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CASE REPORT – OPEN ACCESS

Celiac Disease and Autoimmune Hepatitis Presenting with Fulminant Hepatic Failure: A Case Report

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ABSTRACT

Background: Fulminant hepatic failure (FHF) may be a rare presentation of autoimmune hepatitis (AIH) in previously asymptomatic adolescents. Celiac disease (CD) is a chronic immune disease that may be associated with severe forms of liver disease and coexists with AIH. We report a patient presenting with an FHF at the diagnosis of AIH and CD.

Case Report: An 8-year-old female patient who had no known background or family history of liver disease was referred to our center with an FHF diagnosis. Her clinical and laboratory findings fulfilled the criteria of seronegative AIH and CD. After 7 days of starting the medical treatment, encephalopathy and liver function tests gradually improved.

Conclusion: AIH and CD usually follow a chronic course and rarely coexist. However, they should be considered the etiologies of FHF and should be treated promptly.

Keywords: Autoimmune hepatitis, celiac disease, children, fulminant hepatic failure

INTRODUCTION

Celiac disease (CD) is a chronic immune disease, which activates after exposure to gluten in genetically predisposed individuals (1). Pediatric autoimmune liver disease is characterized by inflammatory liver histology, circulating autoantibodies, and increased levels of immunoglobulin (Ig)G in the absence of a known etiology (2). Two diseases rarely coexist (3) and may lead to serious liver damage (4). The focus of this report is a pediatric patient who was introduced as having fulminant hepatic failure (FHF) and then diagnosed with CD and autoimmune hepatitis (AIH).

CASE REPORT

An 8-year-old female patient, who had no known background or family history of liver disease, was referred with an FHF diagnosis. For 10 days before her admission, the patient had taken single-dose paracetamol for abdominal pain. On examination, it was noted that she was confused, restless, agitated, pale, and icteric. In addition, her pupillary light reflex was reduced, and her bilateral deep tendon reflexes were increased. These symptoms concluded as Stage II on the systems for grading hepatic encephalopathy. She weighed 24.7 kg (Z-score: –0.12 SD) and her height was 128 cm (Z-score: 0.43 SD). An abdominal examination revealed mild distention. Her liver and spleen were impalpable. Percussion of Traube's space was not dullness. The other systemic examinations were normal. Laboratory tests showed the following results: Hemoglobin was 9.6 g/L, white blood cell count was 7.5 K/μL, platelet count was 253 K/μL, erythrocyte sedimentation rate was 2 mm/h, total serum bilirubin was 8.7 mg/dL, direct bilirubin was 6.2 mg/dL, ALT was 540 U/L, aspartate aminotransferase (AST) was 616 U/L, gamma-glutamyl transferase was 185 U/L, albumin was 2.4 g/L, total serum protein was 4.2 g/L, the international normalized ratio was 6.1, and serum ammonia was 234 μg/dL. The patient was admitted to the pediatric intensive care unit; she was also selected as a possible candidate for liver transplantation. Four courses of plasmapheresis treatment were implemented. Sodium benzoate, N-acetyl cysteine, Vitamin K, and lactulose were started. Encephalopathy improved thereafter, and the acute liver failure (ALF) stopped. Extensive laboratory evaluations excluded Wilson's disease, viral hepatitis, metabolic diseases, cystic fibrosis, and alpha-1 antitrypsin deficiency. Autoantibodies comprising antinuclear, anti-mitochondrial, anti-smooth muscle, anti-liver/kidney microsomal, anti-liver cytosol type 1, and anti-soluble liver antigen/liver pancreas antibodies were negative. Total IgG 23 g/L (normal: 10–19 g/L), anti-tissue transglutaminase IgA: 328 U/ml, anti-tissue transglutaminase IgG was 105 U/ml, and IgA was 2.3 g/L. The haplotype was HLA DR3DQ2. The laboratory findings confirmed the diagnosis of CD; however, a histological biopsy was deemed inappropriate due to the severity of her condition. Abdominal ultrasonography showed a non-homogeneous liver and a small amount of ascites. An magnetic resonance imaging revealed hepatic contour irregularity, heterogeneity of hepatic parenchyma, and mild splenomegaly (Fig. 1). Her cranial CT was normal. Her liver biopsy documented panacinar hepatitis with interphase activity. Periportal interface

