Case Report

Autoimmune liver disease in a toddler

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ABSTRACT

Autoimmune liver disease (AILD) is a rare cause of chronic liver disease in toddlers. We report a 2.5-year-old child who presented with recurrent episodes of jaundice. The child was diagnosed to have AILD type 2. He was successfully treated and is doing well on 5 years follow-up.

Key words: Autoimmune liver disease, Chronic, Liver disease, Toddler

Autoimmune liver disease (AILD) is a treatable cause of chronic liver disease (CLD) in children. The condition has a varied clinical presentation and should be suspected in all patients with liver disease (acute or chronic). It may be associated with other autoimmune disorders. The treatment consists of steroids and immunosuppressants. If not treated in time, it can lead to cirrhosis and liver failure.

CASE PRESENTATION

A 2.5-year-old male child was referred to us with history of intermittent jaundice for the past 6 months. He was a first born child and a product of second-degree consanguinity. He had four such episodes in the past 6 months. The episode would start without prodromal symptoms. The child would have high-colored urine staining the diapers and last for 15–20 days, followed by a relative symptom-free interval. He was referred to us in the fourth episode as the patient had more jaundice than the previous three episodes. He also had an intermittent fever for the past 20 days. There was a history of fall from stairs while playing before 15 days, following which he had bleeding from gums. There was no history of hematemesis or melena. There was no history suggestive of encephalopathy. The patient had received two doses of inactivated hepatitis A vaccine and three doses of hepatitis B vaccine. There was no history of any hepatotoxic drug, traditional medicines, or supplements consumption before the illness. There was no history of the use of copper vessels.

On physical examination, the child had icterus, mild pallor, wasting, and stunting. There were no dysmorphic features. On abdominal examination, liver was found palpable 3 cm below the right costal margin. It was firm with sharp edges, non-tender, and had a nodular surface. The spleen was 5 cm palpable below the left costal margin. Clinically, there was no ascites. On ophthalmologic examination, there was no cataract, no Kayser-Fleischer ring on slit-lamp examination, and fundus examination was normal. Examination of the oral cavity was normal.

The child was clinically diagnosed as having CLD and was investigated for the same. Hemogram showed a microcytic hypochromic type of anemia (hemoglobin 8.5 g/dl). Liver function tests were suggestive of a direct hyperbilirubinemia (total 3.7 mg/dl and direct 2.8 mg/dl) with raised transaminases (ALT 1600 IU/l and AST 782 IU/L). The international normalized ratio was 1.2. Serum albumin was 3.5 mg/dl. Alkaline phosphatase and gamma-glutamyl transferase were normal. Erythrocyte sedimentation rate was 60 mm at the end of the 1st h, and serum C-reactive protein was 70 mg/l.

The serology for viral hepatitis (immunoglobulin [Ig]M anti-hepatitis A virus, HBsAg, anti-HBc, anti-HEV *IgM*, anti-HCV antibodies**,** IgM for cytomegalovirus, Epstein–Barr, and herpes simplex viruses) was all negative. Serum ceruloplasmin levels, 24 h urine copper was normal. Ultrasound abdomen revealed altered echogenicity of liver, splenomegaly, a raised portal venous diameter, and patent hepatic veins. Hypergammaglobulinemia was detected with increased IgG 0.3 g/l (>1.1 times the normal value for the age) with normal levels of IgM, IgA, and IgE. Anti-nuclear antibody (ANA), anti-smooth muscle antibody (ASMA), and anti-liver cytosol type1 (anti-lc1) antibody were negative at a dilution of 1:20. Anti-liver-kidney microsomal-1 (anti-lkm1) antibody was positive 1:31. A liver biopsy was done, which revealed interface hepatitis and piecemeal necrosis. Upper gastrointestinal endoscopy revealed Grade 1 esophageal

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varices. Proctosigmoidoscopy was normal. Magnetic resonance cholangiopancreatography was normal. Random blood sugar was 74 mg/dl. Workup for celiac disease, hypothyroidism was negative. Thiopurine methyltransferase enzyme activity was normal.

A score of 8 points (two points – negative viral markers, two points = IgG >1.1 times the normal, two points – positive anti-lkm1, and two points – interface hepatitis on liver biopsy) was obtained on the scoring system for diagnosis of juvenile AILD. Hence, a diagnosis of AILD was made. There were no other associated autoimmune disorders.

