Type 1 leukocyte adhesion deficiency complicated by the presence of idiopathic liver cirrhosis

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Received 7 November 2012; received in revised form 12 November 2012; accepted 20 November 2012

Leukocyte adhesion deficiency type 1 (LAD1) is a rare autosomal recessive inherited disease. It results from heterogeneous mutations of the gene on chromosome 21q22.3 encoding the 95-kDa β2 leukocyte integrin subunit, CD18, which lead to impaired leukocyte adhesion and transmigration to inflamed sites.1 The clinical spectrum includes delayed separation of the umbilical cord, neutrophilia, and recurrent bacterial infections; however, liver involvement has never been reported in the literature. Here we describe a rare case of LAD1 with idiopathic cirrhosis.

A 7-year-old boy with LAD1 was diagnosed at 9 months of age. He presented with recurrent sepsis and neutrophilia and a leukocyte count of 20.0–100.0 × 10⁹/L. Molecular analysis showed a homozygous intron 7 (+1) G>A in the gene encoding CD18. Both his biological parents were healthy and non-consanguineous, without a family history of primary immunodeficiency diseases (PIDs). Polymorphonuclear cell dysfunction was observed, including decreased expression of adhesion molecule (CD11b/CD18), impaired chemotaxis, and decreased phagocytosis.2

The patient developed progressive abdominal distension from the age of 4 years. Abdominal sonography showed massive ascites, splenomegaly, and cirrhotic liver changes, but no space-occupying lesions were found. During serial laboratory follow-ups, his aspartate transaminase level was 24–74 U/L, alanine transaminase 12–37 U/L, alkaline phosphatase 285–424 U/L, gamma glutamyl transferase 26–44 U/L, and total bilirubin 1.38–2.73 mg/dL. Serological profiles for hepatitis B virus, hepatitis C virus, Epstein–Barr virus, cytomegalovirus, and human immunodeficiency virus did not show evidence of active or previous infection. Autoimmune profiles, including antinuclear antibodies, mitochondrial antibodies, smooth muscle antibodies, and liver–kidney microsomal antibodies, were also all negative. A stool examination for Cryptosporidia was negative, and magnetic resonance cholangiopancreatography did not reveal any sign of sclerosing cholangitis (Fig. 1). The cause of the patient’s cirrhosis remained unexplained, and a liver biopsy was refused by his family. He received intermittent intravenous albumin supplementation and diuretics; a hematopoietic stem cell transplant (HSCT) was not possible because no appropriate donor was available.

Liver disease is a common manifestation of PID, with a variable incidence ranging from 23.8% to 36.6%.3,4 The most common types of PID involving liver diseases are severe combined immunodeficiency, common variable immunodeficiency and hyper-IgM syndrome.3,4 These hepatic
complications can be attributed to five mechanisms: (i) infection of the hepatobiliary system, such as viral hepatitis, liver abscess, or biliary tract infection; (ii) chronic inflammation of the biliary tract, such as sclerosing cholangitis, which might correlate to Cryptosporidium parvum infection; (iii) secondary to therapeutic intervention, such as drug hepatitis; (iv) autoimmune hepatitis; and (v) malignancies. However, a large proportion of liver disease in PID remains idiopathic. Among the etiologies listed above, none could properly explain the cirrhosis in our patient.

Yokomori et al showed that expression of lymphocyte function-associated antigen 1 (LFA1), composed of CD11a/CD18, increases aberrantly on the surface of lymphocytes in liver biopsy specimens of cirrhosis, suggesting a pivotal role of LFA1 in lymphocyte-mediated bile duct destruction and subsequent cirrhosis. However, this could not be the case in our patient, whose CD18 expression was deficient. His ongoing cirrhosis may be coincident with LAD1, or due to some hepatic infection still not clarified. To the best of our knowledge, this is the first case report of LAD1 with idiopathic liver involvement.

References