



Our second autopsy case of autoimmune pancreatitis: A case report

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Abbreviations: AIP: Autoimmune Pancreatitis; CT: Computed Tomography; ERP: Endoscopic Retrograde Pancreatography; MPD: Main Pancreatic Duct; ERC: Endoscopic Retrograde Cholangiography; CBD: Common Bile Duct; ICDC: International Consensus Diagnostic Criteria.

Introduction

Autoimmune pancreatitis (AIP) is a distinct form of pancreatitis characterized clinically by frequent presentation with obstructive jaundice, histologically by a lymphoplasmacytic infil-

Abstract

Context: Autoimmune pancreatitis (AIP) can convert to ordinary chronic pancreatitis, as shown morphologically and/or functionally. However, few reports have assessed long-term pathological findings in patients with AIP.

Case report: A 62-year-old Japanese man was referred to our department for jaundice in March 2010. Computed tomography showed diffuse enlargement of the pancreas. His serum IgG4 level was increased, and endoscopic retrograde pancreatography images revealed irregular narrowing of the main pancreatic duct. The patient was diagnosed with AIP and underwent endoscopic biliary stenting, but was not treated with steroids. Computed tomography detected biliary carcinoma in November 2010. Despite laparotomy and chemotherapy, the patient died in December 2012. Autopsy examination detected fibrosis, mainly in the periductal and interlobular parts of the pancreas. Focal atrophy of acinar cells was also observed, as was slight infiltration of inflammatory cells, including IgG4-positive plasma cells, into the stroma of the pancreas. Evidence of obliterative phlebitis was observed, but there were few inflammatory cells near the vessels.

Conclusion: This patient was our second autopsy case of AIP. Pathological findings during an inactive phase of AIP were more similar to those of ordinary chronic pancreatitis than to those of active AIP. Obliterative phlebitis may be a diagnostic marker of inactive AIP.

trate and fibrosis, and therapeutically by a dramatic response to steroids [1]. Recently AIP is recognized as a disease entity, which is consisted of two subtypes. Type 1 AIP is now regarded as the pancreatic manifestation of the systemic IgG4-associated



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syndrome, which involves other organs. This subtype is highly abundant in Asian countries. Type 2 AIP presents as IgG4-negative disease with the histological picture of an idiopathic duct centric pancreatitis and is to a higher degree associated with inflammatory bowel disease. This subtype is much more common in European patients than in Asia [2]. Since our presentation of the first autopsy case of AIP in 2007, several reports have described long-term outcomes in patients with AIP. These long-term outcomes included atrophy of the pancreas, pancreatic stone formation, irregular pancreatic duct dilatation, and/or progressive dysfunction of the gland [3-6]. Therefore, in some patients, AIP should change to ordinary chronic pancreatitis, as shown morphologically and/or functionally. Few reports to date, however, have reported long-term pathological findings in patients with AIP. We experienced our second autopsy case of AIP. This report describes the clinical course of this patient, as well as autopsy findings.

Case report

A 62-year-old Japanese man experienced epigastric discomfort after meals, as well as deep colored urine, in March 2010. He was admitted to our department for obstructive jaundice. He had drunk two glasses of distilled spirits daily for 25 years and smoked 20 cigarettes per day for 32 years. His previous history was not contributory. Physical examination on admission revealed jaundice of the bulbar conjunctiva, but no significant findings in the chest and abdominal regions. Laboratory tests showed 7.3 mg/dl total bilirubin, 5.0 mg/dl direct bilirubin, 820 IU/l alkaline phosphatase, 140 IU/l serum amylase, 1.41 mg/dl C-reactive protein, 7.8 g/dl total protein, 4.3 g/dl serum albumin, 309 IU/l serum cholinesterase, 262 mg/dl total cholesterol, 140 mg/dl triglyceride, 9.6 mg/dl serum calcium, 1935.4 mg/dl immunoglobulin G, and 475 mg/dl immunoglobulin G4. Abdominal Computed Tomography (CT) showed diffuse enlargement of the pancreas and bile duct dilatation, as well as a peripancreatic low density rim (Figure 1). Endoscopic Retrograde Pancreatography (ERP) revealed irregular narrowing of the Main Pancreatic Duct (MPD) (Figure 2A). Endoscopic Retrograde Cholangiography (ERC) showed severe stricture of the distal Common Bile Duct (CBD) (Figure 2B). This patient was diagnosed with type 1 AIP. His jaundice was treated by endoscopic biliary stenting, but he refused steroid treatment and was therefore monitored regularly as an outpatient. Follow-up CT in November 2010 revealed a low-density tumor in the right lobe of the liver (Figure 3A), as well as cystic lesions in the body of the pancreas, suspected of being retention cysts (Figure 3B). He was clinically diagnosed with gallbladder carcinoma and, in January 2011, underwent cholecystectomy, extrahepatic bile duct resection and partial hepatectomy. Pathologic examination resulted in a diagnosis of intrahepatic bile duct carcinoma. After 4 months, metastatic lesions were observed in the liver and pelvic cavity. Despite systemic chemotherapy and chemotherapy via the hepatic artery, the patient died in December 2012. CT performed during the month preceding the patient's death revealed severe atrophy of the pancreas (Figure 4). At the time of death, his total steroid dose for antiemetic therapy was equivalent to about 1200 mg of prednisolone.

