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Case report

Sclerosing pancreatitis presenting as a periampullary tumour

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Background

Sclerosing lesions of the pancreatic duct are rare and may be secondary to primary sclerosing cholangitis (PSC) or the result of a primary sclerosing process (the recently described lymphoplasmacystic sclerosing pancreatitis, LSP). Occasionally this process may present as a mass lesion.

Case outline

A 21-year-old man presented with abdominal pain and jaundice, giving a high index of suspicion for a periampullary malignancy. There were minimal symptoms suggestive of PSC. The resected head of the pancreas demonstrated changes of chronic pancreatitis with a fibro-inflammatory process of the pancreatic duct suggesting an underlying ductal sclerosing process.

Discussion

Clinical presentation and imaging characteristics of PSC involving the pancreas are often misleading and may suggest a neoplasm as the underlying disorder. Conclusive diagnosis is usually not determined until after surgical intervention. Although racial differences in pancreatic duct involvement have been suggested, the underlying histopathology is the same as in PSC involving the biliary ducts.

Keywords

primary sclerosing cholangitis, pancreatic duct, periampullary pseudomalignancy, sclerosing pancreatitis

Introduction

Primary sclerosing cholangitis (PSC) is an autoimmune disease associated with inflammatory bowel disease, specifically ulcerative colitis [1, 2]. It typically affects a middle-aged man with a history of ulcerative colitis. Median age of onset is 40 years, and there is a 2:1 male-to-female preponderance [3]. It has been estimated that approximately 70% of PSC patients have inflammatory bowel disease but, conversely, only 5% of ulcerative colitis patients manifest PSC. Classical laboratory findings include an extremely elevated alkaline phosphatase and a positive anti-nuclear antibody [3]. Diagnosis is often made with endoscopic retrograde cholangiopancreatography (ERCP), which characteristically shows multiple strictures of the biliary tree. Liver biopsy, demonstrating the characteristic periductal onion-skinning fibrosis, confirms the diagnosis.

PSC is associated with multiple complications, including intrahepatic and/or extrahepatic bile duct destruction, cholangiocarcinoma (estimates range from 4% to 20%), and rarely chronic pancreatitis [1, 2]. Recent studies suggest that ursodeoxycholic acid at high doses may benefit patients with PSC and preliminary data from short-term randomised control trials have shown improvements in both cholangiographic appearances and biochemical parameters for PSC in patients. Unfortunately, long-term improvement and survival have yet to be realised [4, 5] and presently, without proven effective medical treatment for the disease, the natural history is progression to cirrhosis and end-stage liver disease. Transplantation is the only effective therapeutic option for these patients [3].

Recently a new entity, lymphoplasmacytic pancreatitis (LSP), has been described in the literature. It involves a diffuse lymphoplasmacytic infiltration, interstitial fibrosis, periductal inflammation and periphlebitis in the pancreas. It too masquerades as a neoplastic process and is usually diagnosed after surgical extirpation [6].

In this report we describe an unusual case of a

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sclerosing pancreatic lesion that may be the initial presentation of primary sclerosing cholangitis associated with inflammatory bowel disease.

Case report

A 21-year-old male university student from Syria presented with post-prandial epigastric pain associated with nausea and vomiting. Initial treatment with an H_2 blocker and proton pump inhibitor had no effect. There was no history of jaundice, pancreatitis, parasitic infection or trauma. His medical history included occasional eruptions of oral lesions from herpes simplex-2 virus infection. He had had no previous operations, nor did he smoke or drink alcohol.

