

Diagnosis of autoimmune pancreatitis with intraductal biliary biopsy and treatment of stricture with serial placement of multiple biliary stents

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Autoimmune pancreatitis is increasingly recognized as a cause of pancreatitis.¹ Patients with a mass on imaging or distal common bile duct stricture often undergo surgical resection for possible malignancy, but establishing the correct diagnosis prevents unnecessary surgery, as corticosteroid treatment is highly effective.²⁻⁴ A pancreatic core or surgical biopsy is usually required to establish the diagnosis but carries the potential of serious complications.⁵ We report 2 cases in which the diagnosis of autoimmune pancreatitis was secured by intraductal biopsy of a biliary stricture. This approach to the diagnosis has not been previously reported. Both patients were successfully treated with the aid of multiple biliary stents in addition to corticosteroids.



Figure 1. Finding on ERCP showing a CBD stricture and proximal biliary dilatation.

CASE REPORT 1

A 48-year-old woman with a history of Sjögren's syndrome was admitted with acute pancreatitis. She had no history of gallstones and denied alcohol intake. An abdominal US revealed a dilated common bile duct (CBD) and no evidence of cholelithiasis or choledocholithiasis. The peak lipase level was 1029 U/L (normal range 114-285 U/L). Her liver function tests were normal, and no other metabolic derangements were evident. The patient's symptoms settled and she was discharged on day 4 after admission. After discharge, ERCP revealed a suspicious mid-CBD stricture with proximal duct dilatation (Fig. 1). A 10F 7-cm long plastic stent was placed. Abdominal CT scan and EUS did not disclose any mass or other lesion within the pancreas. Surgical opinion advocated a Whipple's resection because of the probable pancreatic neoplasm. A second ERCP was performed to further assess the stricture and obtain tissue. A 7-mm specimen was obtained by intraductal biopsy. Histological examination revealed the characteristic lymphoplasmacytic infiltrate of autoimmune pancreatitis and dense fibrosis of the duct wall (Figs. 2 and 3). Immunohistochemistry revealed extensive infiltration by immunoglobulin G subtype 4 (IgG4)-positive plasma cells (Fig. 4). Serum IgG4 was elevated (14.51 g/L [0.011-1.040 g/L]). The patient was treated with a daily 40-mg oral dose of prednisolone, which was reduced by 5 mg every fortnight for 4 months, and multiple stenting, with a maximal treatment of 3 10F stents side by side. After 5 months, a final ERCP revealed complete resolution

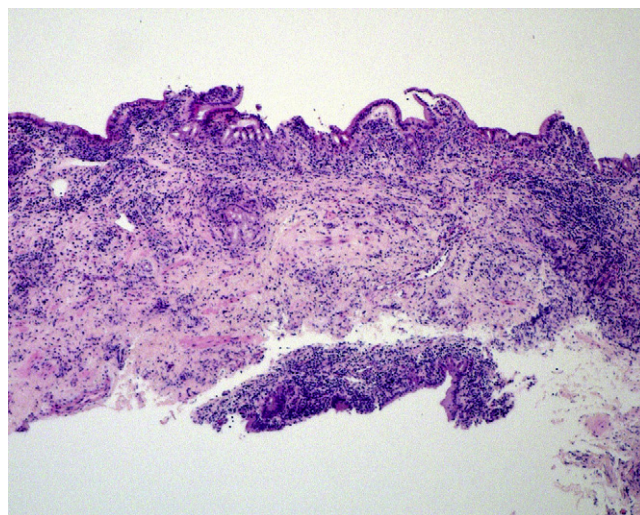


Figure 2. Microscopic appearance of the bile duct stricture biopsy specimen showing subepithelial inflammatory cells, including numerous plasma cells and lymphocytes plus fibrous thickening of the bile duct wall (H&E, orig. mag. $\times 50$).

of the stricture, and the stents were removed (Fig. 5). She has since remained asymptomatic.

