IgG4-Related Autoimmune Pancreatitis Mimic Pancreatic Tumor with Aortitis — A Case Report

Chun-Ming Sun

Department of Medicine, Division of Rheumatology, Allergy and Immunology, Yuan's General Hospital, Kaohsiung, Taiwan

Abstract

IgG4-related diseases (IgG4-RD) are a spectrum of diseases involving many organs. Type 1 autoimmune pancreatitis is the most common disease of IgG4-RD. It often presents with obstructive jaundice and swelling of the pancreas. We report a case of a 56-year-old male with initial presentation of epigastric pain. Endoscopic abdominal sonogram, CT scan and MRI revealed a tumor over pancreatic tail. Pancreatectomy was done and the pathological report revealed IgG4-related autoimmune pancreatitis. In addition, wall thickening of the infra-renal abdominal aorta was also noted, and aortitis was diagnosed. The case emphasizes autoimmune pancreatitis be present with a pseudotumor and complete studies like IgG subclasses, including IgG4, should be included. (J Intern Med Taiwan 2015; 26: 169-173)

Key words: IgG4-RD, Autoimmune pancreatitis, Aortitis

Introduction

IgG4-related disease (IgG4-RD) is a recently recognized systemic disease characterized by elevated serum IgG4 level, IgG4-positive lymphocyte infiltration in histopathology, and fibrosclerotic change in various organs. It involves many organs, such as the pancreas, salivary gland, kidney, lung and blood vessels. Autoimmune pancreatitis is the most common presentation and reported to reach 41% in systemic case series[1]. The main presenting symptoms include jaundice, abdominal pain, pruritus, steatorrhea, and new-onset diabetes mellitus. CT scan is useful in the diagnosis and the typical features are a sausage-shaped pancreas and focal or diffuse pancreatic enlargement. However, rare cases may present with a pseudotumor. We describe a case of IgG4-related autoimmune pancreatitis with the unusual presentation of a pancreatic tumor combined with infrarenal aortitis.

Case presentation

A 56-year-old male was admitted to our emergency room due to epigastric pain radiating to the back 4-5 days previously. CT scan was done and a pancreatic tumor over tail and wall thickening of infrarenal aorta were found. He did not have fever, vomiting, diarrhea or tea-color urine presentations. Physical examination did not reveal jaundice or lymphadenopathy of the neck and inguinal

Reprint requests and correspondence：Dr. Chun-Ming Sun
Address：Department of Medicine, Division of Rheumatology, Allergy and Immunology, Yuan's General Hospital, Kaohsiung, No.162 Cheng Kung 1st Road, Kaohsiung 80249, Taiwan

area. Laboratory findings such as CBC, CRP, GOT/GPT, total bilirubin, BUN/Cr, amylase/lipase, CEA/CA19-9 were within normal limits. Epigastric pain persisted in spite of conservative treatment with analgesics. MRI of abdomen showed a pancreatic tail tumor (Figure 1) and infrarenal aortic wall thickening (Figure 2). Distal pancreatectomy and splenectomy were performed under the impression of pancreatic tumor. Pathological report showed an ill-defined nodular lesion composed of dense inflammatory cell infiltration and fibrosis in a periductal and interlobular distribution with acinar destruction and narrowing of the pancreatic ducts. The inflammatory infiltrate consisted predominantly of lymphocytes and plasma cells with formation of lymphoid follicles (Figures 3A and 3B). In the immunohistochemical study, the lymphocytes were slightly more CD3-positive T cells than CD20 positive B cells and many CD138-positive plasma cells were positive for IgG4 (more than 30 cells/HPF) (Figure 3C). An IgG4-associated autoimmune pancreatitis was diagnosed. Serum IgG4 was checked and shown to be slightly elevated. Other immunological studies were done as shown below (Table 1). After the operation, the patient was followed at OPD and prednisolone was prescribed. The post-operative course was smooth.

Discussion

Autoimmune pancreatitis (AIP) is divided into

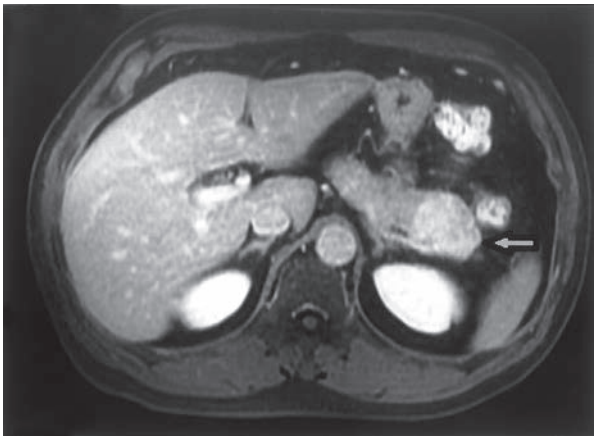

Figure 1. Axial contrast-enhanced MRI scan shows a heterogeneously-enhanced nodule in the pancreatic tail.

