Acute on chronic liver disease due to hepatic infiltration of chronic lymphoproliferative disorder of Natural Killer cells

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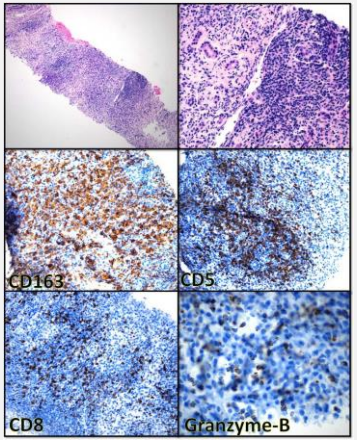
Introduction

We report a case of acute on chronic liver disease with a predominantly cholestatic pattern which was diagnosed as hepatic infiltration of chronic lymphoproliferative disorder of natural killer cells (CLPD-NK) after extensive workup and an initial false-negative liver biopsy.

Figures



Liver with diffuse lymphohistiocytic infiltrate. Sections show an atypical lymphohistiocytic infiltrate of the liver and composed of small to medium-sized cells that stain CD163+, CD5+, CD4 and CD8 with down-regulation, and Granzyme B +.

Case description

A 54-year-old woman with alcohol use disorder, celiac disease, and Hashimoto thyroiditis initially presented with 8-week history of night sweats, fever and jaundice. She reported taking daily naproxen for a few weeks. The physical exam was remarkable for jaundice. Labs showed bilirubin of 2.5, AST 869, ALT 543, alkaline phosphatase 966 and INR with 0.9. Right upper quadrant ultrasound showed no ductal dilation with a non-specific hypoechoic area in the superior right lobe and nodular appearance of the liver. Autoimmune workup revealed positive anti-smooth muscle antibody in a low titer but was otherwise negative.

A liver biopsy showed massive hepatic necrosis with marked pan-acinar lymphocytic inflammation. The leading cause of her liver injury was thought to be drug-induced due to naproxen in a background of chronic liver disease. Her liver disease progressed, developing ascites, encephalopathy and pruritus refractory to treatment. Nine months after initial presentation she presented with a hemoglobin of 7, MCV 104, LDH 590, Haptoglobin < 10, total bilirubin 2.9, and ferritin of 4289. WBC count was noted to have an absolute increase in lymphocytes, bone marrow biopsy showed CLPD-NK. A second liver biopsy was performed showing diffuse lymphohistiocytic infiltrate and flow cytometry revealed atypical lymphocytes/NK cell population. The patient was started on chemotherapy which led to clinical and biochemical improvement of her liver disease.

Discussion

CLPD-NK is a rare and heterogeneous disorder. Unlike other NK cell disorders, CLPD-NKs is not associated with EBV infection. This disorder follows an indolent course, making it difficult to detect it in the initial stages. Hepatic abnormalities in patients with lymphoproliferative disorders can occur from direct infiltration by abnormal cells, bile duct obstruction by lymphadenopathy, paraneoplastic syndrome, hemophagocytic syndrome, and reactivation of viral hepatitis. Our patient is to our knowledge the first case reported of cholestasis and hepatic infiltration from CLPD-NK. Treatment is indicated in symptomatic patients. Hence, early diagnosis is essential so patients can receive timely administration of immunosuppressive therapy.

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