

Pseudotumoral autoimmune pancreatitis mimicking a pancreatic cancer: a very difficult disease to diagnose

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Abstract

Autoimmune pancreatitis (AIP) is a rare disorder, although the exact prevalence is still unknown. It is a type of pancreatitis that is presumed to have an autoimmune aetiology, and is currently diagnosed based on a combination of 5 criteria. However, in this day and age, some patients with AIP are likely to be resected for the suspicion of malignancy. The authors report a case of pseudo-tumoral autoimmune pancreatitis, reviewing some literature about it and underlining the difficulty in the diagnosis. A 56-year-old patient was referred to our unit for upper abdominal pain. In his past medical history we note mellitus diabetes. The clinical examination was unremarkable. Laboratory data showed no abnormal values. Upper endoscopy showed antral gastritis. Transabdominal ultrasonography showed a hepatic steatosis and 5 angiomas. No computed tomography scan was made. Magnetic resonance imaging (MRI) showed 5 angiomas and a lesion of 20x20 mm of the pancreatic tail with decreased signal intensity on T1-weighted MR images, increased signal intensity on T2-weighted MR images. Due to concerns of pancreatic malignancy, the patient underwent open distal spleno-pancreatectomy. Histological analysis of the resected specimen revealed no malignancy. Postoperatively, immunoglobulin G fraction 4 was slightly above of the upper limit of the normal range. After corticotherapy the patient is getting better. This case underlines the difficulties still encountered in the diagnosis of AIP. It has been frequently misdiagnosed as pancreatic cancer and caused unnecessary resection. In order to avoid unnecessary resections for an otherwise benign and easily treatable condition, it is urgent to refine diagnostic criteria and to reach an international consensus.

Introduction

Autoimmune pancreatitis (AIP) is a rare disease. The overall prevalence and incidence have yet to be determined. Three series have

reported the prevalence of autoimmune pancreatitis as between 5% and 6% of all patients with chronic pancreatitis.^{1,2} AIP may closely mimics pancreatic cancer (PC) especially in focal form. It is very important to distinguish between these two entities regarding to differences in treatment and prognosis. AIP can be diffuse or focal form (pseudo-tumoral form). AIP appears to be a disease of the elderly, but vary widely in age, as most patients are more than 50 years old at diagnosis.³ It is reported to be at least twice as common in men as in women.^{2,4} Although diffuse swelling of the pancreatic parenchyma can be morphologically characteristic of AIP, a focal type of this clinical entity has been recently recognized and is still difficult to establish.³ However, in this day and age, even with heightened awareness of AIP and appropriate preoperative workup (including serum immunoglobulin G fraction 4 (IgG4) measurement and, in very select cases, a short steroid trial), some patients with AIP are likely to be resected for the suspicion of malignancy.⁵

Case Report

A 56-year-old patient was referred to our unit for upper abdominal pain since two week and lost of 6 kg in two months. In his past medical history we note mellitus diabetes. His clinical examination was unremarkable. Laboratory data showed no abnormal values. The serum carcinoembryonic antigen and cancer antigen 19-9 (ca¹⁹⁻⁹) level was normal. Upper endoscopy showed antral gastritis. Transabdominal ultrasonography showed a hepatic steatosis and 5 angiomas. Magnetic resonance imaging (MRI) showed the angiomas and a lesion of 20x20 mm of the pancreatic tail with decreased signal intensity on T1-weighted MR images, increased signal intensity on T2-weighted MR images, and discreetly hypovascularized (Figure 1). Due to concerns of pancreatic malignancy (pancreatic adenocarcinoma), the patient underwent laparotomy. We found a tumor about 5 cm in diameter lacking clear margins in the tail of the pancreas, which was removed via an open distal spleno-pancreatectomy. Histological analysis of the resected specimen revealed no malignancy, but dense fibrosis with lymphoplasmotic infiltration and acinar atrophy (Figure 2). Postoperatively, autoantibodies and immunoglobulin were normal but IgG4 was slightly above of the upper limit of the normal range. Patient was treated by 40 mg/j of corticotherapy with a remarkable improvement. In the follow up, the patient had well-being. Because of the past medical history of mellitus diabetes, the young age of the patient, the normalization of the serum IgG4 level, the absence of malignancy in histology, and the clinical improvement after corticoid therapy, the diagnosis of AIP was made.

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Discussion

Autoimmune pancreatitis is a rare type of chronic pancreatitis that closely mimic pancreatic cancer. These two entities can present with obstructive jaundice and/or weight loss and abdominal discomfort.⁶ Although diagnostic criteria were established for AIP, there remains no practical strategy to differentiate PC from AIP.⁷ Making a correct differential diagnosis between the two conditions is of paramount importance as the treatment approaches are different.⁶