CASE REPORT 2

A 78-year-old man presented to the surgical unit with a 3-month history of abdominal pain, jaundice, anorexia, and

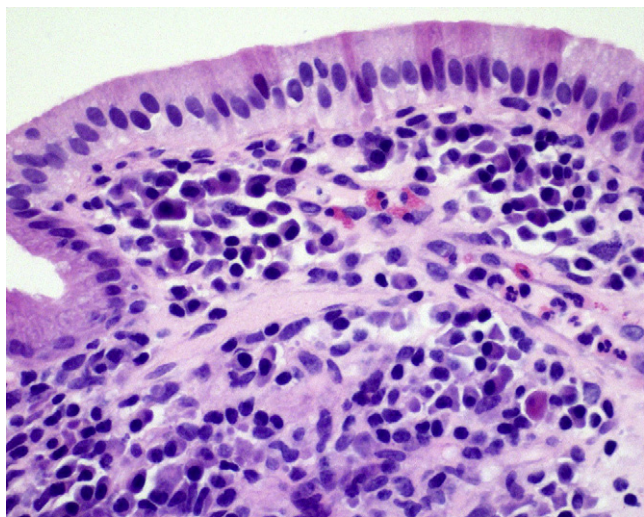


Figure 3. Microscopic appearance of the bile duct stricture biopsy specimen showing plasma cells and occasional eosinophils (H&E, orig. mag. $\times 400$).

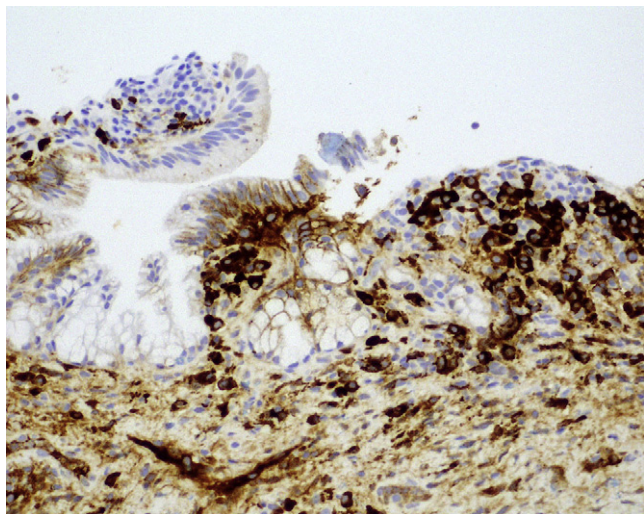


Figure 4. Immunostaining demonstrating >30 IgG4-positive plasma cells/high power field (IgG4 immunohistochemistry, orig. mag. $\times 200$).

5-kg weight loss. His liver function tests showed mixed abnormalities, including bilirubin ($79 \mu\text{mol/L}$ [$0\text{--}17 \mu\text{mol/L}$]). An abdominal CT scan revealed a dilated CBD and an enlarged uncinate process. ERCP revealed a distal biliary stricture (Figs. 6 and 7). A Whipple's resection was planned; however, after discussion of the procedure and its associated risks, the patient declined surgery. Due to his contrast allergy, the patient received 3-day courses of high-dose prednisolone before CT scanning, and over a 4-month period, the pancreatic mass reduced in size on interval CT imaging. However, the CBD stricture remained unchanged, and a repeat ERCP with intraductal biopsies was performed, which revealed extensive IgG4-positive plasma cells. Serum IgG4 at the time of biopsy was elevated at 17.6 g/L . Three



Figure 5. Finding on ERCP showing resolution of the CBD stricture.



Figure 6. Finding on ERCP showing the distal biliary stricture.

monthly multiple stentings in conjunction with a tapering dose of 40 mg oral prednisolone daily, reduced by 5 mg every fortnight, were commenced (Figs. 8 and 9). The patient remains asymptomatic.

DISCUSSION

In up to 40% of cases, patients with autoimmune pancreatitis undergo pancreatic resection either to achieve the



Figure 7. Finding on ERCP showing an attenuated main pancreatic duct.



