

Case Report

IgG4-Related Sclerosing Cholangitis Mimicking Cholangiocarcinoma

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Keywords

Biliary dilatation · Cholangiocarcinoma · IgG4-related disease · IgG4-related sclerosing cholangitis

Abstract

IgG4-related sclerosing cholangitis (IgG4-SC) is a relatively newly identified disease that is frequently associated with autoimmune pancreatitis. The differential diagnosis between cholangiocarcinoma, primary sclerosing cholangitis, and IgG4-SC can be challenging due to significant overlap among the clinical and imaging characteristics. We report the case of a 71-year-old woman who was diagnosed with IgG4-related disease based on increased serum IgG4 levels, imaging, and clinical presentation, which showed systemic involvement, including sclerosing cholangitis and kidneys. The patient presented with chronic jaundice. Magnetic resonance imaging revealed bile duct strictures and the dilatation of upstream bile ducts, smooth wall thickening with uniform enhancement in the delayed phase, and no vascular infiltration. Multiple low-density, wedge-shaped areas were identified in both kidneys, which were hypointense on T2-weighted images and hyperintense on diffusion-weighted images. The serum IgG4 levels of this patient were elevated to nearly 10-fold the normal upper limit. A diagnosis of IgG4-SC associated with IgG4-related kidney was made. Based on this case, pre-surgery IgG4 serum treatment in patients with non-malignant bile duct stenosis was recommended to exclude IgG4-SC.

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Introduction

IgG4-related disease (IgG4-RD) is a chronic inflammatory disease associated with high serum concentrations of serum IgG4 and the marked IgG4-positive plasma cell infiltration of affected tissues. The most commonly affected organs include the pancreas, lymph nodes, and lacrimal and salivary glands [1]. The term IgG4-related sclerosing cholangitis (IgG4-SC) is used when IgG4-RD affects the bile duct. IgG4-SC is a characteristic type of sclerosing cholangitis, associated with high serum IgG4 levels and the infiltration of IgG4-positive plasma cells in the bile duct wall [2, 3]. IgG4-SC is frequently associated with autoimmune pancreatitis. IgG4-SC diagnosis is based on imaging, serological, and histopathological findings, the coexistence of other IgG4-RDs, and the response to steroid therapy [4]. The differential diagnoses for IgG4-SC include primary sclerosing cholangitis and bile duct carcinoma [5]. In this article, we describe a case of IgG4-SC that was long-misdiagnosed as cholangiocarcinoma.

Case Report

A 71-year-old woman was admitted to the hospital due to jaundice and dark urine over the previous 2 years. This patient had previously been diagnosed with cholangiocarcinoma without biopsy and was treated with biliary drainage. The symptoms were relieved after a year, and abdominal magnetic resonance imaging (MRI) was performed. Neither pancreatic nor bile duct tumors were detected.

Laboratory data revealed that total bilirubin level was 39 $\mu\text{mol/L}$, gamma-glutamyl transpeptidase was 311 UI/L, alanine aminotransferase was 34 UI/L, and alkaline phos-

