Autoimmune Pancreatitis Presenting as A Pancreatic Head Tumor：Report of A Case

Chien-Chu Lin[1], Cheng-Chao Liang[1], Meng-Tzu Weng[1], Tzong-Hsi Lee[1], and Kuo-Hsin Chen[2]

[1]Division of Gastroenterology and Hepatology, Department of Internal Medicine, [2]Department of Surgery, Far Eastern Memorial Hospital, Taipei, Taiwan

Abstract

Autoimmune pancreatitis (AIP) is a benign form of chronic pancreatitis that is associated with autoimmune processes demonstrated on clinical images, laboratory, and histopathologic features. We herein report the case of a 67-year-old man with a history of diabetes mellitus for one year who was referred to our emergency department because of painless jaundice for 3 days. Abdominal computed tomography revealed diffuse but uniformly enhanced pancreatic enlargement, especially in the pancreatic head. On endoscopic retrograde cholangio-pancreatography, the main pancreatic duct had an irregular contour and diffuse attenuation. There was also a stricture of the distal common bile duct. Endoscopic ultrasound imaging showed a reticular pattern and diffuse enlargement of pancreatic parenchyma. There was a 3.0 x 2.7 cm relative hypoechoic lesion in the pancreatic head. Tissue diagnosis was made by laparoscopic biopsy, which revealed abundant lymphoplasmacytic cell infiltrates accompanied by periductal inflammation by histopathology. The serum immunoglobulin G4 level was greater than 160 mg/dL. These findings led to a diagnosis of autoimmune pancreatitis for which the treatment of choice is corticosteroids. Our patient was still alive and being treated with oral steroids one year later. The imaging and jaundice improved after treatment, however the pre-existing diabetes mellitus did not improve during the steroid therapy. (J Intern Med Taiwan 2010; 21: 366-372)

Key Words：Jaundice, Pancreatitis, Autoimmune

Introduction

Autoimmune pancreatitis (AIP) was first described by Toshida et al.[1] in 1995. The disease is a benign form of chronic pancreatitis that is associated with autoimmune processes demonstrated on clinical images, laboratory, and histopathologic features. Good treatment response to steroids is also a hallmark of AIP. The incidence of AIP has been reported to be 4.6~6% among patients with chronic pancreatitis[2]. Many other terms share the same clinical entities, such as lymphoplasmacytic sclerosing pancreatitis[3], chronic sclerosing pancreatitis[4], nonalcoholic duct destructive pancreatitis[5], and pseudotumorous pancreatitis[6]. The

Correspondence and requests for reprints：Dr. Chien-Chu Lin
Address：Division of Gastroenterology and Hepatology, Department of Internal Medicine, Far Eastern Memorial Hospital, No. 21, Section 2, Nan-Ya South Road, Banciao City, Taipei, 22050, Taiwan

treatment of choice is corticosteroids[7]. Steroid therapy can lead to a dramatic improvement of symptoms, including biliary obstruction, pancreatic duct narrowing, sugar control, and pancreatic lesions. We present a case of AIP presenting as a pancreatic head tumor and the follow-up treatment response.

Case Report

A 67-year-old man with a history of diabetes mellitus (DM) for one year was referred to our emergency department after suffering from painless jaundice for 3 days. He denied having fever or passage of clay colored stools. A physical examination revealed that the patient had icteric sclera without other stigmata of cirrhosis. Laboratory data showed conjugated hyperbilirubinemia (total/direct bilirubin 4.4/3.23 mg/dL; normal reference limit 1.5/0.3 mg/dL), elevated liver enzyme (aspartate aminotransferase/alanine aminotransferase 99/174 IU/L; normal reference limit 37/41 IU/L), elevated biliary tract enzymes (alkaline phosphatase/r-glutamyl transferase 165/616 IU/L; normal reference limit 104/36 IU/L), elevated globulin level (globulin 5.6 gm/dL; normal reference limit 3.5 gm/dL) and elevated tumor marker: Carbohydrate Antigen 19-9 (CA 19-9 97.12 U/mL; normal reference upper limit 37 U/mL). Other biochemistry data were within normal limits.

