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SHORT REPORT

IgG4-associated ampullitis and cholangiopathy in Crohn's disease

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Abstract

Inflammatory bowel disease (IBD) is reported to be associated with autoimmune pancreatitis and IgG4-related sclerosing disease. We report a case of a 28 year old African American male with a long history of upper gastrointestinal tract Crohn's disease (CD) with multiple surgeries who developed medically refractory disease with small bowel obstruction. He had abnormal liver function tests with imaging evidence of chronic pancreatitis and ampullary inflammatory process. He underwent Whipple's procedure. Histopathological evaluation of surgical specimens of the ampulla and distal common bile duct showed accumulation of IgG4-positive plasma cells in the lamina propria. Preoperative endoscopic biopsies also showed chronic active enteritis involving the duodenum and jejunum with increased IgG4-expressing plasma cell infiltration. His serum IgG4 was 164 mg/dL. The association of IgG4-expressing plasma cell accumulation in the gastrointestinal tract with IBD in patients with hepatobiliary manifestation may have pathogenetic, diagnostic and therapeutic implications.

Abbreviations: AID, autoimmune disorders; AIP, autoimmune pancreatitis; CD, Crohn's disease; CBD, the common bile duct; CARP, chronic antibiotic refractory pouchitis; HPF, high-power field; IBD, inflammatory bowel disease; IAC, IgG4 associated cholangitis; IPAA, ileal pouch-anal anastomosis; MRCP, magnetic resonance cholangiopancreatography; PSC, primary sclerosing cholangitis; TNF, tumor-necrosis factor; UC, ulcerative colitis.

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1. Introduction

Elevation of serum IgG4 is considered to be one of the hallmarks for autoimmune pancreatitis (AIP). At tissue level, pancreas along with other involved organs have characteristic infiltration with abundant IgG4-positive plasma cells.,[1–3] AIP may represent a spectrum of autoimmune disorders (AID), which may also involve extrapancreatic organs, including the bile duct, gallbladder, salivary glands, retroperitoneum, lymph node, pleura, lung, kidney, duodenum, and colon. The cluster of disease process has been termed as IgG4-related sclerosing disease.[4–6] Periarteritis and interstitial lung disease due to infiltrating IgG4-positive plasma cells in the absence of AIP have been described recently.[7,8] Gastrointestinal (GI) tract involvement in AIP may show IgG4-positive plasma cells in endoscopically normal-appearing mucosa.[9]

Association between IBD and AIP has been studied recently. In a study of 71 patients with AIP, of which 3 had concurrent ulcerative colitis (UC) and 1 had Crohn's disease (CD), immunostaining of biopsy of colon specimen from one UC patient revealed greater than 10 IgG4-positive cells per high power field (hpf), consistent with the diagnostic criteria of IgG4-related sclerosing disease[3] IgG4 may play a role in the disease process of IBD in patients with or without a history of pancreatic disease. Similarly, we had recently reported a case in which a young patient with chronic antibiotic refractory pouchitis (CARP) and multiple AID who had the histologic feature of IgG4-positive plasma cell infiltration of greater than 10 cells/hpf in pouch biopsy.[10] His colectomy specimen before ileal pouch anal anastomosis (IPAA) surgery did not reveal infiltration of IgG4-expressing plasma cells. A study presented as an abstract form in which IgG4 was used as a marker to differentiate UC from CD, UC patients had more IgG4-positive plasma cell accumulation than that in CD or microscopic colitis.[11] To our knowledge, the role of IgG4 in CD with hepatopancreatobiliary involvement has not been reported. We report here a case of a 28 year old male with history of upper gastrointestinal CD involving the stomach, duodenum and jejunum who had underwent gastrojejunostomy for duodenal strictures. Following surgery, he developed recurrent anastomotic strictures at gastrojejunostomy site requiring repeat endoscopic dilatations and anti-tumor necrosis factor (TNF) therapy. Biopsy at the duodenum and gastrojejunostomy site showed infiltration of IgG4-expressing plasma cells. He also developed abnormal liver function tests and imaging evidence of chronic pancreatitis because of involvement of the ampulla by CD. He underwent Whipple's surgery and surgical specimen showed evidence of IgG4 accumulation at the ampulla and the common bile duct (CBD). The distal stomach and duodenum showed evidence of active CD with non-caseating granulomas.