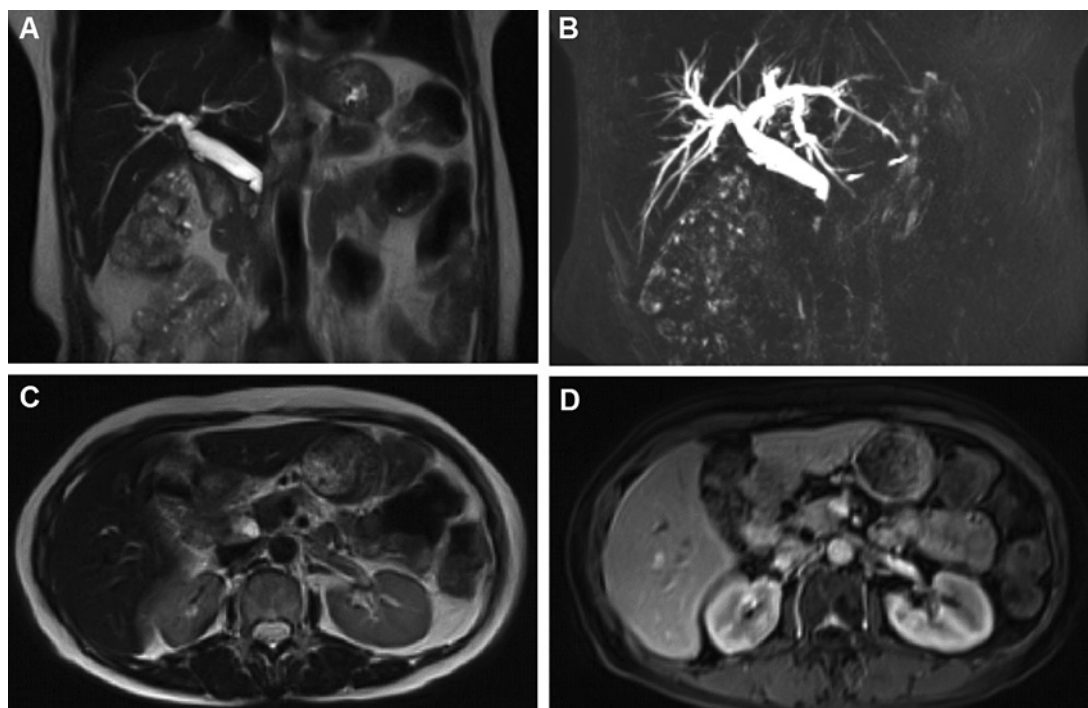


Fig. 1. Abdominal, contrast-enhanced magnetic resonance image, performed in 2018. **A** Coronal T2-weighted magnetic resonance cholangiopancreatography. **B** Axial T2-weighted image. **C** Post-contrast, fat-saturated, T1-weighted image showing the focal stricture of the distal common bile duct (**A**) and upstream dilatation. The bile duct lumen appeared smooth (**C**, **D**). The head of the pancreatic was not enlarged (**C**).

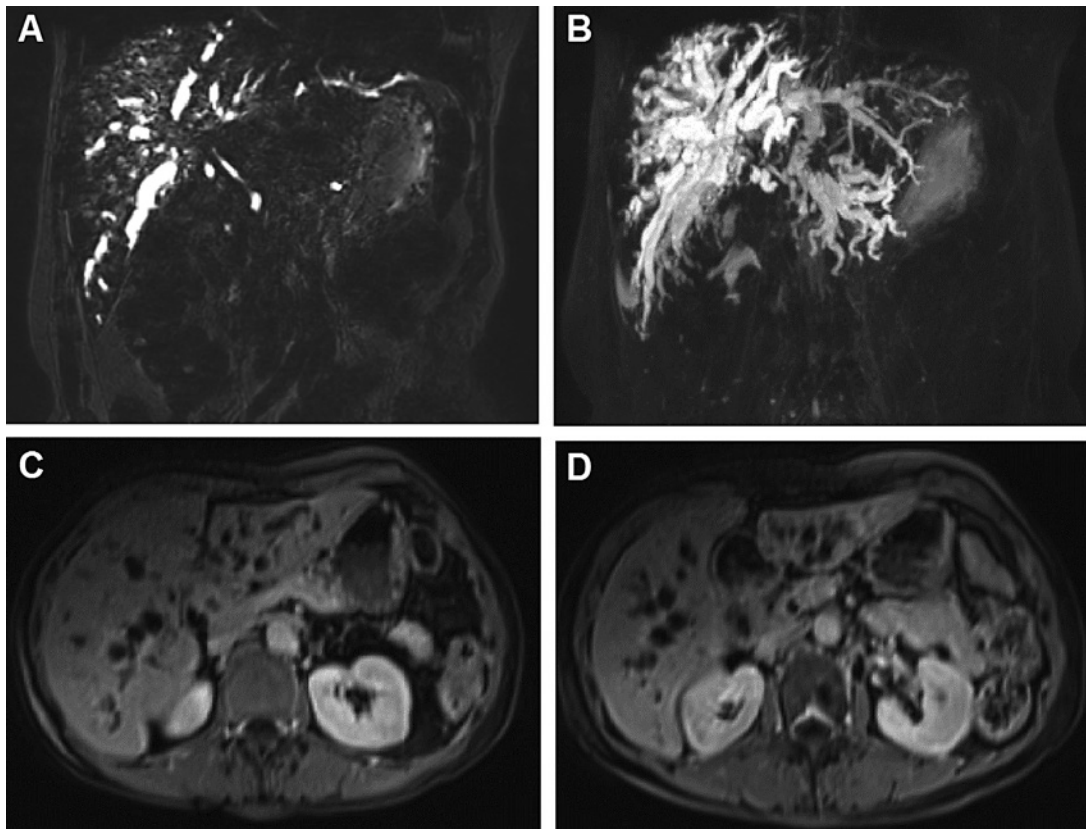


Fig. 2. Abdominal contrast-enhanced magnetic resonance imaging performed in 2019. Magnetic resonance cholangiopancreatography (**A, B**) and axial T1-weighted, fat-saturated imaging, weighted IV contrast in venous phase (**C, D**) showed multiple severe strictures of the perihilar bile duct, whereas the common bile duct was associated with upstream biliary dilatation. The bile duct wall was thickened, and the bile duct lumen appeared smooth.

