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CASE REPORT | LIVER

Facing the Unknown: Idiopathic Giant Cell Hepatitis

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ABSTRACT

Giant cell hepatitis is a rare infiltrative disease associated with several viruses, drugs, malignancies, and autoimmune conditions. To date, treatment aims at controlling the underlying etiology, and there are limited data on the clinical course and treatment of idiopathic cases. We present a case of idiopathic giant cell hepatitis in an otherwise healthy adult man and review the literature regarding treatment and outcomes in this population.

KEYWORDS: giant cell hepatitis; granulomatous hepatitis; post-infantile giant cell hepatitis; idiopathic

INTRODUCTION

Giant cell hepatitis (GCH) is a relatively common form of liver disease in neonates, but remains exceedingly rare in adults. Idiopathic cases, in particular, represent only 25%–30% of 200 reported cases.[1,2] GCH is defined by giant, multinucleated cells believed to arise from an abnormal hepatocyte response to various stimuli. Pathophysiology remains poorly understood, although a multitude of medications, viruses, autoimmune conditions, and malignancies have been implicated.[3] Prognosis ranges from spontaneous resolution to fulminant hepatic failure and death.[4] As such, identifying the underlying cause is important in preventing disease progression. To date, management of idiopathic cases remains uncertain. We report a case of idiopathic GCH in an otherwise healthy adult man and offer management considerations based on our experience in conjunction with established literature.

CASE REPORT

A previously healthy man in his mid-30s was referred to gastroenterology for evaluation of chronic epigastric pain and bloating. Physical examination was unremarkable with no notable scleral icterus or hepatosplenomegaly. Laboratory test results revealed an elevated alkaline phosphatase of 278 U/L. After lapse in care because of the coronavirus disease 2019 pandemic, laboratory test results 1 year later showed an increase in alkaline phosphatase to 976 U/L with elevated aspartate transaminase to 71 U/L and alanine aminotransferase to 57 U/L. Total bilirubin was 1.2 mg/dL. Imaging showed no biliary obstruction. Liver biopsy demonstrated granulomas with giant cells in portal and periportal areas extending to lobular areas, consistent with giant cell granulomatous hepatitis (Figure 1). Owing to extensive granulomatous involvement, fibrosis staging could not be assessed. Fungal, alpha-fetoprotein, and viral stains were negative.

A detailed review of potential medications, environmental exposures, and toxic exposures was unrevealing. Herbal supplements were notable only for ginger extract, which had recently been discontinued. He had no recent travel or occupational exposures. He previously lived on the West Coast and has lived in the Northeast for several years. Family history was unknown.

The patient was started on prednisone 10 mg. This was stopped 2 months later given the lack of response, and he was referred to hepatology for a second opinion. Extensive laboratory workup, including viral hepatitis serologies, alpha-1 antitrypsin, ceruloplasmin, autoimmune panel, angiotensin-converting enzyme, gamma globulin, urine histoplasma, Lyme, syphilis, cytomegalovirus, Epstein-Barr virus, HIV, toxoplasmosis, schistosomiasis, aspergillosis, cryptococcus, and celiac panel, was unrevealing.

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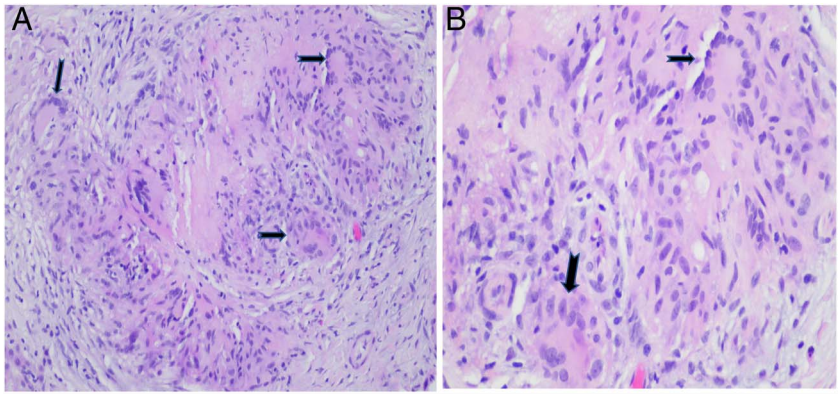

Figure 1. (A) Liver biopsy showing noncaseating epithelioid granulomas with multiple multinucleated giant cells (arrows) effacing the portal tracts and lobular areas. Mild portal and lobular inflammation are also present consisting of lymphocytes with scattered plasma cells and eosinophils. (B) A higher magnification of a granuloma showing multinucleated giant cells (arrows).

He was started on ursodiol 300 mg twice daily and had laboratory improvement at 3-month follow-up (aspartate transaminase 48 U/L, alanine aminotransferase 94 U/L, alkaline phosphatase 548 U/L, and total bilirubin 1.0 mg/dL). He remains well without symptoms of cholestasis with plans for laboratory monitoring every 3 months.

DISCUSSION

Although most cases of GCH have a known underlying etiology amenable to targeted therapeutics, idiopathic cases are poorly understood and treatment strategies remain ill-defined.[3,4] Mortality upwards of 15% have been reported in idiopathic cases because of progressive cirrhosis and liver failure.[5] Supportive care lacks consistent clinical benefit,[5,6] and effective pharmacotherapy remains overall elusive. Many of the reported cases are embedded within larger case series, making assessment of outcomes particularly challenging.[2,6,7] Immunosuppressive therapy has been used with mixed outcomes. Of 11 cases identified in the literature who received immunosuppressive therapy, only 4 (36%) showed some form of laboratory and/or clinical stability or improvement. Six (55%) progressed to cirrhosis and/or liver failure. Of the 6 requiring liver transplantation, 3 ultimately had to undergo retransplantation because of recurrent disease and liver failure.[2,6–11]

It is important to note that the majority of reported cases of idiopathic GCH is decades old. The underlying etiology may have been missed because of lack of biotechnology. Because the outcomes in idiopathic cases are poor and evidence-based treatment options are limited, it is essential to pursue an extensive workup in hopes of identifying a potential etiology that may guide treatment.

Although the literature is mixed, it is reasonable to offer steroids or other immunosuppressive therapy in cases of idiopathic GCH. Patients should be monitored for possible clinical improvement based on laboratory studies, fibrosis assessment, and clinical presentation, and therapy should be withdrawn if response is lacking. Given its benign side effect profile and common use in other granulomatous and cholestatic liver diseases, ursodiol can be considered despite limited evidence. Treatment of progressive disease remains uncertain, although evaluation for liver transplantation should be considered early once the patient has developed progression to cirrhosis and/or clinically significant portal hypertension because of the high risk of liver failure and death. In the future, targeting subtypes of immune cells found on biopsy may be of benefit.[9]

DISCLOSURES

Author contributions: M. McGoldrick reviewed the literature, wrote the manuscript, and approved the final article. C. Castrodad-Rodríguez provided the histology figures, revised the article for intellectual content, and approved the final article. Y. Huang provided the histology figures, revised the article for intellectual content, and approved the final article. C. Tow edited and revised the article for intellectual content, approved the final article, and is the article guarantor.

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