IgG4-related autoimmune hepatitis with pathological characteristics of giant-cell hepatitis: A case report

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Case Report

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Abstract

Background Immunoglobulin (Ig)G4-positive plasma cells are thought to be present in some cases of autoimmune hepatitis (AIH), and giant-cell hepatitis (GCH) or synchronous giant hepatocytes are rare in some patients with AIH.

Case presentation : A 68-year-old woman was hospitalized with asthenia, poor appetite, and yellow urine for more than 20 days. accompanied by obvious abnormal liver function, elevated IgG and IgG4 levels. Liver biopsy was performed, and the pathology showed extensive proliferation of fibrous tissue, formation of pseudolobules, moderate and severe interfacial inflammation, bridging necrosis and fibrosis, edema of hepatocytes as rosette-forming cells, multinucleated hepatocytes in each portal area, extensive monocyte lymph infiltration, dense plasma cells in the portal area, and positive plasma cells stained by IgG4 (more than 10 per portal area). The pathological diagnosis was IgG4-related AIH and GCH. Methylprednisolone was administered (20 mg/day). Two weeks later, her liver function gradually improved, and the immune indexes began to decline.

Conclusion: we report a case of cirrhosis caused by AIH, which has the characteristics of IgG4 correlation and GCH in the hepatic pathology. Whether there is an inevitable relationship between them remains unclear.

Introduction

Giant-cell hepatitis (GCH) is often found in neonates and infants with severe liver disease and rarely in adults. Therefore, it is also known as post-infantile or synchronous GCH[1–3]. It is believed that viral (hepatitis A, B, and C viruses; cytomegalovirus virus; Epstein–Barr virus; human immunodeficiency virus) infections[4], drugs, autoimmune diseases (autoimmune hepatitis, AIH), and metabolic diseases may be the underlying causes[5]. Recently, chronic leukemia has also been reported as a cause. We report a rare case of cirrhosis caused by AIH associated with immunoglobulin (Ig)G4 and GCH.

Case Presentation

A 68-year-old woman was hospitalized with asthenia, poor appetite, and yellow urine for more than 20 days. There was no history of hepatitis, blood transfusion, water contact with schistosomiasis, alcohol abuse, or drugs prone to causing liver damage taken recently. The patient denied hypertension, diabetes, coronary heart disease, and other chronic histories. Physical examination revealed the following: blood pressure, 106/88 mmHg; heart rate, 71 beats/min; body temperature, 36.8 °C. The skin and sclera were slightly yellow; no liver palms and spider nevi were found. The abdomen was flat and soft, and there was no tenderness or rebound pain in the whole abdomen, no palpation under the sword under the liver rib, no palpation under the spleen rib, no percussion pain in the liver area, negative mobility dullness, and no edema in both lower limbs. A liver function test revealed the following: total bilirubin (TBIL), 65.21 μmol/L; direct bilirubin, 45.19 μmol/L; alanine aminotransferase (ALT), 441.2 U/L; aspartate

aminotransferase (AST), 466.6 U/L; alkaline phosphatase (ALP), 330.4 U/L; -glutamyl transpeptidase, 489.6 U/L; lactate dehydrogenase, 222.6 U/L; total cholesterol, 6.43 mmol/L; albumin, 31.2 g/L; globulin (38.6 g/L); and prealbumin, 102.3 mg/L. A blood routine test revealed the following: white blood cells, 3.61×10^9/L; red blood cells, 3.38×10^{12}/L; hemoglobin, 89 g/L; platelets, 75×10^9/L; neutrophil count, 1.97×10^9/L; and neutrophils, 55.4%. Antinuclear antibody (85 U/L; <10 U/L, enzyme-linked immunosorbent assay), anti-smooth muscle antibody, anti-liver/kidney microsomal antibody type 1, anti-nuclear glycoprotein antibody, anti-soluble acid nucleoprotein antibody, anti-hepatocyte cytoplasmic antigen type 1 antibody, anti-soluble liver antigen/hepatopancreatic antigen antibody, and other test results were negative, whereas the IgG, IgG4, and IgM levels were 29.4 g/L (<17.1 g/L), 2.93 g/L (<2.01 g/L), and 4.33 g/L (<4 g/L), respectively. Viral hepatitis (A–E), Epstein–Barr virus, and cytomegalovirus infections were ruled out. Computed tomography of the upper abdomen revealed cirrhosis and splenomegaly.