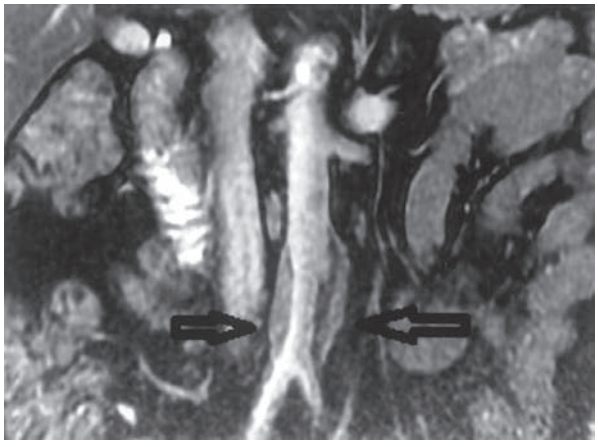

Figure 2. Coronal FIESTA MRI scan shows segmental infrarenal aortic wall thickening.

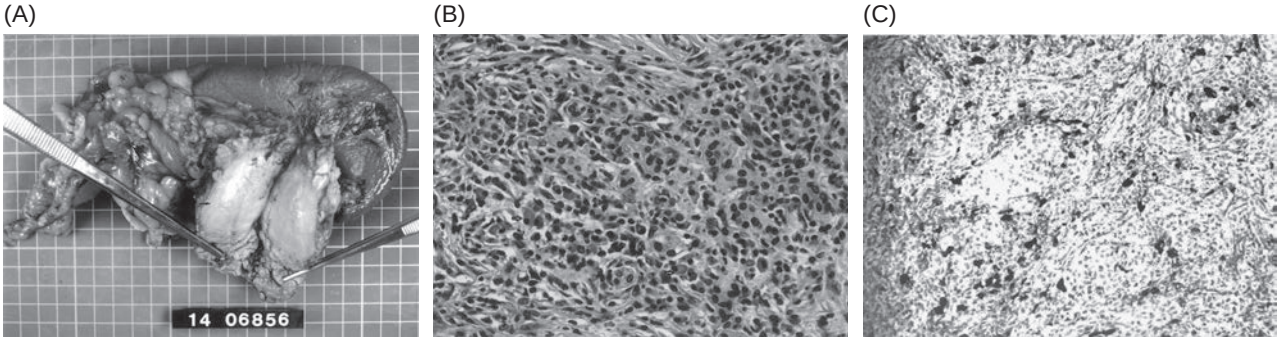

Figure 3. (A) An ill-defined, yellowish-white and firm pancreatic tumor measuring 5.0 × 3.5 × 3.0 cm in size. (B) Hematoxylin and eosin staining shows dense lymphoplasmacytic infiltrate in a fibrotic stroma (× 200). (C) Immunoglobulin G4 (IgG4) staining shows markedly increased (>30/high power filed) periductal IgG4+ plasma cell infiltrate (×200).

Table 1. Immunological profile

ANA	RF (≦15)	C3	C4	ESR (0-15)
1:80H	34.7	137	29.5	44
CRP (≦0.3)	IgG	IgG4 (3.9-86.4)		
0.32	1210	107		

types 1 and 2. Type 1 AIP is IgG4-related pancreatitis, which is also called lymphoplasmacytic sclerosing pancreatitis (LPSP) because of its histopathological findings. Type 1 AIP is considered as being in the group of IgG4-RD. The typical findings of IgG4-RD show diffuse or focal organ enlargement and mass-forming or nodular/thickened lesions in various organs. The organs known to be affected include the pancreas, biliary duct, lacrimal/salivary glands, retroperitoneum, central nervous system, thyroid gland, lungs, liver, gastrointestinal tracts, kidneys, prostate gland, and lymph nodes. The etiology of IgG4-RD is unknown. Recently, abnormal innate immunity has been demonstrated in patients with IgG4-RD. In addition, IgG4 may play a role of pathogenesis. A recent study suggested that Fc-Fc interactions are compatible with intact IgG4 molecules and may provide a model for the formation of aggregates of IgG4 that can cause disease pathology in the absence of antigen[2]. However, another data suggested that IgG4 does not act as a pathogenic factor, but as an anti-inflammatory factor in IgG4-RD. Further studies are necessary to clarify the precise role of IgG4 in IgG4-RD.

We present the rare case of type 1 autoimmune pancreatitis presenting with a tumor-like lesion and not associated with other typical symptoms. He was not icteric and not febric. Serum amylase and lipase were normal. The course of illness is not characteristic of obstructive jaundice or acute pancreatitis. Our explanation is that the tumor was located at the pancreatic tail and the focal inflammation was not severe. According to the literature[3], the type 1 AIP is characterized in old age and male patients, which is consistent with our case. In addition, type 1 AIP is more often related with other organ involvement. In our case, the AIP was synchronously associated with aortitis. The biochemistry findings in type 1 AIP are not specific. The inflammatory markers are usually high. Specific immunological markers for IgG4-RD are IgG, IgG4 and IgE. Because the AIP was not included in the differential diagnosis before operation, the immunological markers were checked after the diagnosis was made. IgG level was normal and IgG4 level was mildly elevated. These findings are not characteristic of AIP patients. The radiologic finding of our case was a tumor-like lesion of pancreatic tail. There was no focal or diffuse swelling in the pancreas like most type 1 AIP patients. The differentiation of focal type AIP and pancreatic cancer has been studied, and it was found that accuracy of diagnosis of AIP was high if serum IgG4 was over 280 mg/dL and CA19-9 was below 85.0 U/ml[4].