phatase was 32 UI/L, and a normal renal function blood test was recorded. Anti-nuclear antibodies, anti-liver kidney microsomal antibodies, anti-Smith antibodies, and anti-neutrophil cytoplasmic antibodies were negative. The serum IgG4 level was very high, up to 7,596 mg/L (normal range: 39–864 mg/L).

Imaging Findings

MRI of the abdomen with contrast showed dilated bile ducts with stricture, and the wall of bile ducts appeared to be thickened, showing a smooth inner wall with no evidence of any masses or stones in the bile duct or the head of the pancreas (Fig. 1–3). Both kidneys showed multiple, hypointense, wedge-shaped lesions on T2-weighted images. The diffusivity of the lesions revealed restricted diffusion, and the kidneys were enhanced inhomogeneously (Fig. 4, 5). A computed tomography scan performed in 2020 after drainage showed a decrease in dilation (Fig. 6), and the lesions in both kidneys were late-enhancing, with the density levels of the pre-contrast, arterial, and venous phases recorded as 37, 66, and 90 Hounsfield, respectively (Fig. 7).

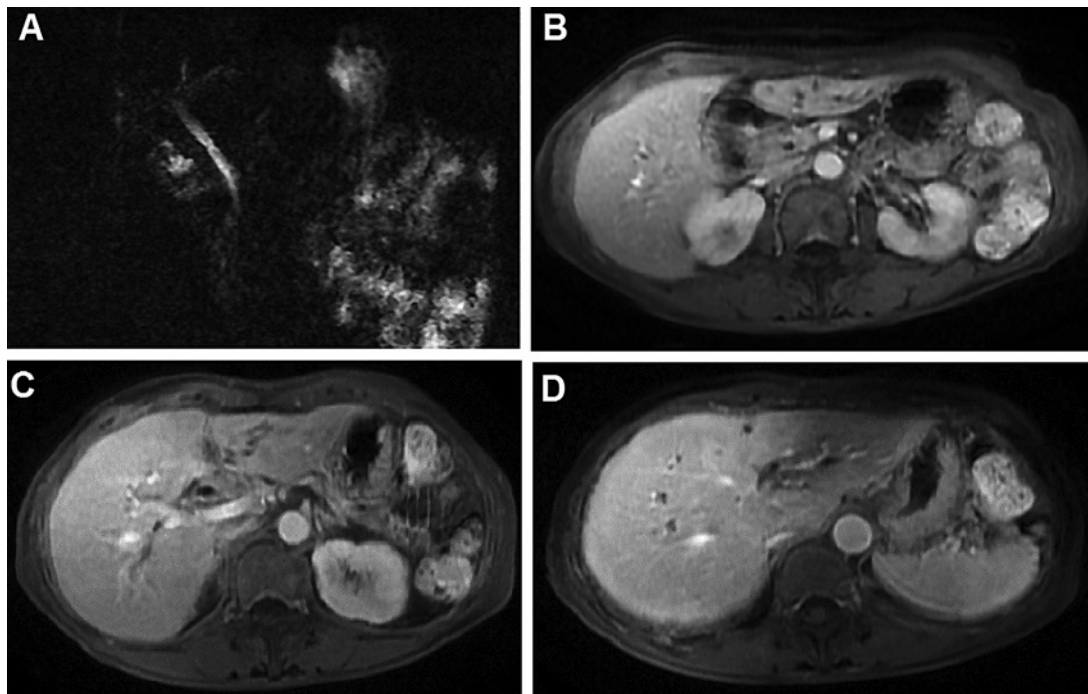


Fig. 3. Abdominal contrast-enhanced magnetic resonance imaging performed in 2020. Magnetic resonance cholangiopancreatography (**A**) and axial T1-weighted fat-saturated imaging with IV contrast in venous phase (**B–D**) showed biliary dilatation. The bile duct wall was thickened, and the bile duct lumen was smooth.

