Clinical and Experimental HEPATOLOGY

Clin Exp HEPATOL 2018; 4, 3: 205–209
DOI: https://doi.org/10.5114/ceh.2018.78126
Received: 03.12.2017, **Accepted:** 21.01.2018, **Published:** 05.09.2018

Case report

A good response to steroid therapy in IgG4-related sclerosing cholangitis: a case report

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Abstract

IgG4-related sclerosing cholangitis is a rare autoimmune liver disease. Biliary tract imaging, serum IgG4 concentration, and histopathological examination are the major diagnostic criteria for IgG4-related sclerosing cholangitis. In this paper, we report a male patient with yellowish skin, in whom classical liver-protection drugs were initially given, but the efficacy was poor. After that, IgG4-related sclerosing cholangitis was diagnosed, and he achieved a good response to steroid therapy.

Key words: IgG4, cholangitis, liver, steroid, relapse.

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Introduction

IgG4-related sclerosing cholangitis is a rare autoimmune liver disease, in which other organs, such as the pancreas and salivary glands, are often involved [1]. The major clinical presentations of IgG4-related sclerosing cholangitis include abdominal pain, jaundice, pruritus, and weight loss [2, 3]. The current diagnostic criteria for IgG4-related sclerosing cholangitis include serum IgG4 level, biliary tract imaging, and steroid trial as well as histopathological examination [4]. Prednisolone 40 mg/day orally can improve the liver function in IgG4-related sclerosing cholangitis [5, 6]. However, relapse after steroid withdrawal is common [7]. Other treatments include rituximab and immunomodulators [8, 9].

Herein, we report an elderly male patient with yellowish skin and sclera who was diagnosed with IgG4-related sclerosing cholangitis and achieved a complete response after oral methylprednisolone.

Case description

On July 14, 2017, a 66-year-old man was admitted to his local hospital due to jaundice and abdominal discomfort. At his local hospital, laboratory tests demonstrated that total bilirubin (TBIL) was 177.4 μmol/l (reference range: 5.1-22.2 μmol/l), direct bilirubin (DBIL) was 104.8 μmol/l (reference range: 0-8.6 μmol/l), aspartate aminotransaminase (AST) was 111 U/l (reference range: 15-40 U/l), alanine aminotransaminase (ALT) was 179 U/l (reference range: 9-50 U/l), alkaline phosphatase (ALP) was 164 U/l (reference range: 45-125 U/l), and γ-glutamyl transpeptidase (γ-GGT) was 554 U/l (reference range: 10-60 U/l). He was treated with ursodeoxycholic acid, magnesium isoglycyrrhizinate and S-adenosylmethionine. Contrast-enhanced abdominal computed tomography revealed a distal bile duct stricture. Magnetic resonance imaging showed dilatation of the upper middle segment of the common bile duct and stenosis of the lower part of the common bile

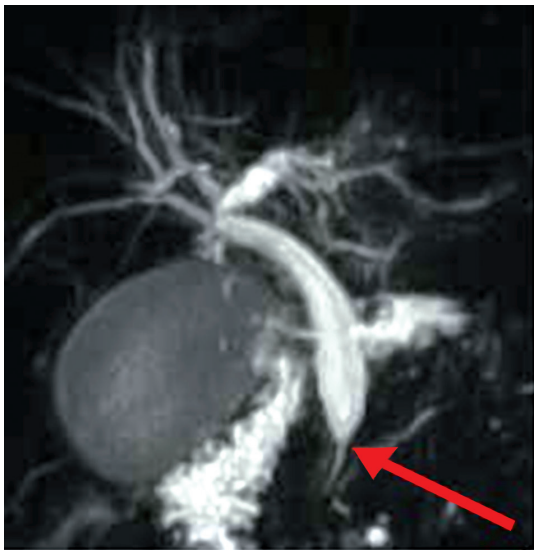

Fig. 1. Magnetic resonance cholangiopancreatography upon admission. It revealed stenosis of the lower part of the common bile duct and dilatation of the left and right intrahepatic duct and the top part of the common bile duct