Figure 8. Finding on ERCP showing resolution of the CBD stricture.

diagnosis or due to the mistaken diagnosis of pancreatic cancer.^{2,6} However, correct preoperative diagnosis can drastically alter the management of these patients and eliminate clinical uncertainty. EUS has become an important part of the diagnostic algorithm and combined with FNA can help establish the diagnosis of autoimmune pancreatitis.⁷ However cytopathologic assessment of EUS-FNA aspirated material is limited by the lack of tissue architecture preservation.⁸ In a series of 14 patients in whom 12 underwent EUS-FNA, 9 specimens showed evidence of lymphocytes, plasma cells, and fibrosis; however, 10 of these patients still underwent surgery.⁷ Although it is a technique that is currently not widely practiced, obtaining EUS Tru-cut specimens with 19-gauge caliber needles enables acquisition of core samples with preserved tissue architecture. In a series of 14 patients with proven autoimmune pancreatitis, EUS Tru-cut specimens were shown to be either diagnostic or strongly suggestive of autoimmune pancreatitis in 12 patients. However, the larger needle is more difficult to use and has an uncertain safety profile.⁸

While the involvement of the pancreas in autoimmune pancreatitis may be patchy, the inflammatory process often involves the intrapancreatic portion of the CBD.^{9,10} In up to 94% of cases, it also leads to marked bile duct thickening and narrowing due to diffuse lymphoplasmacytic infiltration and fibrosis.¹¹ Therefore, an intraductal biopsy may provide an efficient, safe, sufficient, and easily obtainable

sample for histology and immunohistochemistry in those who present with a biliary stricture or cholangiographic abnormality. The presence of numerous IgG4-positive plasma cells confirms the diagnosis of autoimmune pancreatitis.¹²

Biliary strictures in autoimmune pancreatitis may not respond to steroid therapy alone in up to 50% of cases.¹¹ Based on these cases and on the experience from refractory biliary strictures associated with other benign conditions, the strictures associated with autoimmune pancreatitis should be considered for treatment with serial placement of multiple side-by-side stents.¹³⁻¹⁶ However, before a general recommendation on side-by-side stenting for biliary strictures in autoimmune pancreatitis can be made, further prospective randomized studies with substantial patient numbers are required.

In conclusion, intraductal biliary stricture biopsy should be considered in patients with suspected autoimmune pancreatitis and biliary strictures. The finding of the characteristic histological changes with IgG4-positive plasma cells confirms the diagnosis and eliminates the need for more invasive diagnostic procedures. A similar strategy of intraductal biopsy in patients who do not have biliary involvement may be applicable with distal pancreatic strictures.

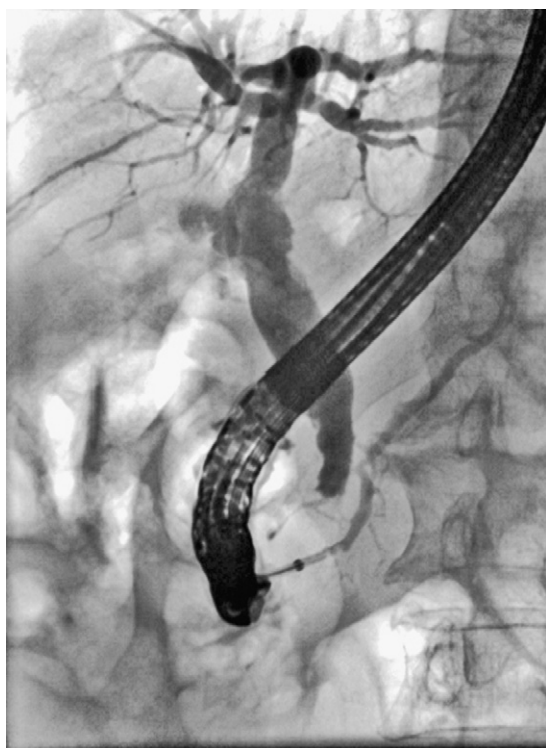


Figure 9. Finding on ERCP showing normalization of the pancreatic duct.

DISCLOSURE

The authors report that there are no disclosures relevant to this publication.

Abbreviations: CBD, common bile duct; IgG4, immunoglobulin G subtype 4.

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