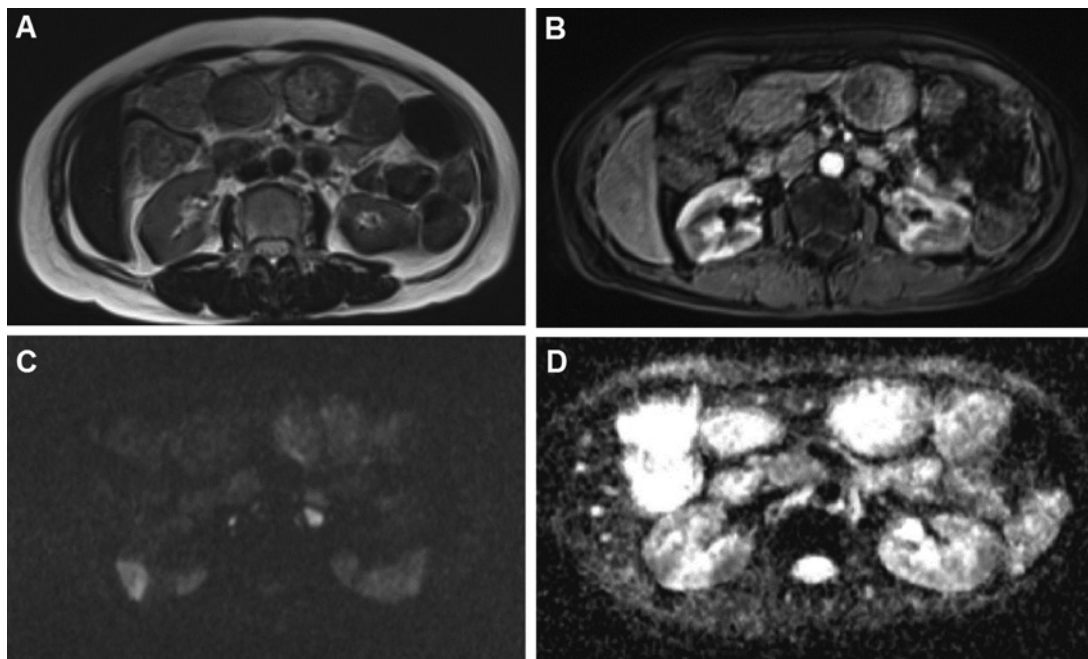


Fig. 4. Abdominal contrast-enhanced magnetic resonance imaging performed in 2018. Axial T2-weighted (**A**), diffusion-weighted (**B**), and apparent diffusion coefficient images (**C**), and axial T1-weighted, fat-saturated images with IV contrast in the arterial phase (**D**) demonstrated multiple wedge-shaped areas, which were hypointense on T2-weighted images (**A**), restricted diffusion (**B, C**), with reduced kidney enhancement (**D**).