Oesophogastroduodenoscopy was normal. At follow-up 3 months later, the patient was noted to have scleral icterus and a liver biochemical profile revealing a total bilirubin of 154 μmol/L, an alkaline phosphatase of 871 IU/L and an AST of 385 IU/L. An abdominal ultrasound scan revealed a large irregular mass in the head of pancreas with resultant dilatation of the extrahepatic/intrahepatic biliary tree. Computed tomography (CT) of the abdomen failed to show any irregularity in the head of pancreas or dilatation of the pancreatic duct, but did reveal intrahepatic biliary tree dilatation and an abrupt cut-off of the distal common bile duct. A subsequent endoscopic retrograde cholangiopancreaticogram (ERCP) demonstrated similar findings (Figure 1). The pancreatic duct could not be cannulated during ERCP, suggesting possible stricturing or stenosis. During that procedure a stent was placed, but it failed to relieve the jaundice. Therefore, a percutaneous transhepatic cholangiogram (PTC) drain was inserted and adequate decompression of the biliary tree was achieved. Again, a distal bile duct stricture was visualised. The patient's jaundice improved, but his pain, vomiting and weight loss (6.5 kg since onset of symptoms) persisted.

Nine days later the patient was transferred to our facility for re-evaluation. A trans-abdominal ultrasound scan showed a normal textured pancreas with no focal mass or adenopathy and a pancreatic duct with normal calibre. The biliary tree was mildly dilated with the indwelling PTC drain in place. A magnetic resonance cholangiopancreatography (MRCP) and abdominal CT revealed normal pancreatic and peripancreatic tissue and failed to clarify presence of a stricture. Although not

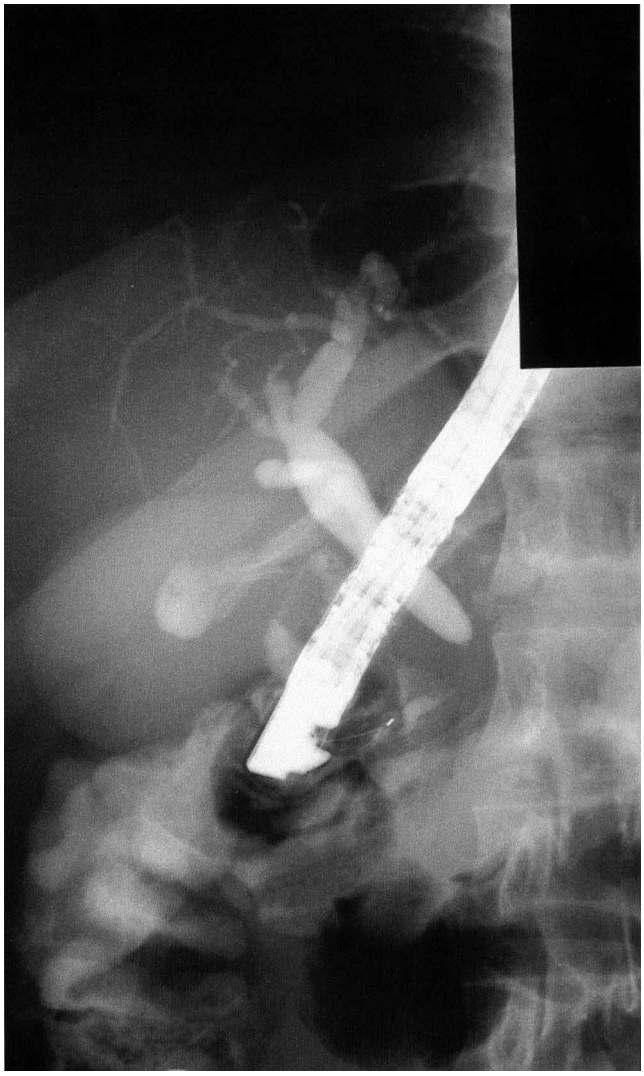

Figure 1. *Endoscopic retrograde cholangiopancreatography showing cannulation and contrast injection into the biliary tree. Note the dilated common bile duct and distal stricture in the head of the pancreas.*

diagnostic of inflammatory bowel disease (IBD), colonoscopy with mucosal biopsy revealed focal active inflammation with only minimal architectural changes and suggested an IBD. Endoscopic ultrasound revealed a mass in the head of pancreas. Given that the mass was suspicious for a neoplasm, pancreatoduodenectomy was advised.

