Two Cases of Autoimmune Pancreatitis with Coexisting Features of Tumor-Forming Pancreatitis.

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Abstract

Case 1: A 61-year-old male was hospitalized for evaluation of jaundice. The antinuclear antibody (ANA) titer was 160, and rheumatoid factor (RF) was positive. Contrast abdominal CT showed diffuse enlargement of the pancreas and a mass in the pancreatic head. ERCP revealed localized narrowing in the main pancreatic duct in the pancreatic body. The patient was diagnosed as having autoimmune pancreatitis (AIP). Treatment with prednisolone (PSL) improved the pancreatic enlargement and reduced the size of the mass in the pancreatic head. Case 2: A 74-year-old male was hospitalized with suspected cancer of the pancreatic head. Serum IgG was 2,212 mg/dl, IgG4 was 915 mg/dl, and the anti-DNA antibody titer was 4. Abdominal US and abdominal contrast CT showed diffuse enlargement of the pancreas and a mass in the pancreatic head. As the jaundice decreased with endoscopic naso-biliary drainage, the pancreatic enlargement improved, and the mass in the pancreatic head decreased in size. Based on the clinical course, the patient was diagnosed with AIP. Both of these patients appear to have had AIP with coexisting features of tumor-forming pancreatitis (TFP). Thus, AIP should be considered as an etiology of nonalcoholic TFP. One of the two patients initially diagnosed based on the 2002 diagnostic criteria for AIP had a confirmatory diagnosis based on the 2006 revised clinical diagnostic criteria for AIP. Patients should be re-evaluated based on the later criteria.

Key Words

Autoimmune Pancreatitis, Tumor-Forming Pancreatitis

Introduction

Autoimmune pancreatitis (AIP) was first described in 1961 by Sarles et al.¹ as a chronic inflammatory sclerosis of the pancreas involving an autoimmune mechanism. In Japan, since 1992, when Toki et al.² reported a case of chronic pancreatitis with diffuse irregular narrowing of the main pancreatic duct, the number of cases has increased. On the other hand, tumor-forming pancreatitis (TFP) is often referred to clinically in the differential diagnosis of pancreatic cancer, but TFP is not a well-defined clinical entity.³ In this report, we describe two patients with AIP and coexisting features of TFP.

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Case 1: This 61-year-old male developed generalized malaise and dark urine in late August of 2002 and was hospitalized by his physician for evaluation of hepatic dysfunction. The history was negative for alcohol consumption. Physical examination revealed jaundice and scleral icterus. Abdominal examination revealed a palpable, nontender mass beneath the right subcostal margin. Laboratory data on admission included a blood sedimentation rate of 61 mm/h (moderately elevated), a direct bilirubin of 5.1 mg/dl, an antinuclear antibody (ANA) titer of 160, and a positive rheumatoid factor (RF). Contrast abdominal CT during the parenchymal phase showed diffuse enlargement of the pancreas and a mass in the pancreatic head, but a corresponding low-density area suspicious of pancreatic cancer was not present (Fig. 1a, b). MRCP showed narrowing of the lower common bile duct and localized narrowing of the main pancreatic duct (Fig. 2a). PTBD was performed for obstructive jaundice. PTC showed smooth extrinsic narrowing of the lower common bile duct margin (Fig. 3a). On ERCP, localized narrowing of the main pancreatic duct in the pancreatic body, but no post-stenotic dilation, was observed. In addition, there was no narrowing or obstruction of the main pancreatic duct in the pancreatic head (Fig. 3b). On cholangioscopy, there was no irregularity or redness of the common bile duct mucosa; thus, the narrowing was due to extrinsic compression. Based on these findings, the patient was diagnosed as having AIP, and treatment with prednisolone (PSL) 30 mg per day.
was started. The pancreatic enlargement and narrowing of the lower common bile duct improved (Fig. 2b).