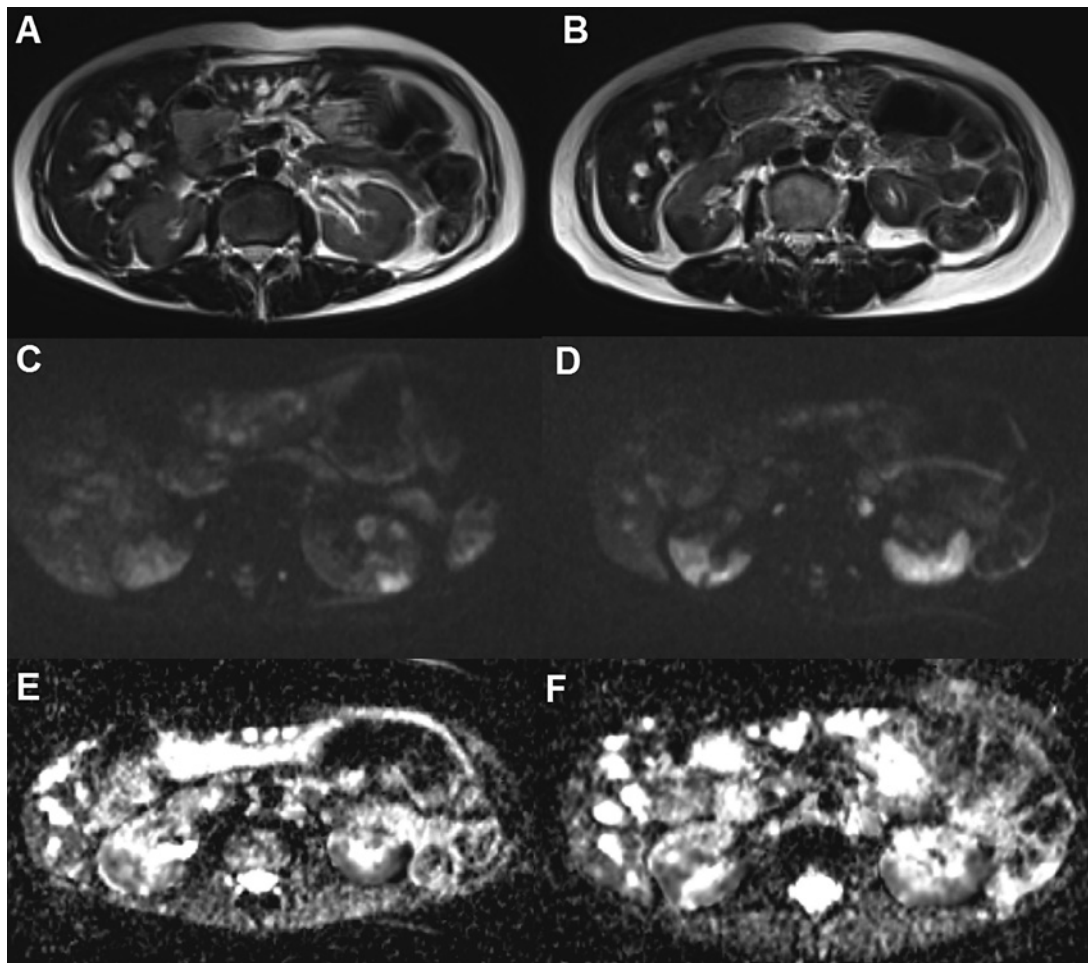


Fig. 5. Magnetic resonance imaging of the abdomen performed in 2019. Axial T2-weighted (**A, B**), diffusion-weighted (**C, D**), and apparent diffusion coefficient images (**E, F**) showed multiple wedge-shaped areas that were hypointense on T2-weighted (**A, B**) imaging, with restricted diffusion (**C–E**) and increased size compared with the imaging results from 2018.

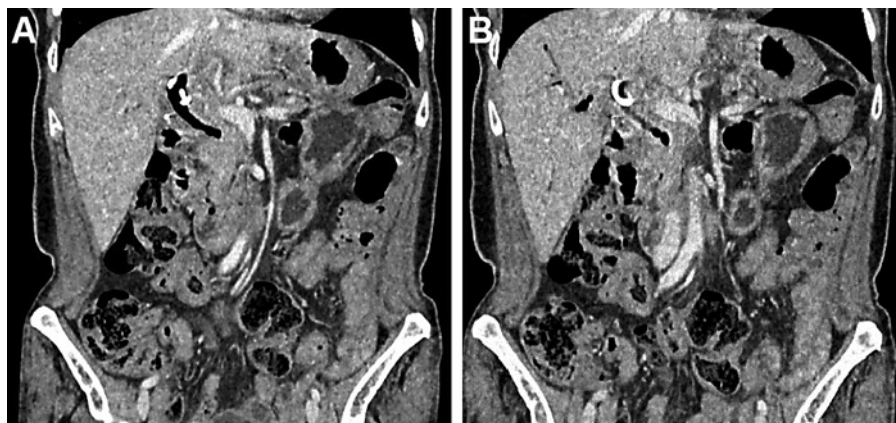


Fig. 6. Abdominal contrast-enhanced computed tomography performed in 2020. Coronal computed tomography imaging of the abdomen in the venous phase displayed a dilated bile duct, with gas and a draining tube placed within it. No mass was detected in the bile duct.



Fig. 7. Abdominal contrast-enhanced computed tomography performed in 2020. Axial computed tomography scans of the abdomen, without contrast (**A**), in the arterial phase (**B**) and venous phase (**C**), showed multiple wedge-shaped areas, with low density, hypoenhancement, and late enhancement, in both kidneys (average density of the lesion in the non-contrast phase: 37 HU, arterial phase: 66 HU, venous phase: 90 HU).

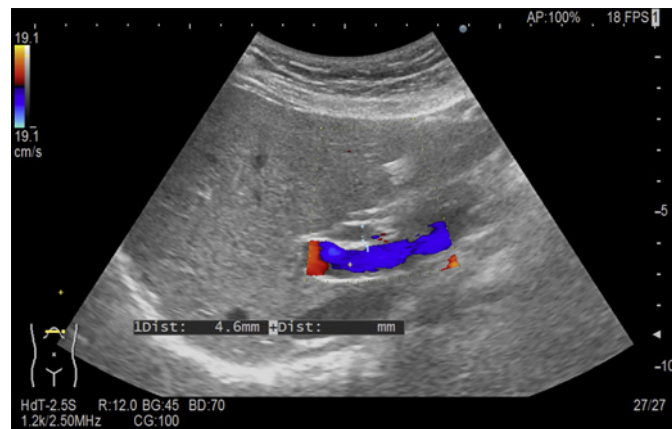


Fig. 8. Abdominal ultrasound showed non-dilated common bile ducts and intrahepatic bile ducts.