At laparotomy, the entire pancreas was very firm with distinct fullness appreciated in the head. The superior mesenteric vessels were spared, and the mass otherwise met criteria for resectability. A classical Whipple's resection was performed. The patient had an unremarkable postoperative course with the exception of chronic

opioid-dependent pain. He was discharged home on day 21.

Histopathological examination revealed chronic pancreatitis with parenchymal fibrosis and extinction of acinar cells. The islet cells were preserved. The large pancreatic ducts were surrounded by fibrous tissue with a regional lymphoplasmacytic infiltrate and there was proliferation of small pancreatic ducts (Figure 2). The intrapancreatic bile duct showed similar histological changes, but the extrapancreatic bile ducts did not demonstrate fibrotic thickening. Despite the absence of classic 'onion skin' fibrosis and mucosal flattening, the appearance of the large ducts was similar to that seen in the biliary ducts of primary biliary cirrhosis. Unlike chronic pancreatitis, the inflammation was focused on ductal structures and not the pancreatic parenchyma. The gallbladder showed acute and chronic cholecystitis, but did not show fibrotic thickening of the cystic duct.

The histological findings, in conjunction with the abnormal colonic biopsy suggestive of IBD, suggested the possibility of underlying PSC. We were unable to confirm the diagnosis of PSC by liver biopsy or autoimmune serology as the diagnosis of PSC was not suspected preoperatively, and the patient was lost to follow-up.

Discussion

PSC is considered to be an immune-mediated phenomenon with polygenic inheritance. Evidence to support this hypothesis includes the recognition of polymorphisms of the genes associated with immunity (particularly the MHC complex) [7], the association of the disease with certain HLA haplotypes, the presence of autoantibodies, and an increase in total serum immunoglobulins. Additional aetiological factors are suggested by the infrequency of the disease in women, as well as its unresponsiveness to immunosuppression [8]. A genetic predisposition with subsequent exposure to toxic or infectious agents has been proposed to be the aetiopathogenic basis of the disease [8].