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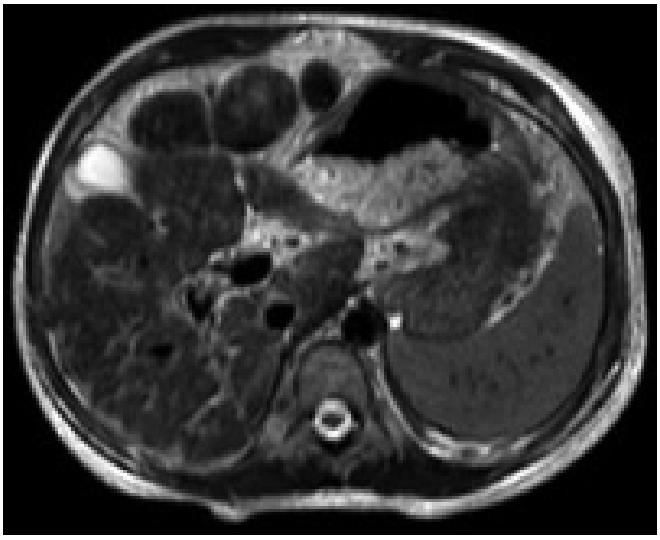

Figure 1. Heterogeneous liver parenchyma on magnetic resonance imaging

hepatitis, confluent necrosis, focal necrotic hepatocytes, and portal inflammation were noted. The fibrosis score was 3 (according to Ishak scoring system). A diagnosis of seronegative AIH besides CD was thus given. She was commenced on 1 mg/kg/day of prednisolone and introduced to a gluten-free diet (GFD). Five days after starting treatment, the steroid dose was gradually reduced within 3 months and the maintenance dose was continued as 4 mg/day. After 5 weeks on prednisolone and a GFD, her ALT decreased to 51 U/l and anti-tissue Tg IgA was 328 U/L. Azathioprine was then introduced at 12.5 mg (0.5 mg/kg/day); after 4 weeks, the maintenance dose was continued as 25 mg/day. She remains in remission with normal liver function tests (LFTs) and celiac serology 12 months after the admission of prednisolone. At the time of her most recent follow-up, 1 year post-diagnosis, her treatment was a GFD, 4 mg of prednisolone daily, and 25 mg of azathioprine daily.

DISCUSSION

CD is a chronic immune disease which activates after exposure to gluten in genetically predisposed individuals. The classic symptoms are diarrhea, chronic constipation, abdominal distention, and recurrent abdominal pain (1). Recently, extraintestinal symptoms of the disease have increased. The liver in celiac patients may be affected by cryptogenic and autoimmune. A GFD reverses enzymes to normal in almost all cases of cryptogenic hepatitis, while autoimmune involvement including AIH, primary sclerosing cholangitis, and primary biliary cirrhosis may lead to fibrosis and cirrhosis. Fibrosis and cirrhosis are generally unaffected by gluten withdrawal, therefore necessitating an immunosuppressive treatment (5). Liver involvement may be life threatening in celiac patients. Pavone et al. (6) reported a 14-year-old girl with CD who did not adhere to a GFD; she was affected by severe hepatic failure and underwent a liver transplant. Long-term exposure to gluten in celiac patients is a known cause of ALF. To the best of our knowledge, our patient who presented with fulminant hepatitis without any known systemic disease, newly diagnosed AIH, and atypical CD differs from celiac patients who have ALF after prolonged exposure to gluten.

Di Biase et al. (7) surveyed 350 children with CD; 40% had hypertransaminemia, 2% had AIH, and one patient had relapsed after discontinuing immunosuppressive therapy. It was reported that a GFD is insufficient to restore liver damage and the risk of AIH is high in CD patients whose ALT and AST are 5 times higher than the normal upper limit. A number of hypotheses can be raised, although there is no definitive answer to the following question: "Why is it rarely accompanied by AİH in CDs that make up 1% of the population?" As an answer to this question causes to accuse are the following: In patients diagnosed as having CD with hypertransaminemia, intestinal permeability was increased compared to patients with normal LFTs (8); anti-tTG antibodies spread to the liver and extraintestinal areas to increase inflammation in the liver (9); and HLA-DQ2, the major genetic marker in celiac patients is associated with HLA-DR3-the leading risk factor for AIH (10). It has been suggested that exposure to gluten in CD increases the risk of ALF, but Quail et al. (11) reported a 13-year-old celiac patient diagnosed with seronegative AIH a year after starting a GFD. The patient had normal LFTs at diagnosis and demonstrated strict compliance to her GFD. It is not known how immunological and genetic factors are triggered.

The serum aminotransferases of celiac patients should be checked at regular intervals, much like the celiac markers of AIH patients (4, 7). Celiac patients with elevated serum aminotransferases should be further investigated for an autoimmune predisposition. Particular attention should be paid to the risk of acute FHF in the presence of a triggering factor.

CONCLUSION

The serum aminotransferases of celiac patients should be checked at regular intervals, much like the celiac markers of AIH patients (4, 7). Celiac patients with elevated serum aminotransferases should be further investigated for an autoimmune predisposition. Particular attention should be paid to the risk of acute FHF in the presence of a triggering factor.

Informed Consent: Written informed consent was obtained from the patient's parents to publish the case report and the image.

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