In addition, some specific findings of CT scan are highly suspected in focal AIP, including homogeneous enhancement during the portal phase, dotted enhancement during the pancreatic phase, duct-penetrating sign, enhanced duct sign and capsule-like rim[5].

AIP may be associated with other autoimmune diseases, such as Sjogren syndrome, idiopathic retroperitoneal fibrosis and inflammatory bowel disease. The rheumatoid factor and ANA were positive in our patient; however, there was no skin rash, arthralgia, dry mouth or dry eye, nor other associated symptoms compatible with autoimmune diseases in our patient.

Autoimmune pancreatitis may be associated with other extrapancreatic lesions. In one study, 45% of autoimmune pancreatitis had extrapancreatic lesions[6]. The extrapancreatic lesions include sclerosing cholecystitis/cholangitis, swelling of bilateral salivary glands, retroperitoneal mass, cervical

lymphadenopathy, and inflammatory pseudotumor of the lung. Our case is synchronous with aortitis, which is rare in the past. Reviewing the literature, only one case has been reported in Taiwan[7]. In one study of CT findings of the IgG4-related periaortitis and periarteritis, the most common location is the abdominal aorta to iliac arteries[8]. The typical findings are well-circumscribed circumferential wall thickening, no cystic change or calcification, and no lymph nodes in the adjoining region. These characteristics are compatible with our case.

Corticosteroid treatment is the first line therapy for IgG4-RD. The optimal doses of steroid for IgG4-RD are still unclear. For AIP, an initial oral prednisolone dose of 0.6mg/kg/day and a maintenance dose of 2.5-5mg/day have been recommended before[9]. Relapse is noted after steroid discontinuation. An initial dose of 20mg/day was reported to be effective at diminishing the aortic wall thickness[6]. IgG4-RD is an increasingly recognized condition in adults, with a heterogeneous clinically presentation affecting a wide range of organ systems. We present a case with unusual presentation of AIP, which was misdiagnosed as a pancreatic tumor. We emphasize that AIP should be considered in the differential diagnosis of pancreatic tumors.

References

1. Brito-Zerón P, Ramos-Casals M, Bosch X, et al. The clinical spectrum of IgG4-related disease. Autoimmun Rev 2014; 13: 1203-10.
2. Davies AM, Rispens T, Ooijevaar-de Heer P, et al. Structural determinants of unique properties of human IgG4-Fc. J MolBiol 2014; 426: 630-44.
3. Shimosegawa T, Chari ST, Frulloni L, et al. International consensus diagnostic criteria for autoimmune pancreatitis. Guidelines of the International Association of Pancreatology. Pancreas 2011; 40: 352-8.
4. Chang MC, Liang PC, Jan S, Yang CY, Tien YW, Wei SC, Wong JM, Chang YT. Increase diagnostic accuracy in differentiating focal type autoimmune pancreatitis from pancreatic cancer with combined serum IgG4 and CA19-9 levels. Pancreatology 2014; 14: 366-72.
5. Furuhashi N, Suzuki K, Sakurai Y, Ikeda M, Kawai Y, Naganawa S. Differentiation of focal-type autoimmune pancreatitis from pancreatic carcinoma: assessment by multiphase contrast-enhanced CT. Eur Radiol 2015; 25: 1366-74.
6 Takuma K, Kamisawa T, Anjiki H, et al. Metachronous Extrapancreatic Lesions in Autoimmune Pancreatitis. Intern Med 2010; 49: 529-33.
7. Tseng CW, Tsai JJ, Chen CC. Abdominal Aortitis Associated With Autoimmune Pancreatitis. Clin Gastroenterol Hepatol 2009; 7: e3-4.
8. Inoue D, Zen Y, Abo H, et al. Immunoglobulin G4–related periaortitis and periarteritis: CT findings in 17 patients. Radiology 2011; 261: 625-33.
9. Kamisawa T, Takuma K, Hara S, et al. Management strategies for autoimmune pancreatitis. Expert Opin Pharmacother 2011; 12: 2149-59.

第四型免疫球蛋白G相關之自體免疫性胰臟炎合併主動脈炎—病例報告

孫俊明

阮綜合社團法人阮綜合醫院　過敏風濕免疫科

摘　要

有一群和第四型免疫球蛋白G相關的疾病目前被廣泛的討論，其中最常見的就是第一型自體免疫性胰臟炎。第一型自體免疫性胰臟炎經常表現出阻塞性黃疸及胰臟腫大。我們報告一個罕見的病例是以上腹痛及胰臟腫瘤來表現，開刀後病理檢查才證實是第一型自體免疫性胰臟炎。此外，放射線檢查也發現病人的腹主動脈有一段管壁有明顯增厚，證實有主動脈炎。這個病例提醒我們當病人出現不尋常的胰臟腫瘤，自體免疫性胰臟炎必須要當作是鑑別診斷之一。