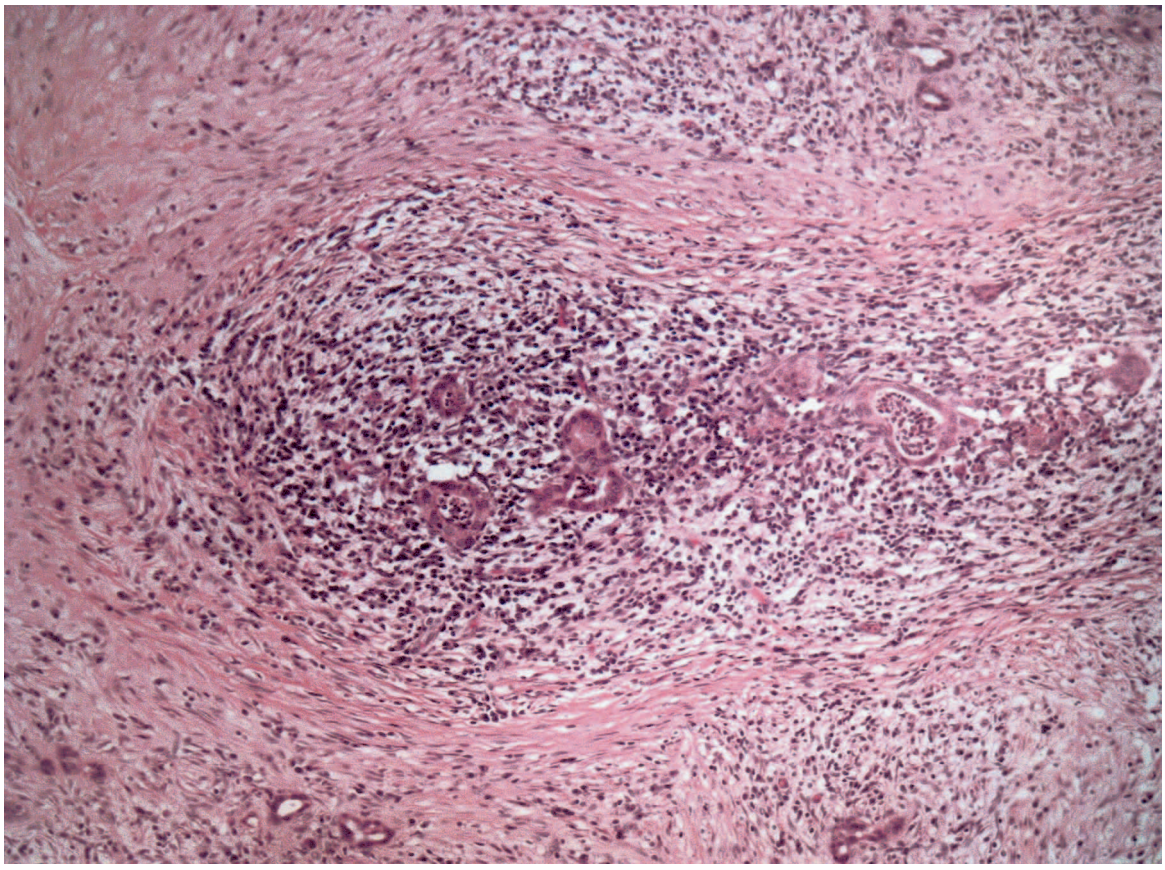

Figure 2. *Histology demonstrating sclerosing lesion of pancreatic duct (H&E, ×100). A dense lymphoplasmacytic infiltrate surrounds the pancreatic duct. There is disruption of the normal ductal epithelium and a ring of concentric fibrosis around the inflamed duct. Focal collections of neutrophils are also seen.*

Case reports of the pancreatic manifestations of PSC have been described over the past decade. Kawaguchi and associates [9] described two patients with clinical presentations of a periampullary malignancy who were ultimately found to have PSC involving the pancreatic duct. Similar to the present case, their pathological assessment included: 1) diffuse lymphoplasmacytic infiltration with lymphoid follicles and marked interstitial fibrosis and acinar atrophy throughout the pancreas, 2) peripancreatic inflammation, and 3) acute and chronic inflammatory changes of the common bile duct and gallbladder [9].

Estimates of the incidence of pancreatic involvement in PSC vary. Schimanski and colleagues reviewed 44 patients with PSC in whom ERCP was used as a diagnostic modality. Only one patient (2%) was found to have any pancreatic pathology [10]. In contrast, Takikawa reported an incidence as high as 15% in a review of 192 patients with PSC from Japan [11]. Clearly, the intrapancreatic biliary duct is an infrequent location for the disease. Features of inflammation characteristic of PSC were identified around the proximal pancreatic duct as well.

Although resection is effective in alleviating symptoms of pancreatitis in patients with PSC, there have also been reports of successful pharmacological treatments. Eerens and co-workers described a case of autoimmune pancreatitis (in the setting of a patient with PSC) that was treated successfully with high-dose steroids [12]. In that case, follow-up MRI 2 months later demonstrated a decrease in size of the pancreas and associated peripancreatic changes.

Lymphoplasmacytic sclerosing pancreatitis (LSP) has recently been characterised in the literature as a mimic for both chronic pancreatitis and pancreatic carcinoma [6, 13, 14]. LSP has been associated with PSC as well as other autoimmune disorders such as ulcerative colitis, Sjogren's syndrome and Riedel's thyroiditis [6, 13]. Weber and colleagues described 31 patents who ultimately were diagnosed with LSP following pancreatic resections performed for suspected pancreatic neoplasms [6]. Jaundice, abdominal pain and weight loss were prominent features in most of them. Imaging characteristics included obliteration or multifocal stenosis of the pancreatic duct. They described a 28% recurrence rate after resection, and determined that residual disease in the body or tail of the pancreas was a risk factor for recurrence. Recurrence typically presented with jaundice and a biliary stricture, which were managed with percutaneous or endoscopic stents. Bolus steroids were only given to two of seven patients with recurrence. Patients with recurrence were closely followed with serial CT scans [6]. Barthet and associates described eight cases in which patients presented with features of chronic pancreatitis, PSC and IBD [13]. They proposed that, in this scenario, the pancreatitis often precedes the more common symptoms of IBD and thus might be used as a marker for future development of disease.