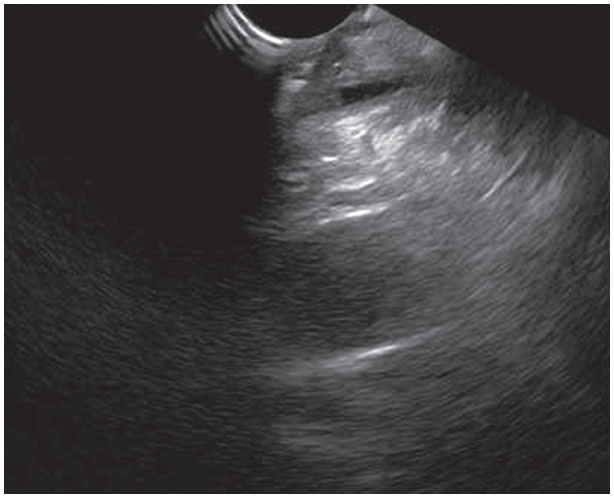

Fig. 2. Endoscopic ultrasound upon admission. It suggested stenosis in the lower part of the common bile duct and swelling of the pancreas

duct. Colonoscopy showed colonic polyps and then he underwent endoscopic resection of colonic polyps. On July 20, 2017, liver dysfunction was worsened. Laboratory tests were as follows: TBIL was 388.1 μmol/l, DBIL 231.9 μmol/l, AST was 104 U/l, ALT was 104 U/l, ALP was 242 U/l, and γ-GGT was 377 U/l.

On July 24, 2017, he was transferred to our department. He denied any history of alcohol abuse. He had a prior suspected diagnosis of autoimmune submandibular gland inflammation by ultrasound and IgG4 test (IgG4: 7.750 g/l [reference range: 0.03-2.01 g/l]) on May 2, 2017. Laboratory tests demonstrated that TBIL was 251.5 μmol/l, DBIL was 203 μmol/l, AST was 91.64 U/l, ALT was 88.48 U/l, ALP was 314.21 U/l, γ-GGT was 178.49 U/l, IgG was 23.29 g/l (reference range: 7-16 g/l), IgM was 0.46 g/l (reference range: 0.4-2.3 g/l), CA199 was 13.67 U/ml (reference range: 0-30 U/ml), and CEA was 1.75 ng/ml (reference range: 0-6 ng/ml). Serum lipase and amylase were within the reference range. Hepatitis B virus, hepatitis C virus, hepatitis A virus, hepatitis E virus, Epstein-Barr virus, antinuclear antibody, antimitochondrial antibody, and rheumatoid factors were negative. Magnetic resonance cholangiopancreatography revealed stenosis of the lower part of the common bile duct and dilatation of the left and right intrahepatic duct and the top part of the common bile duct (Figure 1). Endoscopic ultrasound suggested stenosis of the lower part of the common bile duct and swelling of the pancreas (Figure 2). The patient refused to undergo liver biopsy and histopathological examination. The patient had a probable diagnosis of IgG4-related sclerosing cholangitis according to the Japanese clinical diagnostic criteria 2012 for IgG4-related sclerosing cholangitis. From July 26, 2017, methylprednisolone 24 mg/day orally was given for 2 weeks and then was tapered by 4 mg/week for a total of 7 weeks. On August 13, 2017, laboratory tests were as follows: TBIL was 58.5 μmol/l, DBIL was 46.5 μmol/l, AST was 45 U/l, ALT was 79.79 U/l, ALP was 138.85 U/l, and γ-GGT was 185.19 U/l. Then he was discharged.

On August 30, 2017, laboratory tests demonstrated that TBIL was 27.6 μmol/l, DBIL was 41.7 μmol/l, AST was 23.9 U/l, ALT was 63.53 U/l, ALP was 107 U/l, and γ-GGT was 160.26 U/l. On September 15, 2017, laboratory tests demonstrated that TBIL was 20.4 μmol/l, DBIL was 12.0 μmol/l, AST was 29.28 U/l, ALT was 39.72 U/l, ALP was 105.93 U/l, and γ-GGT was 103.5 U/l. On September 20, 2017, methylprednisolone was stopped.

