the liver and the brain. The majority of cases manifest at the age of 5–35 years. Fulminant hepatitis may be the presenting symptom, and Wilson's disease accounts for up to 12% of patients referred to emergency transplantation. Different clinical manifestations have been associated with Wilson's disease, including hemolysis, renal impairment, and neurological disorders [1]. Here, we report a case of Takotsubo cardiomyopathy (broken heart syndrome) [2].

A 16-year-old Caucasian female was transferred to our transplant center with suspected fulminant hepatic failure (FHF). The patient presented to the referring peripheral hospital with several days of diarrhea and new onset epigastric pain, nausea, vomiting, and icterus, which prompted her to seek medical attention. Her past medical history was unremarkable apart from chronic L-throxine treatment for hypothyroidism. She had been taking an antidiarrheal during the current episode and had had her tongue pierced 2 weeks earlier.

On admission, physical examination demonstrated a fully alert patient, with scleral jaundice, regular heart rate and rhythm, and a systolic murmur over the aortic valve. Abdominal examination revealed increased peristaltic sounds, and a soft, nontender, palpable spleen, without hepatomegaly or stigmata of chronic liver disease.

Blood test results (Table 1) demonstrated increased liver enzymes with prolonged INR and marked hypoalbuminemia. An abdominal ultrasound (US) demonstrated several enlarged lymph nodes up to 15 mm in the hepatic hilum. Intra- and extrahepatic bile ducts were not enlarged. The gallbladder wall was thickened and contents were dense with no cholelithiasis. A small amount of free abdominal fluid was also noted. Other abdominal organs were unremarkable. Doppler US was normal with normal flow in the hepatic artery and hepatic and portal veins.

Additionally, a complete FHF workup was performed, which was negative for autoimmune hepatitis, hepatitis A, B, and C infection, acute Epstein–Barr virus (EBV), and cytomegalovirus (CMV) infections. Additional infectious and toxicological workup was also negative. Blood paracetamol levels were within normal limits, and alpha 1-antitrypsin levels were normal.

An electrocardiogram on admission showed a normal sinus rhythm with ST segment elevation in AVR and V1 as well as diffuse ST depression at the inferior and lateral walls. An echocardiogram demonstrated apical ballooning compatible with Takotsubo syndrome (Fig. 1).

A diagnosis of acute Wilson's disease was performed, based on low serum ceruloplasmin levels [6.8 mg/dl (norm 17–35 mg/dl)] with high copper levels measured in a urine collection [13414 μg/volume (normal 15–50 μg/volume)]. Treatment with penicillamine was initiated in parallel with preparation for liver transplantation.

Several hours after arrival, the patient's mental status deteriorated to the point of grade IV hepatic encephalopathy, and a prophylactic intubation was performed. Noncontrast head CT scan showed no pathologic findings and no signs of cerebral herniation. Repeated blood test showed severe anemia with hemoglobin levels that had dropped to 6.8 G/% (NR 12–14 G/%). After a workup that included a peripheral blood smear and bone marrow aspirate, a massive Coomb's negative hemolysis was diagnosed. Further laboratory results showed deterioration in liver function with model to end-stage liver disease (MELD) score of 37. Plasmapheresis was performed as a rescue therapy, and 48 h after admission, the patient, who was a tourist, was transferred back to her native homeland where she underwent a successful orthotopic liver transplantation.

Fulminant hepatic failure, which is characterized by a rapid decline in synthetic hepatic function with encephalopathy, is a medical emergency. Proper management of patients with FHF requires establishing the diagnosis and etiology, with treatment options ranging from specific therapy when applicable (e.g., N-acetyl cystein in cases of acetaminophen intoxication and other causes of FHF), nonspecific supportive care, and liver transplantation when

 