Trans-abdominal ultrasound (US) disclosed fatty liver, gallbladder sludge, dilated common bile duct (CBD) (Figure 1, black arrow) and a 4.0 x 3.3 cm hypoechoic lesion in the pancreatic head (Figure 1, white arrow). There was no dilatation of the main pancreatic duct. Abdominal computed tomography (CT) revealed diffuse but uniformly enhanced pancreatic enlargement (Figure 2A), especially in the pancreatic head (Figure 2B). There were no definite hypodense lesions in the pancreas. On endoscopic retrograde cholangio-pancreatography (ERCP) (Figure 3), the main pancreatic duct had an irregular contour and diffuse attenuation. There was also a stricture of the distal CBD (Figure 3,

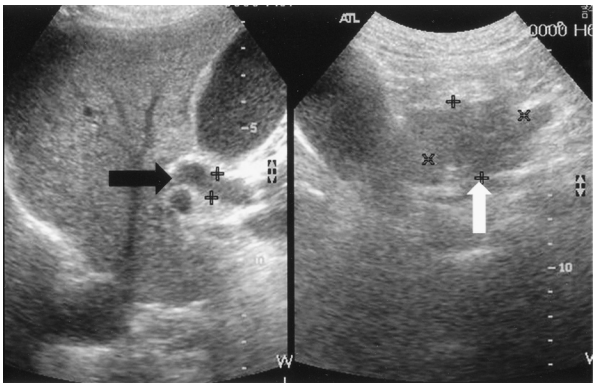

Fig.1. Trans-abdominal ultrasound disclosed fatty liver, gallbladder sludge, dilated common bile duct (black arrow) and a 4.0 x 3.3 cm hypoechoic lesion in the pancreatic head (white arrow).

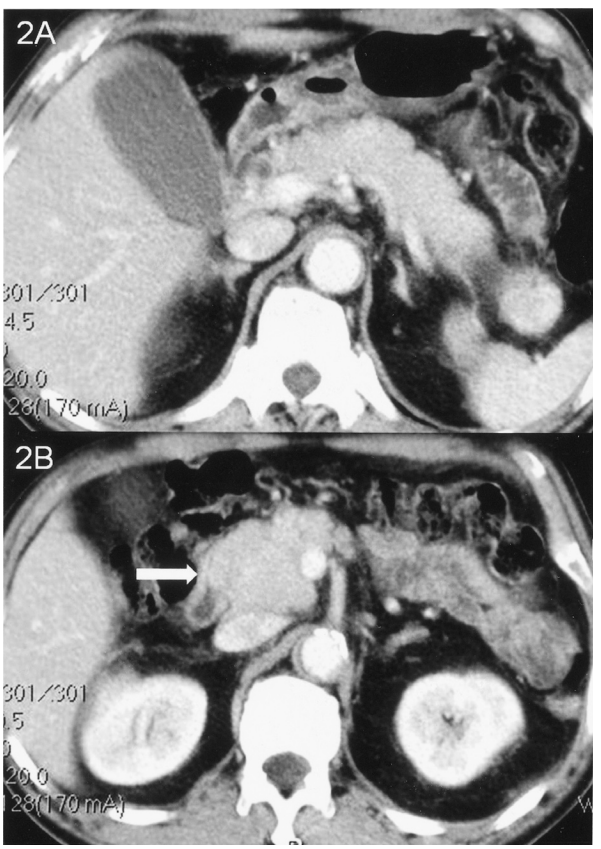

Fig.2.Abdominal computed tomography revealed diffuse but uniformly enhanced pancreatic enlargement (2A), especially in the pancreatic head (2B, arrow).

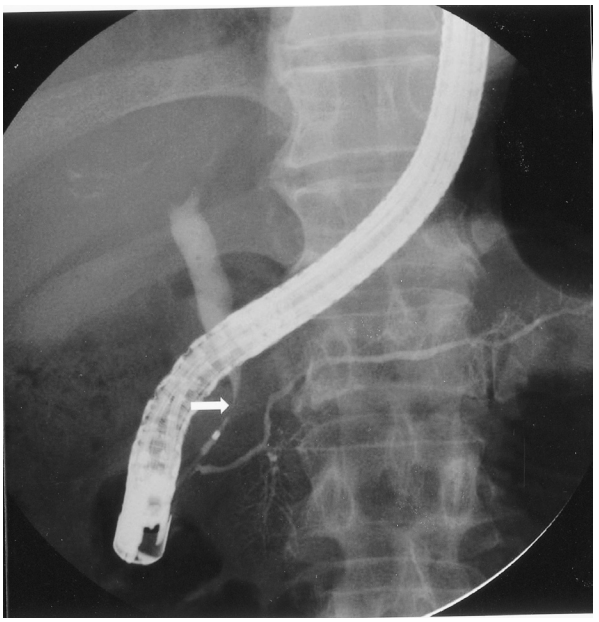

Fig.3. Endoscopic retrograde cholangio-pancreatography showed an irregular contour and diffuse attenuation of the main pancreatic duct, as well as stricture of the distal common bile duct (arrow).

