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Acute liver damage and anorexia nervosa: A case report

LIVER

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ABSTRACT

Anorexia nervosa is an eating disorder predominantly affecting young women and characterized by an intense fear of gaining weight and becoming fat. Liver injury with mild elevation of hepatic enzymes is a frequent complication, and steatosis of the liver is thought to be the major underlying pathology. However, acute hepatic failure with transaminase levels over 1000 u/L is a very rare complication, and the precise mechanism of the liver injury is still unclear. We report a case of a 35-year-old woman with a history of anorexia nervosa who developed acute liver damage with deep coma in relation to profound hypoglycemia. The treatment was hydration, correction of electrolyte and fluid imbalance, and gradual nutritional support to prevent refeeding syndrome. Our patient's consciousness was significantly improved with the recovery of liver function and normalization of transaminase levels. Although the mechanism of pathogenesis is largely unknown, we discuss the two principal hypotheses: starvation-induced autophagy and acute hypoperfusion.

Keywords: Acute liver damage, hypoglycemia, anorexia nervosa, autophagy

Case Report

INTRODUCTION

Anorexia nervosa is an eating disorder characterized by voluntary weight loss, distortion of body image, and intense fear of gaining weight.

Several studies have described an increase in serum liver enzymes in severely malnourished patients who have been affected by anorexia nervosa (1,2).

Such results are usually mild, and normal values are restored when the body weight is normalized.

The mentioned hepatic complications are usually related to an isolated elevation of transaminase levels, but nevertheless, very few cases of acute liver failure in anorexia nervosa have been described (3-7).

We are presenting the case of a 35-year-old woman who suffers from severe anorexia nervosa. She was admitted in June 2011 at our hospital following a hypoglycemic coma and acute liver damage.

CASE PRESENTATION

Our patient, who works as a dietitian, has been under psychiatric care since 1989 due to anorexia nervosa, complicated with amenorrhea and osteoporosis.

She does not take any current regular medication although admits to abusing laxatives (bisacodyl) or diuretics.

Further, she takes occasionally a half-tablet of paracetamol for headaches. She does not consume alcohol regularly and denies any other toxic habits. Her last recorded weight was 32 kg in 2006. Her aminotransferase level was normal at the time (AST=2 u/L and ALT=22 u/L).

The patient was seen initially at the emergency service in view of a decreased level of consciousness secondary to severe hypoglycemia and acute hepatic insufficiency.

At the time of admission, she presented with hypotension, 90/60 mm Hg, and bradycardia at 46 beats per minute, and her body temperature was 36°C.

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The electrocardiogram showed sinus rhythm and a heart rate of 50 beats per minute. She had moderate, diffuse, and unspecific abdominal pain. There were no signs of hepatic encephalopathy. She was dramatically slim on admission. Her weight was 25 kg, and her body mass index (BMI) was 10.5 kg/m^2. She reported a 3-kg weight loss within the previous weeks in the context of extreme anorexia.

Her full blood count showed leukopenia (2400/mm^3) and moderate thrombocytopenia (65,000/mm^3).

Regarding her biochemistry, there was marked hypoglycemia (16 mg/dL) and normal urea (80 mg/dL) and creatinine (0.58 mg/dL) levels. She did not have acidosis. Her pH was 7.36, and her bicarbonate level was normal (40 mEq/L). Her blood test also showed hypokalemia (2.45 mEq/L), hypocalcemia (7.3 mg/dL), hypophosphatemia (0.42 mg/dL), and hypomagnesemia (1.48 mg/dL).

Nutritionally, there was hypoproteinemia (4 g/dL) and hypoalbuminemia (2.4 g/dL).

On admission, she also had a marked elevation of transaminase levels: AST 3758 u/L (reference range 1-40) and ALT 1955 u/L (1-37). GGT levels were 280 u/L (7-32) and alkaline phosphatase 344 u/L (30-106). Plasma bilirubin level was normal. Prothrombin time was 52%, and INR was 1.69.

The serum paracetamol level was negative. The urinary toxicology screen (cannabis, cocaine, amphetamines, opiates, methadone, benzodiazepines) was negative.

Serologic tests for hepatotropic viruses (HAV, HBV, HCV, HEV, CMV, HSV 1-2, EBV, VZV) were negative. Anti-nuclear, anti-mitochondrial, anti-LKM and anti-smooth muscle antibodies were negative. Alpha-1-antitrypsin and ceruloplasmin levels were normal.

Her brain CT scan was normal. Her abdominal ultrasound scan showed a homogeneous hepatomegaly with normal echostructure, moderate ascites, and bilateral pleural effusion. There was no abnormality detected in her gallbladder and biliary ducts. The echocardiogram showed a non-dilated left ventricle with normal systolic function and mild pericardial effusion. There was no cardiac valve dysfunction. Ejection fraction was 63%.

Despite treating her hypoglycemia, her Glasgow Coma Score did not improve, and thus, she was admitted to the intensive care unit for assisted ventilation. After 5 days, the patient was transferred to the endocrinology ward, where she was given vitamin and ionic support, as well as enteral nutrition through a nasogastric tube.

