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CASE REPORT

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IgG4-related sclerosing cholangitis, a mimicker of the cholangiocarcinoma: A case report

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Abstract

An 83-year-old-male patient presented with obstructive jaundice, whose imagings were consistent with the cholangiocarcinoma of the distal common bile duct. The tumor markers were within normal limits. IgG4 level was raised; therefore, IgG4-sclerosing cholangitis was made as the provisional diagnosis. Steroid therapy was started to which he responded well.

KEYWORDS

cholangiocarcinoma, immunoglobulin G4-related disease, sclerosing cholangitis

1 | INTRODUCTION

Immunoglobulin G subclass 4 (IgG4)-related disease (IgG4-RD) is a relatively new and emerging immune-mediated disease with the prevalence of approximately 0.28–1.08 per 100,000 population.[1] Initially linked with autoimmune pancreatitis (AIP) this immune-mediated fibroinflammatory condition now virtually has been described in all organ system: biliary tree, salivary glands, periorbital tissues, kidneys, lungs, lymph nodes, meninges, aorta, breast, prostate, thyroid, pericardium, and skin.[2,3] On histopathology, affected organ/tissue presents as tumor-like lesions with dense lymphoplasmacytic infiltrates enriched with IgG4 positive plasma cells, characteristic "storiform" fibrosis, obliterative phlebitis, and increased eosinophils.[4] Serum IgG4 level is elevated but is not a specific marker of the disease.[5]

IgG4-related sclerosing cholangitis (IgG4-SC) is the most common extrapancreatic manifestation of IgG4-RD. It affects the biliary tree which usually occurs along with autoimmune pancreatitis (AIP).[3,6] Clinically, they present as obstructive jaundice, and cholangiographic findings may suggest cholangiocarcinoma or primary sclerosing cholangitis. Presence of the hypermetabolic bile duct mass goes along with the cholangiocarcinoma. Clinical course, treatment, and prognosis vary between these two, thus needs proper differentiation, though may be difficult.[7] IgG4 responds to glucocorticoid therapy, whereas cholangiocarcinoma may need surgery with or without chemotherapy.[8]

Herein, we report a case of a male patient who presented with features of obstructive jaundice mimicking cholangiocarcinoma without the features of acute pancreatitis, and responded well to the steroid therapy.

2 | CASE PRESENTATION

An 83-year-old male patient presented to the Tribhuvan University Teaching Hospital (TUTH) with complaints of yellowish discoloration of the eyes and abdominal discomfort, insidious in onset and gradually progressive for a month. He had dark-colored urine, clay-colored stool, and pruritus. He also complained of anorexia; however, there

was no significant weight loss. He did not have a fever, abdominal pain, vomiting, abdominal distension, gastrointestinal bleeding, and steatorrhea. There was no past history of jaundice. The patient was hypertensive and was under medication. He smoked 30 pack-years of cigarettes and was a chronic alcoholic. On examination, he was icteric, and the abdomen was soft and non-tender without any organomegaly. Biochemical investigations showed conjugated hyperbilirubinemia and abnormal liver function as outlined in Table 1. Hematological investigations, and serum amylase and lipase were within normal limits.

The ultrasonography (USG) of his abdomen and pelvis showed a normal scan. Contrast-enhanced computed tomography (CECT) scan of the abdomen and pelvis was then carried out which revealed a significantly narrowed lumen and mild thickening of the wall of the distal common bile duct (CBD) at the entrance of the pancreatic head with dilatation of upstream CBD and bilateral intrahepatic bile ducts (IHBDs) (Figure 1). These findings carried us to the possibility of distal cholangiocarcinoma. Therefore, the patient was further evaluated with serum levels of tumor markers, carbohydrate antigen 19–9 (CA 19–9: 8 U/mL; normal range 0–37 U/mL), the carcinoembryonic antigen (CEA: 3.91 ng/mL; range 0–5 ng/mL), and alpha fetoprotein (AFP: 5.24 ng/mL; range 10–20 ng/mL) which were within normal range. An endoscopic retrograde cholangiopancreatography (ERCP) was tried but the cannulation of the CBD failed due to a narrow lumen.