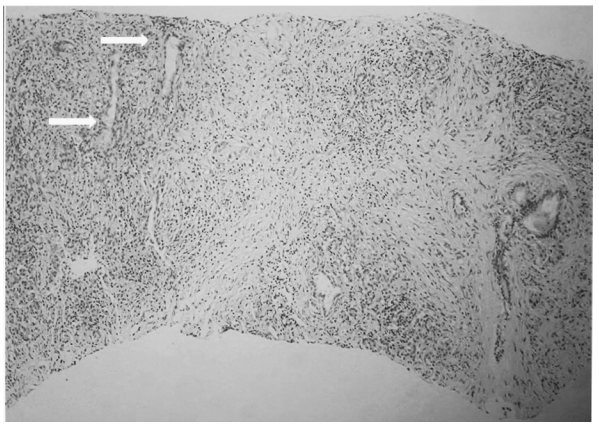

Fig.4. Histopathology showed abundant lymphoplasmacytic cell infiltrates with peri-ductal inflammation (arrows).

arrow). An endoscopic retrograde biliary drainage (ERBD) stent was placed for distal CBD stricture. Endoscopic ultrasound (EUS) imaging showed a reticular pattern and diffuse enlargement of pancreatic parenchyma. There was also a 3.0 x 2.7 cm relative hypoechoic lesion in the pancreatic head.

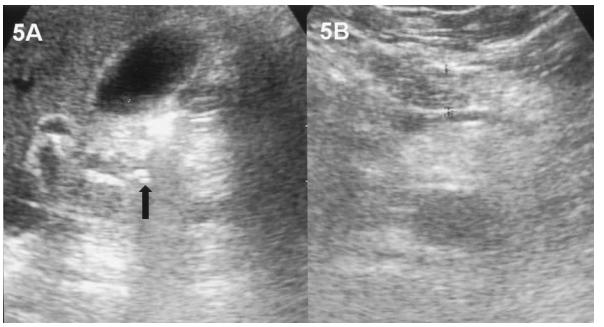

Fig. 5. Follow-up trans-abdominal ultrasound revealed a normal caliber of the CBD with the ERBD in situ (5A, black arrow) and disappearance of the pancreatic head lesion (5B).

Due to inconclusive clinical imaging results, tissue diagnosis was made by laparoscopic biopsy of the head and body portions of the pancreas. Histopathology revealed abundant lymphoplasmacytic cell infiltrates accompanied by peri-ductal inflammation (Figure 4, arrows). The serum immunoglobulin G4 (IgG4) level was greater than 160 mg/dL (normal range 3.9~86.4 mg/dL). These findings led to a diagnosis of lymphoplasmacytic sclerosing pancreatitis with cholangitis or the more general term, "autoimmune pancreatitis".

This patient was treated with oral prednisolone 40 mg/day for one month, tapered by 5 mg every 4 weeks. At the time of this study, he was under maintenance therapy with prednisolone 5 mg per day. Twenty two months after oral prednisolone treatment was initiated, the follow-up IgG4 level was 141 mg/dL. Trans-abdominal ultrasound revealed a normal caliber of the CBD with the ERBD in situ (Figure 5A, black arrow) and disappearance of the pancreatic head lesion (Figure 5B). However, the steroid therapy did not improve the control of pre-existing DM.

Discussion

AIP tends to occur in the sixth and seventh decades of life and predominantly in males[8-9]. Clinical

manifestations of AIP included pancreatic and extra-pancreatic symptoms, but severe abdominal pain is unusual[10]. The most common presenting symptom is obstructive jaundice accompanied by a biliary stricture and a pancreatic mass or diffusely enlarged pancreas[8,11]. The patient in our case was referred to our hospital because of painless jaundice. Extra-pancreatic manifestations such as inflammatory bowel disease[12], sclerosing cholangitis[1], retroperitoneal fibrosis[13], and chronic thyroiditis[12] were absent in this patient.

Trans-abdominal US and EUS showed a pancreatic head mass, but a CT scan only revealed uniformly enhanced pancreatic enlargement without focal lesions. In addition, ERCP did not show a typical picture of pancreatic cancer such as cut off of the main pancreatic duct, upstream ductal dilatation, and localized ductal stricture. This prompted us to investigate other possible causes of obstructive jaundice besides pancreatic head cancer. We consulted a general surgeon for the laparoscopic biopsy of the pancreatic head mass and body portion of the pancreas.