**Case 2:** This 74-year-old male began to experience left-sided abdominal pain in March 2003. In May 2003, he noticed clay-colored stools and jaundice. Since abdominal CT showed enlargement of the pancreatic head, he was admitted to hospital with suspected pancreatic cancer. His alcohol consumption consisted of one bottle beer per day. Physical examination revealed jaundice and scleral icterus. Abdominal examination revealed an elastic, hard mass on the left side; the patient complained of abdominal pain in the area of the mass, with associated tenderness on palpation. Laboratory data on admission showed a blood sedimentation rate of 30 mm/h (mildly elevated), direct bilirubin of 10.8 mg/dl, serum IgG of 2,212 mg/dl, IgG4 of 915 mg/dl, and an anti-DNA antibody titer of 4. Contrast abdominal CT during the parenchymal phase showed diffuse enlargement of the pancreas and a low-density mass in the pancreatic head (Fig. 4a, b). On abdominal US, sausage-shaped enlargement of the entire pancreas, a 5-cm mass in the pancreatic head, and mild dilatation of the main pancreatic duct in the pancreatic body were present (Fig. 5a, b). Contrast abdominal MRI showed no difference in signal intensity between the pancreatic parenchyma and the mass in the pancreatic head. MRCP showed no significant dilatation in the main pancreatic duct of the pancreatic body and tail, but intrahepatic bile duct dilatation and lower common bile duct narrowing were present (Fig. 6). On ERCP, as on MRCP, intrahepatic bile duct dilatation and smooth narrowing of the lower common bile duct margin were observed. Contrast visualization of the main pancreatic duct was difficult. Endoscopic naso-biliary drainage was performed, and the jaundice improved. After catheter removal, there was no exacerbation of jaundice, and contrast abdominal CT showed improvement in the pancreatic enlargement and a reduction in size of the mass in the pancreatic head (Fig. 4c, d). The patient’s symptoms improved during follow-up.

**Discussion**

Interest in AIP has increased, with a growing number of case reports. Etemad and Whitcomb have proposed a new classification for chronic pancreatitis (TIGAR-O), which includes AIP as an etiology. In 2002, the Japan Pancreas Society published diagnostic criteria for AIP. In the present report, the diagnosis of AIP in our patients was based on these 2002 diagnostic criteria for AIP. In patient 1, with pancreatic enlargement, positive ANA, and positive RF, the criteria regarding narrowing of the main pancreatic duct were not met. Patient 2 had a history of alcohol consumption, but pancreatic calcification and irregular pancreatic
Figure 4. Contrast abdominal CT image of case 2 during the parenchymal phase.

a, b: CT showed diffuse enlargement of the pancreas and a low-density mass in the pancreatic head. The arrow indicates a mass in the pancreas head.

c, d: CT showed improvement in the pancreatic enlargement and a reduction in size of the mass in the pancreatic head after endoscopic naso-biliary drainage.

Figure 5. Abdominal US image of case 2.

a: US showed sausage-shaped enlargement of the entire pancreas.

b: US showed a 5-cm mass in the pancreatic head and mild dilation of the main pancreatic duct in the pancreatic body were present. The arrow indicates a mass in the pancreas head.
margins, as defined in the diagnostic criteria for chronic pancreatitis, were not present. Diffuse enlargement of the pancreas was observed. Elevated IgG and IgG4 levels suggested AIP, but ERCP did not visualize the main pancreatic duct, thus not meeting the diagnostic criteria. However, in patient 1, based on the revised clinical diagnostic criteria for AIP in 2006, except for narrowing of $\geq 1/3$ of the main pancreatic duct, the diagnostic criteria were fitted. In addition, elevated IgG4 is reported to be useful in the differential diagnosis between AIP and other disorders, including pancreatic cancer, and in the 2006 clinical diagnostic criteria for AIP, elevated IgG4 is listed. Therefore, in patient 2, even though the main pancreatic duct was not visualized with contrast, the findings were consistent with AIP. Among the case reports that we reviewed, AIP was often diagnosed, as in our patients, based on clinical findings, even though all diagnostic criteria were not fitted. Re-evaluation based on the revised guidelines is necessary.