Liver biopsy was performed, and the pathology showed extensive proliferation of fibrous tissue, formation of pseudolobules, moderate and severe interfacial inflammation, bridging necrosis and fibrosis, edema of hepatocytes as rosette-forming cells, multinucleated hepatocytes in each portal area (Fig 1), extensive monocyte lymph infiltration, dense plasma cells in the portal area, and positive plasma cells stained by IgG4 (more than 10 per portal area) (Fig 2),. The pathological diagnosis was IgG4-related AIH and GCH.

Methylprednisolone was administered (20 mg/day). Two weeks later, her liver function gradually improved (TBIL, 45.3 μmol/L; ALT, 113 U/L; ALP, 143 U/L), and the immune indexes began to decline (IgG, 21.4 g/L; IgG4, 2.21 g/L).

Discussion

The diagnosis of AIH lacks specific biomarkers and relies on pathological abnormalities (mainly interfacial inflammation), elevated transaminase levels (such as ALT and AST), elevated IgG, and more than one positive autoantibody. According to the simple AIH scoring standard introduced in 2008[6], we can diagnose a patient with AIH based on the following criteria: 8 points, ANA+, 2 points; IgG, 2 points, typical pathological characteristics, 2 points, excluding viral hepatitis, 2 points.

IgG4-related diseases (IgG4-RDs) have strong clinical heterogeneity, which varies according to the clinical manifestations of the affected organs. In January 2012, a comprehensive standard of IgG4-RDs was published in Japan[7]. Its contents are as follows: (1) clinical manifestations of diffuse or characteristic enlargement, tumor, nodule, and hypertrophy of single or multiple organs; (2) elevation in serum IgG4 level ≥1.35 g/L; (3) histopathology, involving (i) obvious infiltration and fibrosis of lymphocytes and plasma cells and (ii) IgG4-positive infiltration of plasma cells, wherein the proportion of IgG4-positive/IgG-positive plasma cells is more than 40%, and there are more than 10 IgG4-positive plasma cells per high-power visual field. If conditions (1) + (2) + (3) are met, the diagnosis will be confirmed; if conditions (1) + (3) are met, the diagnosis will be proposed; if conditions (1) + (2) are met, the diagnosis will be suspected,

which has been widely recognized and adopted by the industry peers. The case here is in accordance with IgG4-RD diagnosis based on pathological characteristics of the liver, serum IgG4 levels, and whether there are more than 10 IgG4 plasma cells per high-power field.

Umemura et al. reported a case of IgG4-related AIH in 2007[8]. They also found that IgG4-positive plasma cells infiltrated into the liver tissue in 17 typical AIH cases, so they suggested that IgG4-related AIH exists as a branch of AIH.

IgG4-positive plasma cells can exist in AIH according to the 2019 AIH practice guidance and guidelines from the American Association for the Study of Liver Diseases, but its clinical characteristics and mechanism are still unknown[9].

GCH is believed to be associated with AIH, and the presence of GCH often indicates the severity and progression of the disease[10]. However, whether it is related to IgG4 is a very interesting phenomenon. GCH also existed in the case reported by Umemura et al. and in the other two cases of IgG4-AIH (60 AIH) reported by Umemura et al.[11].

In conclusion, we report a case of cirrhosis caused by AIH, which has the characteristics of IgG4 correlation and GCH in the hepatic pathology. Whether there is an inevitable relationship between them remains unclear.

List Of Abbreviations

AIH: autoimmune hepatitis;

GCH: giant-cell hepatitis;

TBIL: total bilirubin;

ALT: alanine aminotransferase;

AST: aspartate aminotransferase;

ALP: alkaline phosphatase;

IgG4-RDs: IgG4-related diseases;

Declarations

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Availability of data and materials

All data and materials are available from the corresponding author on reasonable request.

Authors' contributions

YW T wrote the manuscript.,XB Z performed Liver biopsy and data collection, SJ H completed liver pathological diagnosis.