The pathologic differentiation between PSC and LSP is not well defined. There is both histological and radiographical overlap between the two phenomena [14]. Both can have a lymphoplasmacytic infiltrate around the intrapancreatic bile ducts with characteristic narrowing. We believe that both disease processes fall within a spectrum of the same pathological phenomenon, and we propose to simplify the term LSP to sclerosing pancreatitis. Both LSP and pancreatic involvement by PSC can result in result in mass lesions and, as the present case suggests, the diagnosis of atypical PSC or sclerosing pancreatitis should be considered in the differential diagnosis of an intrapancreatic stricture of both the bile and pancreatic ducts.

References

1 LaRusso NF, Wiesner RH, Ludwig J, MacCarty RL. Current concept: primary sclerosing cholangitis. *N Engl J Med* 1984;**310**:899–903.

2 Wiesner RH, Porayko MK, LaRusso NF, Ludwig J. Primary sclerosing cholangitis. In: Schiff L, Schiff ER (eds). *Diseases of the Liver*, 7th edn. Philadelphia: Lippincott, 1993;411–26.

3 Raj V, Lichtenstein DR. Hepatobiliary manifestations of inflammatory bowel disease. *Gastroenterol Clin North Am* 1999;**28**:491–513.

4 Mitchell SA, Bansi DS, Hunt N, Van Bergmann K, Fleming KA, Chapman RW. A preliminary trial of high-dose ursodeoxycholic acid in primary sclerosing cholangitis. *Gastroenterology* 2001;**121**:900–7.

5 Harnois DM, Angulo P, Jorgensen RA, LaRusso NF, Lindor KD. High-dose ursodeoxycholic acid as therapy for patients with primary sclerosing cholangitis. *Am J Gastroenterol* 2001;**96**:1558–62.

6 Weber SM, Cubukcu-Dimopulo O, Palesty AF, *et al*. Lymphoplasmacytic sclerosing cholangitis: inflammatory mimic of pancreatic carcinoma. *J Gastrointest Surg* 2003;**7**:129–39.

7 Donaldson PT, Norris S. Immunogenetics in primary

sclerosing cholangitis. *Best Practice and Research in Clinical Gastroenterology* 2001;**15**:611–27.
8 Cullen S, Chapman R. Aetiopathogenesis of primary sclerosing cholangitis. *Best Practice and Research in Clinical Gastroenterology* 2001;**15**:577–89.
9 Kawaguchi K, Koike M, Tsuruta K, Okamota A, Tabata I, Fujita N. Lymphoplasmacytic sclerosing pancreatitis with cholangitis: a variant of primary sclerosing cholangitis extensively involving pancreas. *Hum Pathol* 1991;**22**:387–95.
10 Schimanski U, Stiehl A, Strimmel W, Thielmann L. Low prevalence of alterations in the pancreatic duct system in patients with primary sclerosing cholangitis. *Endoscopy* 1996;**28**:346–9.
11 Takikawa H. Recent status of primary sclerosing cholangitis in Japan. *J Hepatobiliary Pancreat Surg* 1999;**6**:352–5.
12 Eerens I, Vanbeckevoort D, Vansteenbergen W, Van Hoe L. Autoimmune pancreatitis associated with primary sclerosing cholangitis: MR imaging findings. *Eur Radiol* 2001;**11**:1401–4.
13 Barthet M, Hastier P, Bernard JP, *et al*. Chronic pancreatitis and inflammatory bowel disease: true or coincidental association? *Am J Gastroenterol* 1999; **94**: 2141–8.
14 Abraham SC, Wilentz RE, Yeo CJ, *et al*. Pancreaticoduodenectomy (Whipple Resections) in patients without malignancy: are they all 'chronic pancreatitis'? *Am J Surg Pathol* 2003;**27**:110–20.