The first set of proposed diagnosis criteria of AIP was made by the Japan Pancreas Society[14], and there have since been several proposed revisions[8,15-16]. A consensus of Asian diagnostic criteria from the Japan-Korea symposium[17] were as follows: Criterion one: Diffuse, segmental, or focal enlargement of the pancreatic parenchyma, and occasionally with a pancreatic mass lesion, as well as diffuse, segmental, or focal pancreatic duct narrowing, common with bile duct stricture. Criterion two: Elevated serum levels of IgG4 or detection of other autoantibodies. Criterion three: Histopathology reveals lymphoplasmacytic infiltration with fibrosis and abundant IgG4-positive cells. Good response to steroid therapy is an optional criterion. Our patient fulfilled all of the criteria above and avoided an unnecessary Whipple operation. Therefore, AIP can present as a mass in the head of the pancreas that can mimic pancreatic cancer[18].

The pathogenetic mechanism of AIP remains unclear till now. It may be related to genetic factors, humoral and cellular immune mechanisms[19]. In a Japanese population, patients with the HLA haplotype DRB1*0405-DQB1*0401 indicated susceptibility to AIP[20]. There are various autoantibodies in patients with AIP, such as antinuclear antibody, antibodies to smooth muscle, carbonic anhydrase II, rheumatoid factor, and lactoferrin[19,21]. Anti-carbonic anhydrase II antibodies have been observed to be targets of immune response in Japanese and Spanish patients with AIP[22-23]. A recent hypothesis of a biphasic mechanism was proposed by Okazaki et al.[19] for cellular immunity, and included the processes of "induction" and "progression." Treg T cells and pro-inflammatory cytokines (IFN-γ, IL-1b, IL-2, and TNF-α) play important roles in this disease.

The treatment of choice is corticosteroids[7] with varying recommended dosages in the literature. One recommended regimen is prednisolone 40 mg/day for 4 weeks, tapered to 5 to 10 mg/day over 4 to 6 weeks and with a maintenance dose of 5 to 10 mg/day[24]. Another regimen is prednisolone 40 mg per day for one week, tapered by 5 mg per week[18]. The improvement of AIP is often dramatic after steroid therapy[7,25], and if imaging or laboratory data do not improve within 2 to 4 weeks, the diagnosis of AIP should be questioned[10]. However, spontaneous regression of obstructive jaundice, distal CBD stricture and pancreatic mass have been reported[26-27]. Nishimori et al.[28] reported that only about half of AIP patients undergoing steroid therapy experienced a beneficial effect on diabetes mellitus (DM) control.

Our patient was treated with oral steroids for more than one year. Trans-abdominal ultrasound revealed a normal caliber of CBD with ERBD in situ and decreasing size of the pancreatic head

lesion. The follow-up IgG4 level at 22 months after the initiation of steroid therapy was 141 mg/dL. Persistent elevation or fluctuating IgG4 level indicated incomplete resolution or recurrence of AIP[29-30]. In addition, the steroid therapy did not improve the pre-existing DM control. The patient was still alive and under maintenance therapy with prednisolone 5 mg per day at the time of this study.

In summary, AIP can present as a pancreatic head tumor mimicking cancer and should be kept in mind if the results of clinical images are inconclusive. The presenting patient fulfilled the diagnostic criteria of AIP. The imaging and jaundice improved after treatment, however the pre-existing DM did not improve during the steroid therapy.

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自體免疫性胰臟炎以胰臟頭腫瘤來表現：一病例報告

林建助[1] 梁程超[1] 翁孟慈[1] 李宗熙[1] 陳國鋅[2]

亞東紀念醫院 [1]內科部肝膽腸胃科 [2]外科部

摘 要

自體免疫性胰臟炎是一種良性的慢性胰臟炎與自體免疫性疾病有關，期臨床影像、實驗室檢驗、及病理學上有其特殊的表現。我們報告一例67歲男性因爲無痛性黃疸來急診求診，其本身已有一年多糖尿病的病史，腹部超音波顯示出一個在胰臟頭部4.0 x 3.3公分低迴音性的病兆，斷層掃描發現彌漫性胰臟腫大，尤其是胰臟頭部分；逆行性膽胰管攝影顯示主胰管呈現不規則狀瀰漫性狹小合併總膽管末端狹窄；內視鏡超音波則發現非均質性胰臟腫大和一個3.0 x 2.7公分相對低迴音性在胰臟頭部的病兆。因此請外科醫師做一個腹腔鏡的胰臟頭部與體部的組織切片，病理學顯示廣泛性淋巴球與漿胞球浸潤，並無癌細胞的發現；再加上血液中免疫球蛋白IgG4濃度超過160 mg/dL，因此本病例確診爲自體免疫性胰臟炎。治療的首選爲類固醇，此病患治療一年多後仍存活，其影像上及黃疸皆有改善，但糖尿病的控制並無改善。