Ethics approval and consent to participate

Ethics Statement is not applicable for case report according to the Medical Ethics Committee of the Third Hospital of Zhenjiang Affiliated Jiangsu University,

Written informed consent for publication of his clinical details and clinical

Informed consent was obtained from the patient for publication of this case report and accompanying images. The study was conducted in accordance with the Declaration of Helsinki.

Competing interests

The authors declare that they have no competing interests.

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Figures

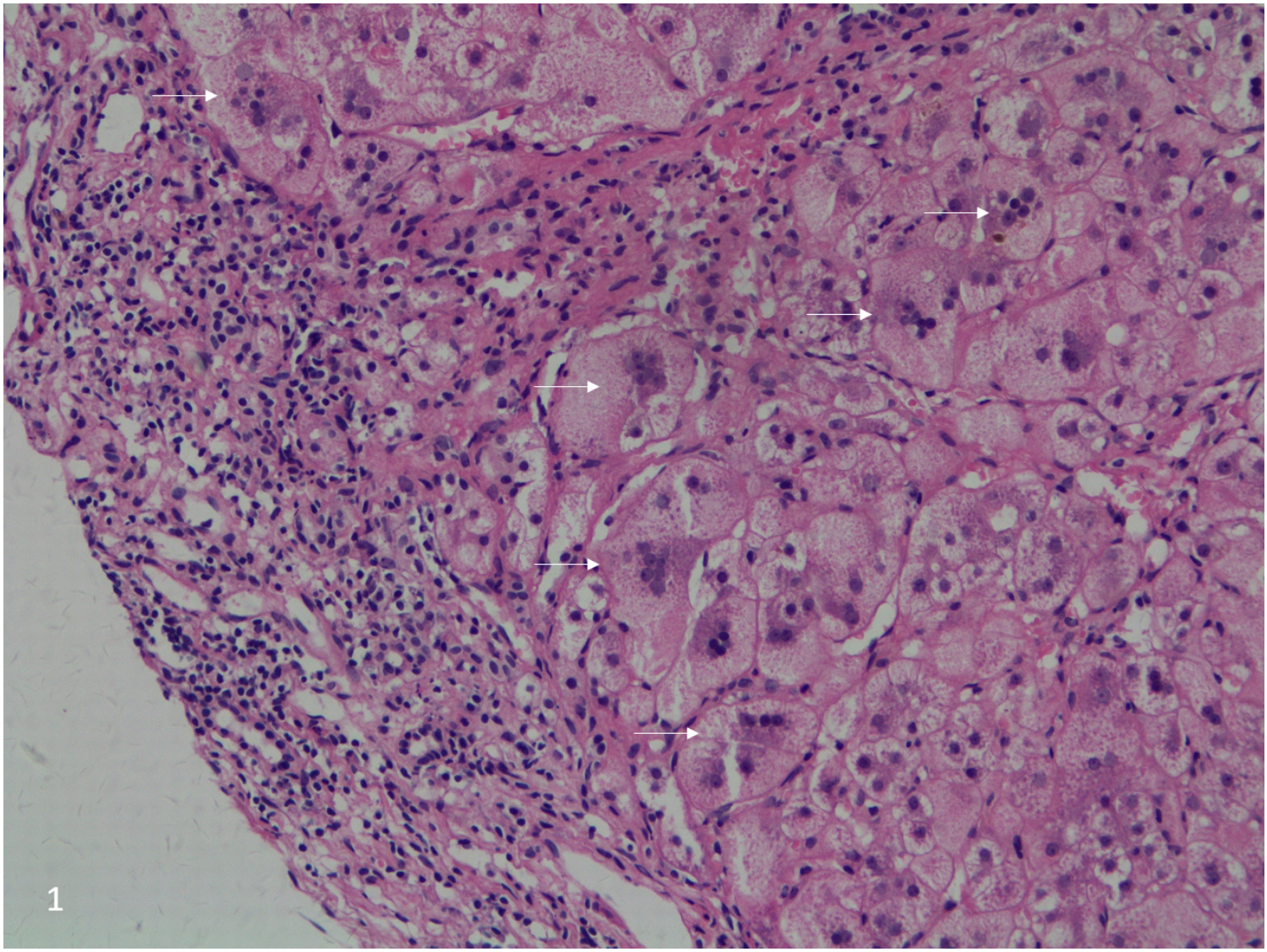

Figure 1

Giant-cell hepatitis. A large number of lymphocyte infiltration, and giant hepatocytes in lobules (Arrow).(Hematoxylin-eosin staining, 200).