2. Case report

A 28-year-old African American male who was initially diagnosed with CD at age 17 presented to our IBD center with worsening epigastric pain, nausea and vomiting. His initial presentation was abdominal pain, nausea and vomiting and investigations then confirmed the diagnosis of CD of upper GI (stomach, duodenum, and proximal jejunum) with granulomas on biopsy specimens. He failed to respond to corticosteroid and 6-mercaptopurine therapy and required a gastro-duodenostomy at Department of Colorectal Surgery (distal duodenum-posterior wall of the stomach) for fibrostenotic CD. Subsequently he was started on infliximab. However he lost response and required a second surgery with proximal jejunal resection (~30 cm) 45 cm from the duodenojejunal flexure with an end–end anastomosis for recurrent stricturing disease at age 20. Three years after, he developed a recurrent stricture at the gastrojejunostomy site and required stricturoplasty at Department of Colorectal Surgery. At age 26, he again had a recurrent stricture at the gastro-jejunostomy site. The anastomosis was resected and a new gastrojejunostomy performed. Since the surgery, the patient had been on adalilumab subcutaneously once every 2 weeks and also had required multiple dilations of the anastomotic stricture and needle–knife therapy. In the interim, colonoscopies, CT enterography, and histologic evaluation showed no evidence of CD at the ileum and colon. Past surgical history also included a complicated cholecystectomy for 'gallstone attacks' with bile leaks and abscess.

The patient presented with worsening epigastric abdominal pain, nausea and vomiting. Physical examination demonstrated mild diffuse abdominal tenderness with involuntary guarding in the epigastric region. A complete blood count and basic metabolic panel showed mild anemia. His liver function tests showed a total bilirubin 0.3 mg/dL, alkaline phosphatase 470 U/L, aspartate aminotransferase (AST) of 193 IU/L and alanine aminotransferase (ALT) of 142 IU/L, total protein of 6.7 g/dL, and serum albumin 3.8 g/dL. His serum lipase was 152 mg/dl. His serum IgG4 was also elevated at 164 mg/dl (normal<112 mg/dl). Computed tomography (CT) enterography revealed mural thickening and wall enhancement of the proximal jejunum and post-surgical changes from previous gastrojejunostomy and jejunojejunal anastomosis. There was also a 2.5-cm anastomotic stricture at the gastrojejunostomy (Fig. 1). Both ultrasound and magnetic resonance cholangiopancreatography (MRCP) showed mild intrahepatic biliary dilation with segmental beading in the peripheral ducts, evidence of cholecystectomy, and a dilated CBD up to 1 cm, and distal biliary stricture. Multiple attempts were made and failed to get an access to the distal CBD with endoscopic retrograde cholangiopancreatography (ERCP) due to complex surgical anatomy. MRCP showed a normally enhanced pancreas with dilation of the main pancreatic duct up to 5 mm and dilation of multiple side branches. The comment was that there may be an ampullary stricture given the dilation of the CBD and pancreatic duct. Primary sclerosing cholangitis (PSC) was listed as a differential diagnosis (Fig. 2).

Percutaneous transhepatic cholangiogram and liver biopsy were performed for persistent abnormal LFTs and distal CBD stricture. Cholangiogram confirmed the smooth stricture of the distal CBD with proximal dilation. The liver biopsy revealed normal hepatic parenchyma with no histologic evidence of PSC and IgG4 immunostaining was negative. An upper endoscopy again showed strictured gastrojejunostomy (Fig. 3). The biopsies from the duodenum and strictured gastrojejunostomy site where there was a focal stricture showed focal active enteritis with ulceration and pyloric gland metaplasia (Fig. 4) and diffuse infiltration of IgG4-expressing plasma cells (Fig. 5). Given his presentation with complex CD, ampullary stricture and CBD dilation and stricturing gastrojejunostomy, the case