Giant-cell Hepatitis—Rare Entity in Adults

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Giant-cell hepatitis (GCH) is characterized by parenchymal inflammation with formation of large multinucleated hepatocytes in response to a variety of insults to the liver. Although it is commonly described in neonates, it rarely occurs in adults. Here we report a case of GCH because of herbal medicine intake. (J CLIN EXP HEPATOL 2016;6:244–245)

INTRODUCTION

GCH is a rare disorder seen by the presence of multinucleated cells in liver as an unusual nonspecific tissue reaction to various stimuli, including drugs, viruses, and toxins. The transformation of the adult liver into extensive giant hepatocytes together with features of hepatitis is referred to as post infantile GCH or syncytial GCH.^{1,2} The exact pathogenesis is not known. It is proposed to be due to an increase in hepatocyte nuclear proliferation without subsequent cell division or membrane fusion of the neighboring hepatocytes.² Some of the drugs that can lead to GCH include methotrexate, 6-mercaptopurine, amitriptyline, chlorthalidone, amoxicillin + clavulanic acid, doxycycline, vinyl chloride, chlorpromazine, and herbal medicines.³ This case demonstrates that GCH although rare in adults do occur as response to insult to liver by alternative medicines intake which is still common in our country.

CASE PRESENTATION

A 30-year-old male presented to the hospital with complaints of yellowish discoloration of eyes and skin, which progressively increased over the course of 3 months. It was associated with pruritus and pale stools. There was no history of prodrome, abdominal pain, gastrointestinal bleed, or vomiting. There was no history of alcohol consumption. On further questioning, he revealed that there was intake of herbal medicine for 21 days prior to the onset of jaundice for weakness and fatigue. There was no past history of jaundice. No history of past environmental or

occupational exposure to hepatotoxins. On examination, there was deep icterus with discoloration of skin. His nails appeared shiny and skin showed scratch marks. Abdominal examination revealed firm and enlarged liver; there was no ascites or splenomegaly. Rest of the systems were unremarkable.

Investigations done showed normal hemogram. Liver function test showed total bilirubin – 24 mg/dl; direct – 17.8 mg/dl; alanine transaminase – 76 U/L; aspartate transaminase – 103 U/L; alkaline phosphatase – 406 U/L; albumin – 3.5 g/dl. His prothrombin time was normal. Ultrasound of the abdomen showed an enlarged liver. Serology for viral hepatitis A, B, C, E, Epstein-Barr virus and cytomegalovirus was negative. The etiological work up for Wilson's disease, hemochromatosis, autoimmune hepatitis was negative. MRCP done was normal to rule out primary sclerosing cholangitis. Percutaneous liver biopsy showed liver architecture was preserved with lobular inflammation (lymphocytes + eosinophils) and multinucleated giant cells seen along with Kupffer cell hyperplasia suggestive of GCH. Histopathology of GCH was shown in Figures 1 and 2. Patient was told to discontinue the drug and was treated with ursodeoxycholic acid 900 mg/day along with

Figure 1 Liver architecture preserved with lobular inflammation (lymphocytes + eosinophils).

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Abbreviations: GCH: giant cell hepatitis; MRCP: magnetic resonance cholangiopancreatography; UDCA: ursodeoxycholic acid
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Figure 2 Multinucleated giant cells seen along with Kupfer cell hyperplasia, suggestive of giant cell hepatitis.

cholestyramine 4 g thrice a day for severe pruritus. He was given high caloric diet with adequate nutrition and was monitored clinically every day during hospitalization. After 2 weeks in the hospital he showed clinical improvement with marginal decrease in serum bilirubin and was discharged. He was followed up regularly up to 3 months, and there was near normalization of the liver function tests. He was better and had joined back work by this time.

DISCUSSION

GCH was first described in 1991 by Phillips¹ as syncytial giant cell hepatitis. The diagnosis of GCH often poses difficulty in adults due to its varied etiology and clinical presentation.⁴ It is characterized by a histological pattern showing multinucleated giant cells and variable inflammation and a common manifestation in pediatric liver diseases, but not so common in adults.⁵

Over 1000 medications and herbal products have been implicated as hepatotoxic. However, they may not always be considered as the etiologic agents. Patients generally consider herbal medicines to be safe and view them as natural alternatives to allopathic medications; hence cases of herbal medicine toxicity may go unrecognized. Establishing a diagnosis of herbal hepatotoxicity can be difficult without a flawless history and even when herbal-related toxicity is suspected, a definitive diagnosis is difficult to establish without proper analysis of the product or plant material.⁶

Giant cell transformation can occur in response to a variety of insults. Causes of GCH include viral hepatitis (hepatitis A, hepatitis B, non A, non B hepatitis, hepatitis C, Epstein–Barr virus), autoimmune hepatitis, and a

variety of drugs including methotrexate, vinyl chloride, chlorpromazine, and even herbal remedies.⁷ There have been reports of giant cell transformation in a setting of autoimmune hepatitis,^{8,9} but this was already ruled out in this patient. In this case, viral, metabolic, and autoimmune diseases have been excluded, so the most likely diagnosis in this patient is giant cell transformation following consumption of native herbal medication, although the contents of the medication are not known. Fraquelli et al. reported a similar case where chronic syncytial GCH occurred in a young adult female following the consumption of herbal medicines.¹⁰ The clinical course varies from spontaneous resolution to progression to cirrhosis and liver cell failure. Liver biopsy is diagnostic, which shows the characteristic giant cells. Our case improved spontaneously with conservative management. However, early diagnosis of this rare entity is vital in patients, who may progress to fulminant hepatic failure as the prognosis is poor without liver transplantation in such settings. Population needs to be made aware about the propensity of herbal supplements in causing severe liver injury, which appear to be more common than realized.

CONFLICTS OF INTEREST

The authors have none to declare.

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