To avoid complications of refeeding syndrome, her caloric input was started at 750 Kcal/day for 1 week; it was then increased to 1200 Kcal/day for a further 2 weeks, and finally, after removing the nasogastric catheter, it was set at 1800 Kcal/day orally.

Oral nutrition was authorized from week 3 following resolution of her abdominal pain, which is usual in these patients (8).

Biologically, there was a marked decrease in her transaminase levels after day 3, achieving normal levels as of day 20. Her prothrombin time also normalized on day 3. Her protein electrophoresis showed an increased of her total protein level at 6 g/dL and serum albumin of 3.2 g/dL on day 45.

Leukopenia and thrombocytopenia normalized. Her pericardial effusion and ascites resolved as soon as her serum albumin returned to normal levels.

The patient was transferred to the psychiatric ward on day 20 for management of her eating disorder, once she had been stabilized biological and nutritionally.

Her weight was 32 kg and her BMI was 13.5 on day 45 after admission.

DISCUSSION

Anorexia nervosa is an eating disorder that develops quickly into a very important feeding restriction.

The illness affects young women mainly, with a prevalence of up to 1% in teenagers (9).

In a meta-analysis done in 2002, mortality reached 5%, the two more frequent causes being suicides and lethal complications of malnutrition (cardiac mostly) (10).

Many of the systemic complications of anorexia nervosa involve the gastrointestinal tract and include pancreatitis (11), gastroduodenal symptoms (12,13), and particularly hepatic disorders.

The presence of hypoglycemia is not usual within the context of this condition. The precise pathogenesis has not been elucidated, but several mechanisms, including excessive exercise, depletion of liver glycogen, defective gluconeogenesis, and failure of glucagon secretion, have been proposed (14).

However, in the context of anorexia nervosa, it is usually severe, recurrent, and difficult to correct (15). It usually happens in young adults rather than adolescents (average age: 34 years) (16,17).

Change in the peripheral blood cell count in these patients is a frequent observation and might be the result of the gelatinous transformation of the bone marrow with hypocellularity, as described by Nishio in 2003 (18). It is usually corrected completely and rapidly by enteral nutrition.

Hypokalemia can be explained by the abuse of laxatives and diuretics. The anasarca is explained by hypoalbuminemia.

Despite the presence of hypokalemia, hypophosphoremia and hypomagnesemia, her clinical situation was not secondarily complicated by heart failure, which could have caused severe arrhythmias due to QT elongation, as has been described in previous studies (19,20).

Pericardial effusion is mostly asymptomatic, not requiring any intervention and spontaneously regressing with refeeding.

Mild elevations in serum aminotransferase levels have been reported in up to 60% of patients with anorexia nervosa (21), but acute liver injury has rarely been described in the Western literature.

In our case, we can not explain her liver failure as secondary to any toxic, drug intake, autoimmune, or infectious agent. Cardiac dysfunction was eliminated by cardiac investigations.

We did not perform a hepatic biopsy, as in most of the previously described cases, due to the resolution of her liver function and clinical and psychological conditions.

Although the mechanism of liver injury in anorexia nervosa remains unclear, it is believed that the marked elevation of transaminase levels, along with hepatic insufficiency, is related to the presence of global dehydration, subsequent hypovolemia and hypotension, and thus hypoxemia and hepatic hypoperfusion (6,7).

But, this hypothesis has not been rigorously demonstrated, and the precise reason could be something else.

The most important series of hepatic biopsies performed in 12 patients who suffered from anorexia (BMI <13 kg/m^2) and hepatic failure dates from 2008: the results showed significant glycogenic depletion but also numerous autophagosomes responsible for autophagy. In only 25% of the cases were signs of apoptosis seen, without any described signs of cell necrosis. It is possible that this "nutrition autophagy," a defense mechanism in the case of anorexia, was the cause for the hepatocyte death. The stress of the endoplasmic reticulocyte might have been the initial trigger (22).

Similar histology data have been seen in a previous case report in 2006 (23).

This autophagy might play a double role: when the loss of weight starts occurring, the liver anomalies are moderate, and the autophagy can endure this state.

After that, when malnutrition worsens and the BMI lowers, peak transaminase level and subsequent liver failure show.

During this time, hepatocytes are formed of numerous autophagosomes, which explains cell death by autophagy. This kind of cell death could be the explanation for the contrast noticed with regards to the significant increase of the aminotransferases detected and the absence of liver necrosis and apoptosis shown in the histology results.

Finally, it is likely that starvation-induced autophagy was the principal mechanism involved in liver cell damage in this population.

We treated a patient suffering from severe anorexia nervosa (BMI 10.5 kg/m^2) complicated with hepatic insufficiency.

Such treatment consisted of rehydration and the correction of her malnutrition, using adapted protocols to avoid the development of re-feeding syndrome.

In view of her successful progress, she was discharged from the hospital on day 50.

Although we did not perform a hepatic biopsy, the mechanism seems to be related to autophagy more than hypoperfusion because of the extremely low BMI.

This observation also highlights the need for following a multi-disciplinary approach in these difficult cases (BMI <13 kg/m^2), involving ICU doctors, gastroenterologists, endocrinologists, and psychiatrists.

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