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A HEPATIC MANIFESTATION OF ANOREXIA NERVOSA

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ABSTRACT

A 30-year-old woman with a history of anorexia nervosa was admitted with weight loss, hypoglycaemia and electrolyte disturbances. During her admission, transaminases peaked at ALP 457 U/l, AST 817 U/l and ALT 1066 U/l. Imaging and laboratory findings were unrevealing, and she declined liver biopsy. Nutrition was introduced via a nasogastric tube and she demonstrated improvement in her laboratory values over several weeks. Her transaminitis was determined to be secondary to severe malnutrition, which has been previously described, but cases with such profound transaminitis are less common. Studies have demonstrated hepatic autophagocytosis as the likely cause.

KEYWORDS

Anorexia nervosa, hepatitis, acute liver injury

LEARNING POINTS

- Anorexia nervosa can cause severe liver injury as manifested in AST and ALT levels in the thousands.
- The slow reintroduction of enteral feeding can reverse liver injury.
- The mechanism is unclear but autophagocytosis of liver cells likely contributes to this phenomenon.

INTRODUCTION

Anorexia nervosa (AN) is defined as restrictive energy intake leading to significantly low body weight, an intense fear of weight gain or becoming fat, and disturbance by one's weight or shape that impacts one's self-worth[1]. It is a common eating disorder with two subtypes, restrictive and binge-eating/purging[1]. AN frequently co-occurs with other medical or psychiatric illnesses, which complicates treatment and increases individual risk for morbidity and mortality[2,3]. The pathogenesis of AN is unknown, but a genetic component and environmental triggers are suggested[3]. AN often has severe accompanying medical conditions affecting all organ systems including the liver[2]. While liver manifestations due to AN are less well characterized, the literature describes liver injury from AN as including increased liver enzymes such as aspartate aminotransferase (AST) and alanine transaminase (ALT) due to injured hepatocytes releasing them into circulation.

CASE DESCRIPTION

A 30-year-old woman with a 17-year history of AN presented with profound weight loss, hypoglycaemia and

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severe electrolyte abnormalities. She had a history of multiple hospitalizations for relapsing and remitting disease with failed attempts at weight gain. She also had a history of major depressive disorder and anxiety along with a family history of eating disorders. On arrival, her BMI was 10.29 kg/m^2. She was hypotensive at 81/59 mmHg, heart rate was 68 bpm, respiratory rate was 14 bpm, and temperature was 36.6°C. She had no scleral icterus, jaundice or angiomas. She reported no alcohol or recreational drug use and was a non-smoker.

Admission laboratory work was significant for a white blood cell count of 1300/mm^3, haemoglobin/haematocrit of 8.3 g/dl/23.6%, and a platelet count of 15,900/mm^3. Initial potassium was 2.0 mmol/l. The hepatic function panel revealed a total bilirubin of 0.7 mg/dl, direct bilirubin of 0.3 mg/dl, AST of 99 U/l (reference range, 0–37 U/l), ALT of 110 U/l (reference range, 0–41 U/l) and alkaline phosphatase (ALP) of 150 U/l (reference range, 35–129 U/l). The patient was admitted to a medicine service for stabilization before transfer to an inpatient psychiatric unit. Caloric intake remained poor during hospitalization, and 9 days after admission her rechecked hepatic function panel was found to be grossly abnormal. As a result, laboratory results were trended. Eleven days after admission AST peaked at 817 U/l, ALT at 1066 U/l, and ALP at 457 U/l. At that time, the patient agreed to enteral feeding via a nasogastric tube.

Abdominal ultrasonography of the right upper quadrant was unrevealing and showed normal hepatopetal flow in the portal vein. Laboratory evaluation with an acute viral hepatitis panel, ceruloplasmin, iron studies, and immunoglobulin levels did not reveal the aetiology of the liver injury. The patient declined liver biopsy, which was recommended by hepatology consultants. Liver function laboratory values trended down slowly after the initiation of enteral feeding, suggesting that the transaminitis was due to severe malnutrition in the setting of AN. As feeding was continued, electrolyte abnormalities slowly corrected and hypoglycaemic episodes became more infrequent. Ultimately, the patient stabilized and was transferred to an inpatient psychiatric unit of the hospital for continued treatment of her AN. At discharge, 45 days after her initial admission, her AST had decreased to 87 U/l, ALT to 151 U/l, and ALP to 158 U/l.

DISCUSSION

Transaminitis is a well-known complication of eating disorders and has been previously described in the literature. Multiple studies have found that over 40% of patients admitted with anorexia have elevated AST or ALT with varying ALP levels[4,5]. Studies have revealed that a subset of patients with severe anorexia (defined as BMI <15 kg/m^2) had a greater occurrence of transaminitis than patients with anorexia with higher BMIs[2,5]. ALT levels specifically are associated with lower BMI and more significant anorexia, suggesting causation between anorexia and transaminitis[4]. This causation appears to be linear in nature[5]. Despite the linear relationship, it has been noted that transaminase levels rarely exceed 1000 U/l in the setting of this disease[6].

Multiple mechanisms have been postulated to cause elevated transaminases in AN. These include hepatic necrosis from ischaemic hepatitis, hepatic autophagy, and refeeding-induced transaminitis. Worsening transaminitis during refeeding, often called refeeding steatosis, is a classic manifestation. This is due to excessive deposition of glucose in liver cells and can be seen on imaging and biopsy[6,8,9]. However, Rautou et al. described several hepatic biopsy samples of patients with severe AN prior to refeeding which were examined under electron microscopy. These revealed autophagosomes but did not show hepatocyte necrosis, apoptosis or hepatic blood flow changes, suggesting that autophagocytosis is a significant cause of transaminitis in severely malnourished patients. This study showed that an increase in cellular membrane permeability in hepatocytes undergoing autophagocytosis could potentially explain why severe transaminitis is seen in these patients when overt hepatocyte necrosis is not seen[7]. Ultimately, these studies reveal transaminases return to normal values with careful refeeding, as in our case.

This case is unique because our patient displayed a profound level of transaminitis with AST >1000 U/l prior to refeeding. At their peak 11 days after admission, her AST and ALT levels were 22 times and 26 times the upper limit of normal, respectively. As she had no history of previous liver disease, her severe transaminitis put her at increased risk of fulminant hepatic failure and higher mortality[10]. However, as in previously reported cases of starvation-induced hepatitis, she had no physical signs of liver disease or significant derangements of hepatic synthetic function (i.e., coagulopathy, thrombocytopenia). Studies have shown that patients with profoundly elevated ALT values were more likely to display hypoglycaemia and hypothermia, findings our patient exhibited during her hospital course[3,6]. This case adds to the evidence that anorexia causes silent liver dysfunction. It rarely produces physical manifestations, but if not recognized, has the potential for severe outcomes if anorexia is left untreated.

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