At autopsy, his pancreas was atrophic with no cystic lesions. Severe fibrosis was observed in the broad area of the pancreas, particularly in the inter-lobular and periductal areas. Atrophy and defluxion of the acinar cells were also observed (Figure 5A,B). There were a few inflammatory cells, including IgG and IgG4-positive plasmacytes (Figure 5C, D, E). These findings were

more similar to those observed in patients with ordinary chronic pancreatitis than to those in patients with active AIP. There was evidence of obliterative phlebitis, but very few inflammatory cells near the vessels (Figure 5F). As for other specific pathological findings of type 1 AIP, neither abundant IgG4-positive cells nor storiform fibrosis was found in the pancreas. Sclerosing cholangitis and retroperitoneal fibrosis were seen and these were compatible for extrapancreatic lesions of IgG4-related disease. Besides these, infiltration of IgG4-positive plasmacytes was observed in the spleen, bone marrow and lymph nodes, which was also seemed compatible for extrapancreatic manifestations of the IgG4-related disease. Metastatic sites of the intrahepatic bile duct carcinoma were proved to be the lungs, duodenum, cecum, rectum, urinary bladder, peritoneum, and lymph nodes in addition to the liver.

Discussion

Reports of AIP have increased, with AIP widely recognized as a distinctive type of pancreatitis. Since the Japan Pancreas Society first proposed diagnostic criteria for AIP in 2002, several groups in Korea, other Asian countries, and the United States have published diagnostic criteria, based on the region of origin [7-11]. In 2011, a multinational group proposed the International Consensus Diagnostic Criteria (ICDC) for AIP [12]. Our patient presented with diffuse enlargement of the gland, irregular narrowing of the MPD, and serum IgG4 concentrations more than twice the normal value. This patient met the 2006 Japanese diagnostic criteria for AIP [11], as well as the ICDC for type 1 AIP [12].

As more patients with AIP have been reported, insights into long-term outcomes have increased [3-6]. A recent large, international, multicenter analysis of long-term outcomes in 978 patients with type 1 AIP reported stone formation in the pancreatic duct of 7% of these patients [3]. Another study reported that three of 21 patients with AIP developed chronic pancreatitis after long-term observation (mean 40.8 months) [5]. Moreover, approximately 40% of patients with AIP were reported to experience pancreatic stone formation over the long term (median, 72 months), and nearly 20% progressed to chronic pancreatitis according to the revised Japanese Clinical Diagnostic Criteria [4]. Taken together, these reports indicate that, in some patients, AIP can transform to ordinary chronic pancreatitis. A proposed mechanism of progression begins with pancreatic head swelling and narrowing of both Wirsung's and Santorini's ducts, causing pancreatic juice stasis in the upstream pancreatic duct. This would result in increased pressure on the intrapancreatic duct and resistance to AIP-specific MPD narrowing in the pancreatic body, causing non-narrowing of the MPD in this region. Finally, those events could result in severe calcification of the entire pancreas [4].

Although these reports analyzed long-term morphological and/or functional outcomes, long-term pathological findings remain unclear, likely because inactive AIP is generally asymptomatic and does not mimic malignancy. The patient described in this report is our second autopsy case of AIP. The previous patient died due to interstitial pneumonia 8 years after a diagnosis of AIP without steroid therapy, which was published in the *Journal of the Pancreas* in 2007. Although autopsy findings of these two patients were similar, including marked fibrosis and atrophy of the acinar cells, there were some differences. Obstructive phlebitis, observed in our second patient, was not observed in our first case. In addition, the two patients differed in the extent of infiltration of inflammatory cells, including IgG4-

positive plasmacytes. These characteristics may be dependent on steroid usage or the extent of inflammation in the active phase of the disease. Evidence of obliterative phlebitis may be a marker of chronic pancreatitis originating from AIP.