As a way out of this diagnostic riddle, the mass was suspected to be due to IgG4-SC and the serum level of IgG4 was tested which was found to be increased (more than 3.65 g/L). An oral steroid (40 mg OD) was started and the patient showed significant clinical improvement within a month, which further pointed the diagnosis toward IgG4-SC. The steroid was tapered by 5 mg every two weeks and stopped at the end of the three months. The clinical improvement of the patient was accompanied by normalization of the liver functions (Table 1), and a subsequent abdominal CT scan which showed normal CBD. The biopsy of the mass was planned during follow-up for the definitive diagnosis. However, the low financial status of the patient and his improvement with the steroid therapy curtailed its necessity. The patient was followed up for three years during which he had no symptoms of obstructive jaundice and abdominal pain. Also, abdominal CT scan and liver function tests (Table 1) that were repeated during the follow-up were normal. Therefore, the higher level of serum IgG4, rapid improvement with steroid therapy, normal level of tumor markers, and no recurrence of symptoms in the follow-up period of three years ruled-out malignancy, and the diagnosis of IgG4-SC was made.

3 | DISCUSSION

IgG4-SC has been classified into four types based on the location of the stenosis in the bile duct. Of them, type 1 (stenosis located at the distal CBD) is mostly associated with AIP and presents with features of obstructive jaundice, abdominal pain, weight loss, steatorrhea, and new-onset diabetes mellitus.[8–10] The IgG4-SC should be distinguished from primary sclerosing cholangitis (PSC), pancreatitis, and cholangiocarcinoma which have similar manifestations. In AIP, pancreatic imaging shows diffuse pancreatic enlargement and irregular narrowing of the pancreatic duct. Similarly, serum CA 19-9 and CEA levels can be used to rule out cholangiocarcinoma.[10,11] PSC is a progressive and chronic disease. It has a poor prognosis and does not respond to steroid therapy.

Autoimmune pancreatitis is the commonest systemic manifestation of the IgG4-SC. However, up to 18% of the patients can have extrapancreatic manifestations such as sialadenitis, dacryocystitis, retroperitoneal fibrosis, and involvement of lung, kidney, and aorta.[12] Very few cases of exclusive IgG4-SC in the absence of the pancreatitis have been reported.[10] The case being presented here is one of those.

An important biomarker frequently used in the diagnosis of the IgG4-RD is serum IgG4 level. The exact mechanism of increased IgG4 levels in IgG4-SC is not clear. It might directly mediate the inflammation or could be produced by anti-inflammatory cytokines.[13,14] But, the definitive diagnosis of IgG4-SC is based on the HISORt criteria (Histology, Imaging, Serology, Other organ involvement, and Response to therapy).[9,13]

The histopathological (H) analysis of the resection specimen shows three diagnostic hallmarks:

TABLE 1 Comparison of laboratory findings among the time of initial presentation, at the end of steroid therapy and after three years.

S.N.	Parameters	At the time of initial presentation	At the end of steroid therapy	After three years	Reference range
1.	Total bilirubin (mg/dL)	4.09	0.9	0.46	0.2–1.2 mg/dL
2.	Direct bilirubin (mg/dL)	2.10	0.23	0.11	0.2–0.5 mg/dL
3.	Alanine aminotransferase (U/L)	93	46	25	5–45 U/L
4.	Aspartate aminotransferase (U/L)	105	100	35	5–40 U/L
5.	Alkaline phosphatase (U/L)	534	192	130	<306 U/L