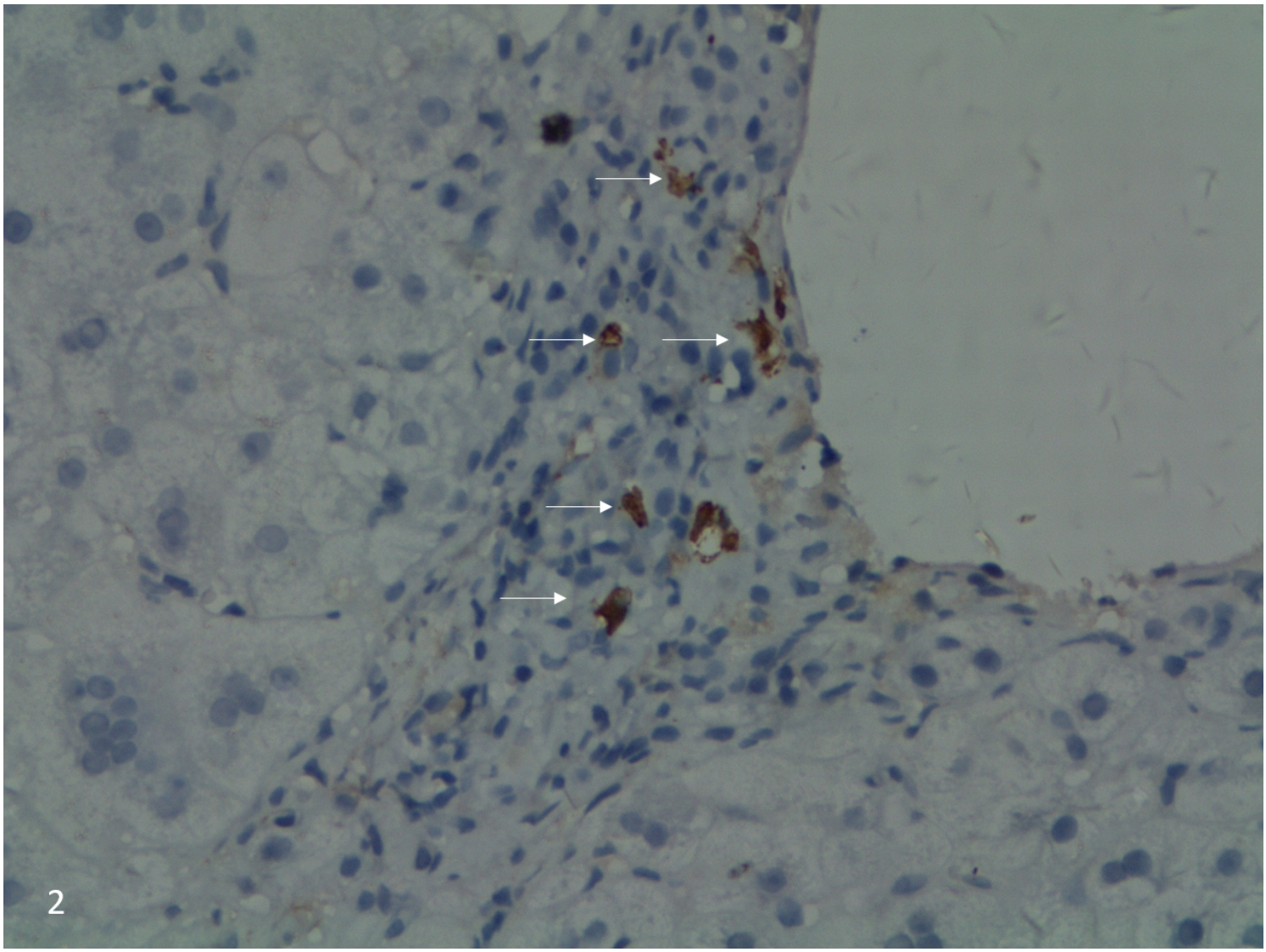

Figure 2

IgG4-positive infiltration of plasma cells (Arrow)..(IgG4 Immunohistochemistry,200)

Supplementary Files

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