**Table 1.** Patient's laboratory results.

| Test | Result | Normal range | Test | Result | Normal range |
|---|---|---|---|---|---|
| Albumin | 21 G/l | 30–50 G/l | INR | 2.64 | |
| Total protein | 66 G/l | 60–80 G/l | Factor II | 21.49% | 70–140% |
| Sodium | 136 mM | 135–145 mM | Factor V | 49.82% | 70–140% |
| Potassium | 5.9 mM | 3.5–5 mM | Factor VII | 22% | 70–140% |
| Chloride | 109 mM | 95–105 mM | Factor VIII | 199.63% | 70–140% |
| Alkaline phosphatase | 26 U/l | 40–130 U/l | Factor IX | 38.94% | 70–140% |
| Alanine transaminase | 27 U/l | 6–53 U/l | Factor X | 23.31% | 70–140% |
| Aspartate aminotransferase | 261 U/l | 2–60 U/l | Factor XI | 20.2% | 70–140% |
| Total billirubin | 728 μM | 0–17 mM | C3 | 106 | 80–160 m/dl |
| Direct bilirubin | 502 μM | 0–3.4 mM | C4 | 17.4 | 15–35 mg/dl |
| LDH | 699 U/l | 300–620 U/l | Ammonia | 37 | 10–60 mM |
| pH | 7.36 | 7.38–7.42 | Lactate | 3.9 mM | 0.5–2.4 mM |
| pCO2 | 43 mm/Hg | 41–51 mm/Hg | WBC | 14.1 K/μl | 4–10 K/μl |
| pO2 | 23 mm/Hg | 30–40 mm/Hg | HGB | 8.6 G% | 12–14 G% |
| HCO3 | 24.3 mM | 18–24 mM | PLT | 22.4 K/μl | 14–40 K/μl |
| | | | Diastase | 50 U/l | 20–100 U/l |
| | | | Uric acid | 266 μM | 150–380 μM |

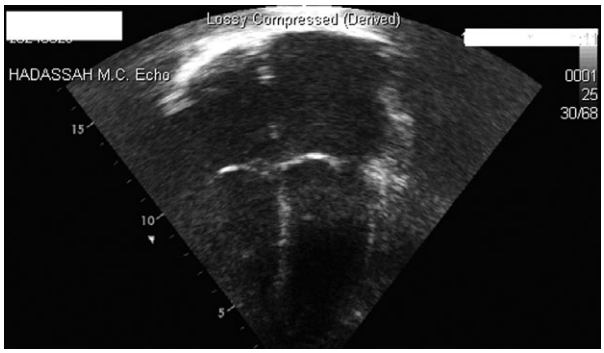


**Figure 1** Echocardiogram in the same patient demonstrated moderately reduced LV function with dyskensia of the mid- and apical anterior and septal wall, consistent with LAD territory. The mitral leaflet is thickened and the anterior leaflet is prolapsing, resulting in moderate posterior jet regurgitation. An apical aneurysm can be seen on the echo presented.

indicated. FHF may also be associated with circulatory dysfunction [3,4].

Takotsubo cardiomyopathy occurs in the setting of acute emotional of physical stress (hence the term "broken heart syndrome"). Takotsubo [5] cardiomyopathy is associated with elevated serum catecholamine levels, and several mechanisms have been suggested to play a role in its pathogenesis, including epicardial coronary artery spasm, coronary microvascular impairment, catecholamine cardiotoxicity, and others. The prognosis of Takotsubo [5] cardiomyopathy is considered good, although recurrence and mortality have been reported. Even though animal models have suggested that the use of estrogen may be beneficial; no specific treatment has been validated in humans [2].

Takotsubo cardiomyopathy has been described in the postoperative course following liver transplantation [5]. In these cases, Takotsubo cardiomyopathy may be attributed to the stress of undergoing major surgery such as liver transplantation, rather than the underlying liver disease and hepatic failure *per se*.

In this case report, a young previously healthy female presented with FHF secondary to Wilson's disease. An abnormal electrocardiogram on admission, which could represent a myocardial infarction with left main artery involvement, prompted echocardiographic investigation, which demonstrated apical ballooning and supported the diagnosis of Takotsubo cardiomyopathy. The patient was transferred to her native homeland where she underwent orthotopic liver transplantation with complete resolution of symptoms. On explant liver pathology, Wilson's disease was confirmed.

This case is unique as it is the first report of Takotsubo cardiomyopathy as a possible complication of FHF, which in this case was secondary to Wilson's disease. It is still unknown whether Takotsubo cardiomyopathy resulted from the hepatic failure, regardless of its etiology, or whether its occurrence was specific to Wilson's disease. We believe it is important for hepatologists and cardiologists to be aware of the possibility of Takotsubo cardiomyopathy in these specific settings. In this specific case, the diagnosis of Takatsubo cardiomyopathy was not considered an absolute contraindication to transplantation (which also required transferring the patient to a different center). No large randomized control trial is expected to be performed to validate this approach; in case, such a condition is diagnosed in a patient with FHF, and decision


 

making is to be made according to the patient's status and local expertise.

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## Conflicts of interest

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