On October 16, 2017, he was admitted to our department for endoscopic resection of gastric polyps. Pathological findings revealed gastric polyps without any malignant lesion. Laboratory tests showed that TBIL was 13.0 μmol/l, DBIL was 6.0 μmol/l, AST was 26.97 U/l, ALT was 27.56 U/l, ALP was 78.39 U/l, and γ-GGT was 61.23 U/l (Figure 3).

Discussion

IgG4-related sclerosing cholangitis is often misdiagnosed as other biliary disorders, such as hilar cholangiocarcinoma, primary sclerosing cholangitis, and pancreatic cancer [10-13]. All of them often have jaundice and similar imaging features, such as a stenosis at the bile duct. However, there was some difference among them. Primary sclerosing cholangitis is char-

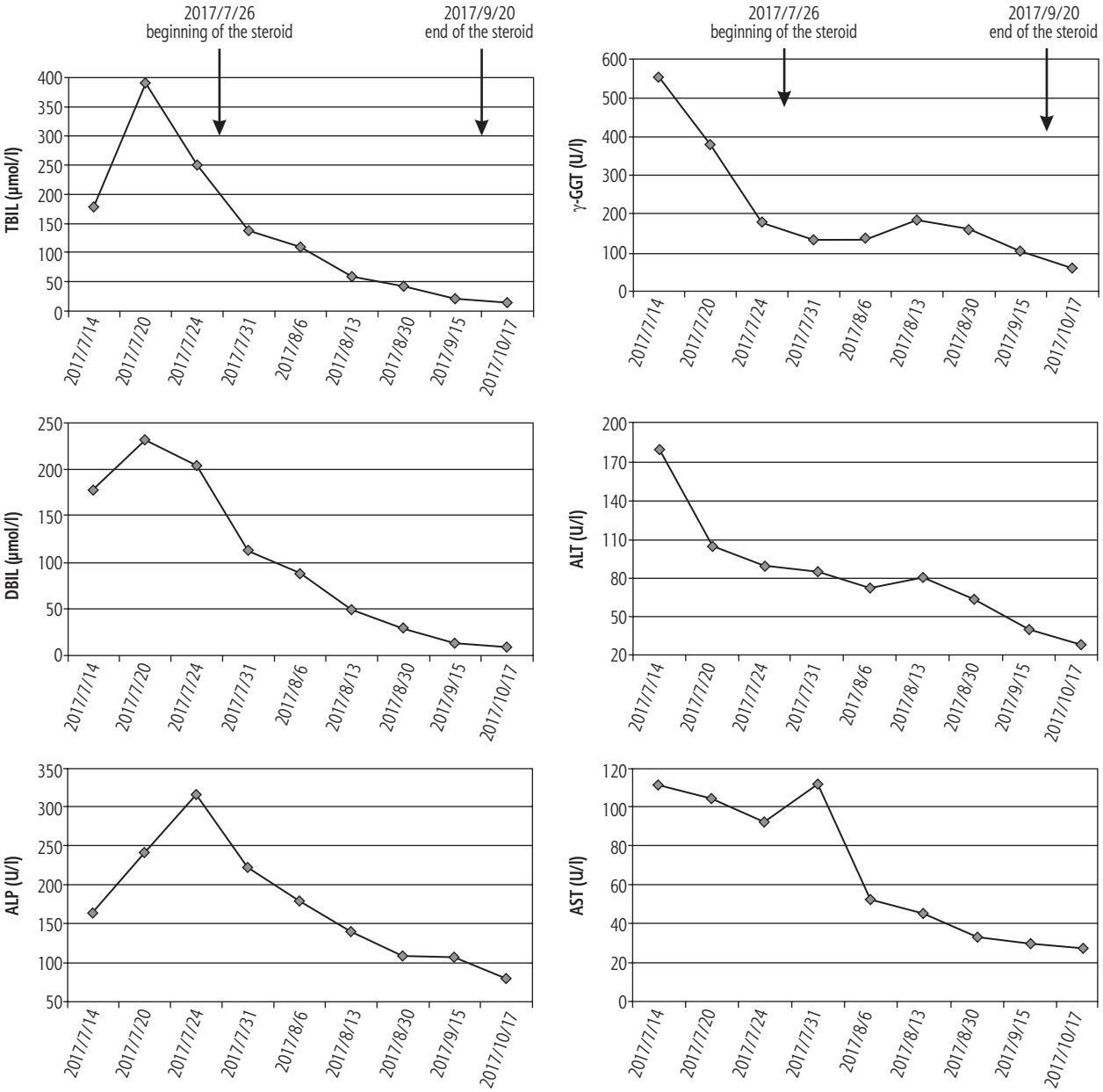

Fig. 3. Changes of total bilirubin (TBIL), direct bilirubin (DBIL), alkaline phosphatase (ALP), γ-glutamyl transpeptidase (γ-GGT), alanine aminotransaminase (ALT), and aspartate aminotransaminase (AST)

acterized by fibrosis and multifocal stenosis of the bile ducts [14-16]. Furthermore, primary sclerosing cholangitis is always associated with inflammatory bowel disease [17, 18]. The characteristics of hilar cholangiocarcinoma are hilar mass and malignant stenosis of the bile ducts [19, 20]. Elevated tumor markers, such as serum cancer antigen 19-9, may be helpful to distinguish hilar cholangiocarcinoma from IgG4-related sclerosing cholangitis [21, 22]. The imaging findings of pancreatic head cancer include a focal mass at the pancreatic head and dilatation of the main pancreatic duct [23]. Serum pancreatic enzymes and tumor markers are also useful for a diagnosis of pancreatic cancer [24]. Certainly, the histology is the golden test for a differential diagnosis.