To our knowledge, only one other autopsy case of AIP, in addition to ours, has been reported [13]. That patient died of dissemination of renal cell carcinoma, and autopsy findings of the pancreas were similar to those of AIP rather than ordinary chronic pancreatitis. Abundant IgG4-positive plasma cell infiltration into the parenchyma of the pancreas was observed, along with dense interstitial fibrosis. Moreover, despite steroid therapy, that patient showed an extra pancreatic relapse in the intrahepatic bile duct, suggesting highly active AIP. Although that report did not describe morphological findings of the pancreas at the time of death, that patient may have died during an active phase of AIP. Few reports to date have described pathological findings during inactive phases of AIP. Our findings, showing clinical and pathological characteristics in a patient with AIP, may provide insights into the pathobiology of AIP.

Figure 1

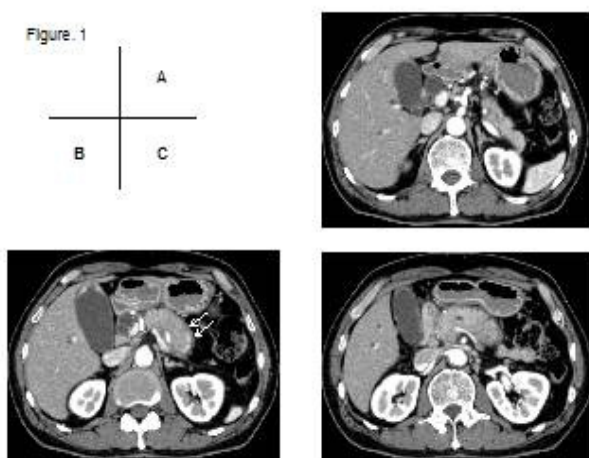


Figure 1(A-C): Abdominal computed tomography findings at first admission. Note the diffuse enlargement of the pancreas and dilatation of the biliary tract, as well as a peripancreatic low density rim (arrows).

Figure 2



Figure 2: Endoscopic retrograde cholangiopancreatography findings. Note the irregular narrowing of the main pancreatic duct (A), and the severe stricture of the distal bile duct (B).

Figure 3 A | B



Figure 3: Abdominal computed tomography findings in November 2010. (A) A low-density tumor present in the right lobe of the liver (arrow). (B) Cystic lesions in the body of the pancreas.

Figure 4 A | B



Figure 4A,B: Abdominal computed tomography findings in the month preceding the patient's death. Note the severe atrophy of the pancreas (arrows).

Figure 5

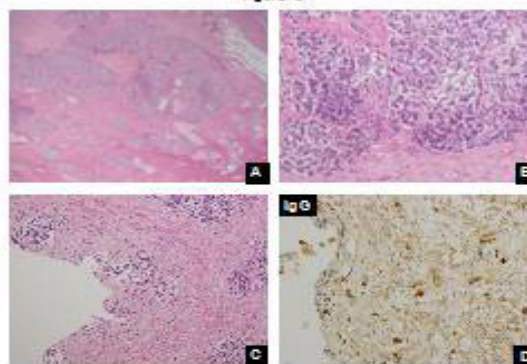


Figure 5

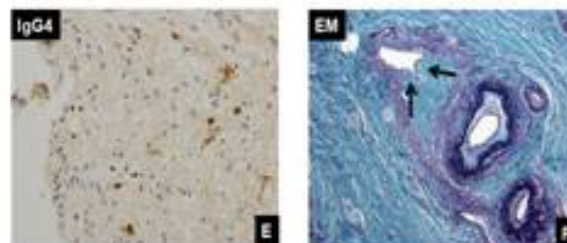


Figure 5: Histology of the autopsy specimens of the pancreas, showing (A,B) severe fibrosis and atrophy of acinar cells; and (C) mild infiltration of inflammatory cells. (D,E): Immunohistochemical staining showing a few IgG- and IgG4-positive plasmacytes. (F) Evidence of obstructive phlebitis (arrows, Elastica Masson staining).

Figures

Conclusion

Few reports have described autopsy findings in patients with AIP. We present our second autopsy case of AIP. The findings in this patient suggest that the pathological characteristics of inactive AIP are similar to those of ordinary chronic pancreatitis, as described in our first case report. The evidence of obliterative phlebitis is a novel finding and may be a marker of chronic pancreatitis originating from AIP.

Authors' contributions

MI, SY and YK provided medical treatment to the patient. YK wrote the manuscript. KY, IH, KT, KW and YM critically reviewed the manuscript. YN reviewed the pathological findings and suggested a lot for this manuscript. TO made final approval of the manuscript to be published.

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