The common presenting symptoms of the pseudo tumoral autoimmune pancreatitis are mild abdominal pain, jaundice, and weight loss.^{3,4} Cholestasis was seen in 75-100% of a Japanese series, mild pancreatitis, acute recurrent pancreatitis, biliary duct strictures are a various clinical forms of AIP.^{4,8} The definitive diagnosis of AIP is relatively easier in diffuse form than focal form. It is made by radiologic computed tomography scan finding of a narrowing of the pancreatic duct and parenchymal edema of the pancreas (a sausage shape).^{8,9} Isolated focal pancreatic mass is difficult to be diagnosing without doubt as a focal AIP. Magnetic resonance cholangiopancreatography, demonstrates biliary abnormalities such as cholangitis. It can show focal AIP as a low-attenuation or an iso-attenuation mass.⁴ On the other hand, features highly suggestive of pancreatic cancer were a pancreatic low density mass, main pancreatic duct obstruction, distal pancreatic atrophy, and metastases.⁷ Endoscopic ultrasonography provides the opportunity for fine needle aspiration, but does not have pathognomonic findings on its own.⁴ Immunological abnormalities include hypergammaglobuli-

naemia, elevated serum IgG4 levels and the presence of autoantibodies including antinuclear antibody, anti smooth muscle antibody, rheumatoid factor, antilactoferrin antibody and anticarbonic anhydrase antibody II.⁹⁻¹¹ The specificity and sensitivity of a high serum IgG4 level in the diagnosis of AIP are >90%.¹² However, a pancreatic cancer with elevated serum IgG4 was reported.³ After resection, histological changes in AIP show predominantly periductal inflammation consisting of a dense interstitial lymphoplasmacytic infiltrate, thus causing duct obstruction with acinar tissue fibrosis.⁴ AIP is frequently associated with other autoimmune diseases. In addition, AIP has been seen in association with retroperitoneal fibrosis,

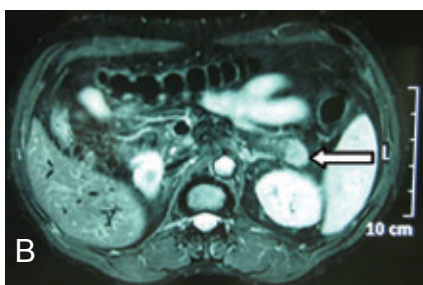
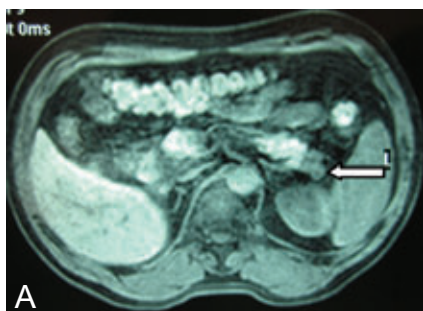


Figure 1. Magnetic resonance imaging shows the affected pancreatic lesion involving tail with decreased intensity on the T1-weighted image (A) and increased intensity on the T2-weighted image (B) compared with the signal intensity in the liver.

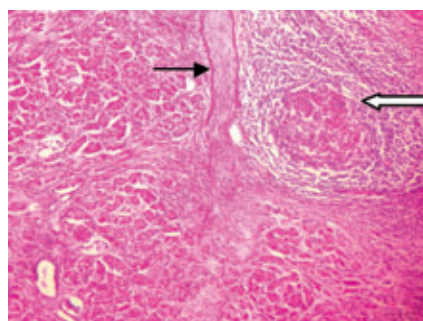


Figure 2. The histologic findings of the resected specimen of the pancreas include: dense fibrosis (black arrow), lymphoplasmacytic infiltration, and acinar atrophy (white arrow). Hematoxylin and eosin (HE, x250).

kidney involvement and lung nodules.^{3,4,8,11} These features are considered as extrapancreatic signs of AIP and might be helpful to diagnose especially in focal form. Our patient had no extrapancreatic features. Because of the difficulty of the diagnosis, several types of diagnosis criteria have been proposed. Since there is currently no diagnostic serological marker for AIP, and approach to the pancreas of histological examination is generally difficult, AIP is currently diagnosed on the basis of presence of a combination of abnormalities unique to AIP.¹³ For practical purposes, the revise Japanese clinical diagnostic criteria (2006)¹⁴ and HISORT criteria from the Mayo Clinic¹⁵ and in 2011 international consensus diagnostic criteria for AIP¹⁶ were proposed. In this set of diagnostic criteria, the diagnosis of AIP is made using one or more positive criteria on: i) imaging criteria: diffuse enlargement of the pancreas and diffuse or segmental irregular narrowing of the main pancreatic duct; ii) laboratory criteria: elevated levels of IgG and/or IgG4 or the presence of autoantibodies; iii) histopathologic criteria: fibrosis and lymphoplasmacytic infiltration; iv) association with other autoimmune diseases; and v) response to steroid therapy.^{3,4,12} Despite all these investigations procedures and the existence of these criteria, 3-5% of patients undergoing pancreatic resection for presumed PC in fact has AIP,⁷ as was the case of our patient. Kamisawa *et al.* reported that 7 of 37 (18.9%) AIP patients had surgery because they were misdiagnosed as having PC or bile duct cancer.³ Steroids are the first choice of therapy in patients with AIP. This treatment may represent a diagnosis test, considered as one of the main diagnosis criteria. The response to steroid therapy is usually phenomenal. Pancreatic and extrapancreatic clinical signs disappear within two weeks. Laboratory parameters of AIP also improve. Imaging studies have demonstrated that improvement can be observed within 1-2 months.¹⁷

Conclusions

Focal AIP remains difficult to distinguish from malignancies. Extrapaneatic features, IgG4 level, endoscopic ultrasound guided fine needle aspiration and corticotherapy are helpful to evoke AIP. The preoperative diagnosis should prevent unnecessary surgery causing a high morbidity comparing to medical treatment (corticosteroid) of AIP.

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