TFP is a clinical entity that is often difficult to distinguish from cancer and may represent the so-called tumor-forming stage of dynamically changing chronic pancreatitis. The etiology of TFP is broadly classified as alcoholic and nonalcoholic, and in the latter, an autoimmune mechanism is thought to play a role. TFP often involves the pancreatic head, but as compared to pancreatic cancer, the incidence of jaundice and obstruction / narrowing of the main pancreatic duct is lower. Even if the main pancreatic duct is narrowed, dilation of the common bile duct is often observed. The differential diagnosis between TFP and pancreatic cancer, especially with tumor fibrosis, can be difficult based on CT or MRI contrast effects in the parenchyma. In these cases, the “duct penetrating sign” may be useful in the differential diagnosis. AIP is usually associated with diffuse pancreatic enlargement, but localized enlargement can also occur. This can be a factor in TFP, and, in particular, when the pancreatic head is enlarged, the differential diagnosis with pancreatic cancer may be difficult. However, when pancreatic head enlargement is part of more diffuse pancreatic enlargement, the presence of a capsule-like rim around the pancreas is helpful in diagnosis. Histologically, this is a fibrous capsule, so on dynamic CT or MRI, there is gradual enhancement. Our each patient also had mass in the pancreatic head, making it difficult to distinguish from pancreatic cancer, but the diffuse pancreatic enlargement and absence of main pancreatic duct dilation helped in the differential diagnosis.

However, in AIP, narrowing of the common bile duct within the pancreas can cause obstructive jaundice, thus making it difficult to differentiate from pancreatic head cancer or bile duct cancer. The narrowing often occurs in the lower common bile duct and is relatively smooth; it is probably due to compression by the enlarged pancreas, but coexisting biliary lesions in AIP have also been reported. It is necessary to care for diagnosis because CT and/or intraductal ultrasound show thickening of the bile duct wall, and the findings in some cases may resemble primary sclerosing cholangitis. Both of our patients had smooth narrowing of the lower bile ducts, but no other findings were evident.

Conclusions
1. We reported two patients with AIP and coexisting features of TFP.
2. Much remains unknown about the etiology of TFP, but in nonalcoholic TFP, underlying AIP should be kept in mind.
3. Suspected cases of AIP should be re-evaluated based on the revised clinical diagnostic criteria for AIP.

Figure 6. MRCP image of case 2.
MRCP showed no significant dilation in the main pancreatic duct of the pancreatic body and tail, but intrahepatic bile duct dilation and lower common bile duct narrowing were present.
Reference


2) Toki F, Kozu T and Oi I. An unusual type of chronic pancreatitis showing diffuse irregular narrowing of the entire main pancreatic duct on ERCP-A report of four cases. Endoscopy 1992; 24: 640.


腫瘤形成性膵炎像を呈した自己免疫性膵炎の2症例

抄録

症例1：61歳の男性。黄疸にて入院。抗核抗体160倍、リウマチ反応陽性。腹部造影 CTにて膵全体の腫大と膵頭部の腫瘤が認められた。ERCPでは体部主膵管に限局性狭細像がみられた。自己免疫性膵炎と考え、プレドニゾロン投与を経て、膵腫大の改善と膵頭部腫瘤の縮小が得られた。症例2：74歳の男性。膵頭部疑いにて入院。IgG2212mg/dl、IgG4915mg/dl、抗DNA抗体4倍。腹部US、腹部造影CTにて膵頭部の腫瘤と膵全盤の腫大がみられた。減黄とともに膵腫大的改善、膵頭部腫瘤の縮小が得られ、経過より自己免疫性膵炎と診断した。我々は自己免疫性膵炎に腫瘤形成性膵炎の病態が合併したと考えられる2症例を経験した。非アルコール性の腫瘤形成性膵炎の病因に自己免疫性膵炎も念頭に置く必要があると考えられた。また診断当初は疑い症例であった2症例のうち1症例は自己免疫性膵炎診断基準2002年から自己免疫性膵炎診断基準2006への改訂により確診例となり、症例の再検討も必要と考える。

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