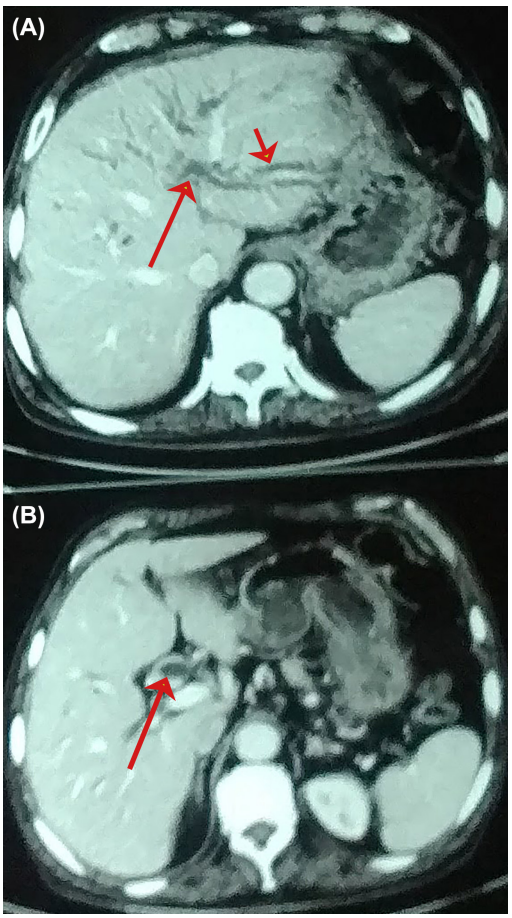

FIGURE 1 CECT of abdomen showing dilated upstream common bile duct (CBD) and bilateral intrahepatic bile ducts (IHBDs) (A), and narrowed lumen and mild thickening of the wall of distal CBD (B).

lymphoplasmacytic infiltration, obliterative phlebitis, and storiform fibrosis.[15] Cholangiogram or computed tomography (CT) scan of the abdomen (I) is used to identify the strictures at any point in the biliary tree.[9,16] Serological study (S) is positive when the levels of IgG4 in serum are elevated (>1.4 g/L). Involvement of other organs (O) and response to steroid therapy (Rt), which shows the normalization of liver enzymes or the resolution of stricture (radiologically), are the other components of HISORt criteria.[16] Either (H and Rt) or (S and I) are required for the definitive diagnosis.[17] In our case, serum IgG4 level was increased (S), CT scan showed the stricture in the distal CBD (I) and the patient responded to steroid therapy (Rt), thus confirming the diagnosis of IgG4-SC.

The treatment of choice in IgG4-SC is a steroid, which has been proven to induce quicker and consistent remission. Joshi and Webster[16] recommended starting dose of prednisolone 30–40 mg OD for four weeks and reducing by 5 mg every subsequent two weeks. However, the patient should be reviewed for biliary cholangitis/sepsis and biliary obstruction. Clinical recovery, improvement in bile duct strictures in radiological study, and normalization in liver function tests are detected within weeks of steroid therapy.[16,18] The patients need to be monitored for relapse during the steroid therapy or thereafter, which is treated with immunomodulatory drugs, in addition to the steroid.[16,19] The three-year follow-up of the patient being presented here showed remission on clinical, radiological, and biochemical grounds.

It is critical for physician to be aware of IgG4-SC without involvement of pancreas as this condition can be easily misdiagnosed. Due to its rarity and poor recognition, there have been cases where it was erroneously treated as cholangiocarcinoma with surgical resection.[10,20] Thus, IgG4-SC should also be suspected in all cases of unexplained biliary strictures to prevent unnecessary surgical interventions.

4 | CONCLUSION

IgG4-SC is a steroid-sensitive immune-mediated fibroinflammatory disorder that should be considered as one of the differentials in patients with biliary strictures. The clinical and the radiographical findings of this disease might mimic that of cholangiocarcinoma but low levels of tumor markers and high levels of serum IgG4 should prompt consideration of IgG4-SC, as this entity responds well to medical therapy thus, obviating the need for surgery.

AUTHOR CONTRIBUTIONS

Siddinath Gyawali: Conceptualization; formal analysis; visualization; writing – original draft; writing – review and editing. **Biraj Pokhrel:** Conceptualization; formal analysis; writing – original draft; writing – review and editing. **Pratik Uprety:** Supervision; writing – review and editing. **Arun Gnawali:** Supervision; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare that there is no conflict of interest regarding the publication of this paper.

DATA AVAILABILITY STATEMENT

Not applicable.

CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent will be made available for review to the editor in chief of this journal if asked.

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