Patients with IgG4-related sclerosing cholangitis have good responses to steroid treatment [1]. The treatment strategy of IgG4-related sclerosing cholangitis is similar to that of autoimmune pancreatitis [5]. The treatment strategy is mildly different among regions. In Japan, prednisolone 0.6 mg/kg/day orally is prescribed for 2-4 weeks and then is gradually tapered to be maintained within 2.5-5 mg/day for at least 3 years [25]. At the Mayo Clinic, the treatment strategy is that prednisone 40 mg/day orally is initially prescribed for 4 weeks and then the dose of prednisone is tapered

Table 1. Selected clinical trials on treatment with steroid for IgG4-related sclerosing cholangitis

First author	Steroid treatment	Response rate (%)	Recurrence rate (%)
Ghazale	Prednisone 40 mg/day for 4-6 weeks, taper 5 mg/week for 11 weeks	97.00	53.00
Tanaka	Prednisolone	90.00	19.00
Liu	Prednisone 40 mg/day for 4 weeks, taper 5 mg/week for 13 weeks	86.10	66.10
You	Prednisolone 0.5 mg/kg/day for 1-2 months, taper 5 mg/month	72.30	38.98

by 5 mg/week for a total of 11 weeks [26]. In the UK, the steroid treatment is that prednisolone 30 mg daily is prescribed for 2 weeks and then is tapered by 5 mg every 2 weeks for 3-4 months [27]. In China, prednisone 40 mg/day orally is prescribed for 4-6 weeks and then is tapered by 5 mg/week for 13 weeks [28]. In our case, the therapeutic strategy is that methylprednisolone 24 mg/day orally is prescribed for 2 weeks and then is tapered by 4 mg/week for 7 weeks.

We also summarized the findings of 4 clinical trials on the treatment of IgG4-related sclerosing cholangitis. The response rate with steroid was 72.3-97% [26, 28, 29], while the disease relapse rate was 19%-66.1% after steroid withdrawal [2, 26, 28, 29] (Table 1). Our patient achieved a complete response to the steroid treatment.

In conclusion, it is crucial for patients with IgG4-related sclerosing cholangitis to receive an accurate diagnosis and to initiate steroid treatment as soon as possible. Response to steroids is common. However, considering the relatively high relapse rate after steroid withdrawal, we should perform a watchful follow-up of patients with IgG4-related sclerosing cholangitis.

Disclosure

The authors report no conflict of interest.

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