Treatment

This patient had previously been treated with drainage of the biliary system for 1 month, which relieved her symptoms. She had refused steroid therapy; however, her condition remained stable after 5 months, and no sign of obstruction was observed for either the intra- or extra-hepatic biliary ducts on ultrasound (Fig. 8). Serum IgG4 levels remained high, at 6,417 mg/L.

Discussion

IgG4-SC is a chronic inflammatory disease and tends to occur in older individuals, aged 60–70 years. The clinical presentation depends on the location, disease activity, and organs involved. Patients with IgG4-SC often present with obstructive jaundice, pruritus, cholangitis, weight loss, and abdominal pain. However, the symptoms are not specific [6, 7]. We can use the 2019 American College of Rheumatology/European League Against Rheumatism classification criteria for IgG4-RD or the HISORt (histology, pancreatic imaging, serology, organ, response to treatment) criteria, which was developed for autoimmune pancreatitis and adapted for IgG4-SC [6, 8]. Imaging findings showed the thickening of common bile duct wall,

the narrowing of the long segments and the dilation of the upstream biliary system, homogenous enhancement, with smooth inner and outer margins, and the absence of biliary masses.

Nakazawa et al. [9, 10] classified IgG4-SC into four categories:

The differential diagnosis for IgG4-SC includes cholangiocarcinoma and primary sclerosing cholangitis. The differential diagnosis between cholangiocarcinoma and IgG4-SC remains still challenging because the clinical presentations of IgG4-SC and cholangiocarcinoma can be similar. In contrast, imaging characteristics can distinguish IgG4-SC from primary sclerosing cholangitis. The presence of increased serum IgG4 levels and the involvement of extra biliary organs also suggested IgG4-SC. Glucocorticoids remain the first-line treatment to improve symptoms and restore organ functions, but patients with IgG4-SC are at high risk of relapse [3, 8, 11]. Patients who develop disease relapse after steroid therapy can be treated with immunomodulatory drugs. Because IgG4-SC is a relatively new disease, our knowledge regarding the risks of malignancy and long-term outcomes remain limited. In cases that are not treated with steroids, substantial spontaneous improvement has been reported, most often for type 1 IgG4-SC but rarely for the other types [12, 13]. Progression to cirrhosis and portal hypertension has also been described. Overall, IgG4-SC appears to have a favorable prognosis, likely due to the excellent response to corticosteroid therapy.

Some reports have described IgG4-SC cases associated with normal or only mildly elevated IgG4 serum levels that were misdiagnosed as cholangiocarcinoma, leading to an unnecessary partial hepatectomy [14, 15]. In our case, the patient was diagnosed with cholangiocarcinoma in 2018. Biliary dilation increased with time, but no mass was identified in the biliary duct. The imaging study results from 2019 displayed severe biliary duct constrictions, which appeared similar to a Klatskin tumor, but the mass was too ambiguous on MRI to perform a biopsy. Moreover, the patient refused treatment and only accepted biliary drainage for symptom relief, which was remarkably effective. The definitive diagnosis of IgG4-SC was based on increased serum IgG4 levels, imaging features, and multiple organ involvement. She refused steroid therapy; however, her condition remained stable after 5 months, and no obstructions were identified on imaging in either intra- or extra-hepatic biliary ducts. This appears to be the long-term natural course of IgG4-SC, which displays spontaneous regression without steroid therapy. However, this case requires long-term follow-up to assess disease relapse.

The primary limitations associated with this case report are the lack of tissue confirmation, and the follow-up procedure was not strict.

Conclusion

In conclusion, we presented a rare case of IgG4-SC, with a long-term natural course that was initially misdiagnosed as cholangiocarcinoma. These two entities can be difficult to differentiate, but IgG4 serum levels can be helpful. Therefore, we recommended that IgG4 serum levels should be examined whenever IgG4-SC is suspected.

Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors report no conflicts of interest.

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Author Contributions

Pham Minh Thong and Nguyen Minh Duc contributed equally to this article as co-first authors.

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