The child was started with prednisolone 2 mg/kg/day, which was tapered over 8 weeks as transaminases were reduced. Azathioprine was started at 4 weeks at a dose of 0.5 mg/kg/day, which was gradually increased to 2.5 mg/kg/day. At the end of 8 weeks, prednisolone dose was reduced to 2.5 mg daily, and azathioprine was dosed at 2.5 mg/kg/day. The treatment led to excellent biochemical response and clinical improvement within 2 months with cleared anemia and reduced transaminases. After 2 years of symptom-free interval, the patient stopped medicine on their own and had a relapse which was treated with the same regime. At present, it's 5 years since the diagnosis; the child is completely asymptomatic with normal transaminases on oral azathioprine 37.5 mg (2.5 mg/kg/day) and Tab. prednisolone 2.5 mg once a day along with fat-soluble vitamins and calcium as supplements.

DISCUSSION

AILDs are a group of progressive inflammatory disorders of the liver characterized by raised transaminases, positive autoantibodies, IgG, and interface hepatitis on histology in the absence of a known etiology [1]. AILD consists of three main categories: Autoimmune hepatitis, primary biliary cirrhosis, and primary sclerosing cholangitis. An high alkaline phosphatase level in a patient with CLD would give a clue of sclerosing cholangitis. An "overlap syndrome" occurs when there are overlapping features within the spectrum of AILDs [2]. The worldwide prevalence has been reported as 2–17/100,000 children [3].

It has various clinical phenotypes ranging from an asymptomatic elevation of transaminases, acute hepatitis, cirrhosis, or liver failure [4]. Few patients may present with periods of increased or decreased activity [5]. It may even be asymptomatic and detected on routine examination. Some patients have non-specific symptoms, such as fatigue, anorexia, nausea, abdominal pain, itching, arthralgia involving the small joints, or a transient erythematous rash may also be present [6]. Patients may have other autoimmune disorders such as celiac disease, type-1 diabetes mellitus, autoimmune thyroiditis, rheumatoid arthritis, ulcerative colitis, and systemic lupus erythematosus, vitiligo syndrome [7], and autoimmune hemolytic anemia [8].

There are two types of autoimmune hepatitis reported in children. Type 1 is characterized by the presence of ANAs and/or ASMA. It presents around puberty. Type 2 AILD is mainly seen in children and also in infants and toddlers. It is associated with anti-lkm1 [9] and/or anti-lc1 [10]. Patients who have anti-lkm-1 positivity present more frequently with fulminant liver failure [9]. The European Society for Paediatric Gastroenterology, Hepatology, and Nutrition has proposed scoring criteria for diagnosing juvenile AILD. It is based on aggregate scores assigned to history, clinical presentation, laboratory findings, and liver histology.

AILD responds well to steroids and immunosuppressants. Prednisolone is started in the dose of 2 mg/kg/day (maximum 60 mg/day) and tapered over 6–8 weeks to a maintenance dose of 2.5–5 mg daily. The timing of the addition of a steroid-sparing agent, azathioprine, varies as per different protocols. It is usually started at a dose of 0.5 mg/kg/day and increased up to 2–2.5 mg/kg/day if no toxicity along with fat-soluble vitamins (A, D, E, and K) and calcium as supplements.

For refractory cases, drugs such as mycophenolate mofetil, tacrolimus, cyclosporine, rituximab, and infliximab have been used. Except for fulminant liver failure, AILD responds well to immunosuppressive treatment with a remission rate of 90%. Treatment is given for at least 2–3 years and withdrawn only if transaminases and autoantibodies have been negative for at least 1 year. A repeat biopsy should be done to guide regarding the same. Liver transplant is a treatment option for AILD patients with end-stage CLD, hepatic malignancy, intractable symptoms, and severe acute liver failure unresponsive to steroid treatment [11].

CONCLUSION

This article reports the importance of suspecting an autoimmune etiology in a child with CLD with recurrent episodes of jaundice. With timely treatment, most patients experience remission in AILD. An attempt should be made to rule out other associated autoimmune disorders.

AUTHORS' CONTRIBUTIONS

All authors read and approved the final manuscript.

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