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A Case of Immunoglobulin G4-Related Autoimmune Pancreatitis With Extreme Hypergammaglobulinemia

To the Editor:

Autoimmune pancreatitis (AIP) is an infrequently recognized disorder of presumed autoimmune etiology that belongs to the spectrum of immunoglobulin G4 (IgG4)-related diseases.¹ In 2006, the Mayo Clinic proposed the diagnostic criteria for AIP, according to characteristic clinical, histologic, and morphologic findings.² Typical AIP patients present with obstructive jaundice and have a good response to glucocorticoid. However, few reported cases of AIP patients had extreme hypergammaglobulinemia, hypoalbuminemia, and long duration.

A 78-year-old male patient was admitted to Peking Union Medical College Hospital in 2017 with persistent enlargement of the pancreas head in imaging and intermittent abnormal liver function for over 9 years. Edema of his eyelids appeared for 1 month. In 2008, the elderly man was first diagnosed as having enlargement of the pancreas head (Figs. 1A, B) in health examination with normal serum carbohydrate antigen 19-9. From 2009 to 2016, he was regularly followed up with abdominal magnetic resonance imaging or computed tomography (CT), and the size of the pancreas head ranged from 4.7×3.7 cm to 2.4×2.0 cm (Figs. 1C, D). During this period, the patient had only minor abnormality of elevated alkaline phosphatase without dominant jaundice and insulin-controlled diabetes mellitus. He was treated with biliary stent implantation and replacements via endoscopic retrograde cholangiopancreatography several times, and his liver function improved. During the 9 years, the patient was in good condition without loss of weight.

One month ago, the patient presented with edema of both eyelids and referred to our hospital. He was in good general condition. Normal bilirubin, liver enzymes, and carbohydrate antigen 19-9 were found. The inflammatory markers showed a C-reactive protein of 2.42 mg/L (reference range, 0–5 mg/L) and erythrocyte sedimentation rate of 101 mm/h (reference range, 0–15 mm/h). The obvious laboratory abnormalities illustrated globulin of 111 g/L (reference range, 14–52 g/L), IgG

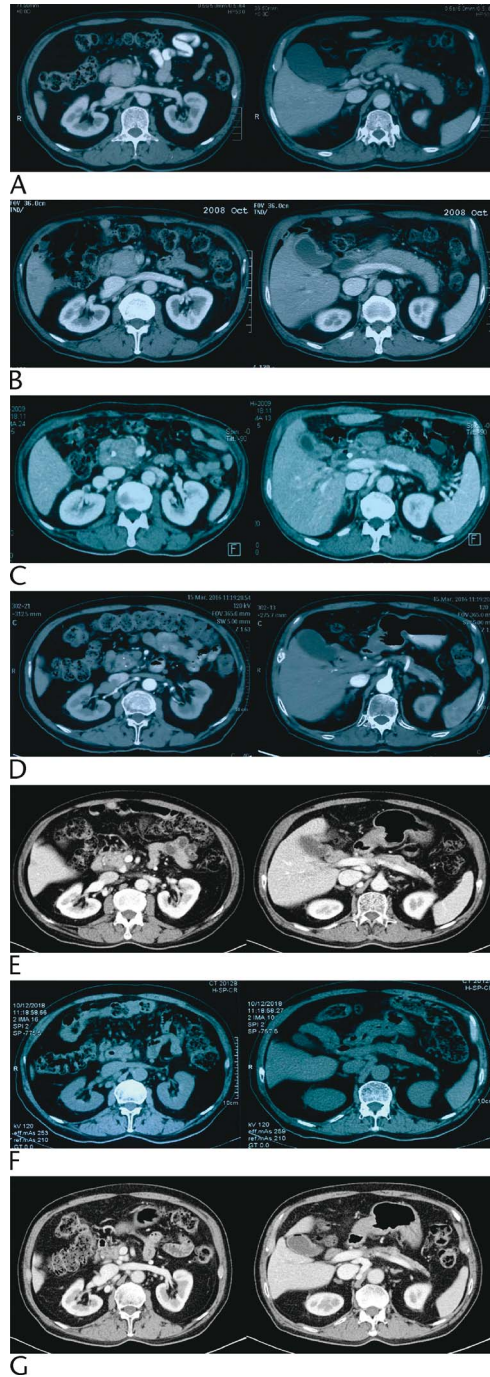


FIGURE 1. Images of the pancreas from 2008 to 2019. A, An enhanced CT scan from March 2008 showed an enlarged head of the pancreas with a smooth contour and even enhancement. The body and tail of the pancreas were slightly swollen and appeared sausage-like with low-density capsular margin. B, In October 2008, the swelling of the pancreas seemed to be slightly resolved and a low-density “sheath-like” structure around the pancreas was clearly demonstrated. C, In June 2009, the enlargement of the pancreas head was more obvious than before, and the common bile duct was dilated. D, In May 2016, the pancreatic head was significantly reduced in size. The body and tail of the pancreas atrophied. E, In April 2017, the enlarged pancreatic head and atrophied pancreatic body/tail were found, with uneven thicknesses and local stenosis of the pancreatic duct and common bile duct. F, In 2018, after treatment, the head of the pancreas was significantly smaller than before, the tail of the pancreas was atrophied, the pancreatic duct showed no obvious expansion, and there were no obvious sheath-like changes in the pancreatic circumference. G, In September 2019, with a maintenance dose of 5 mg/d, the head, tail, and duct of the pancreas had no significant differences from those in 2018.

of 91.13 g/L (reference range, 7–17 g/L), and IgG4 of 31.5 g/L (reference range, 0.08–1.4 g/L). Serum protein electrophoresis revealed that the percentage of γ protein was elevated at 61.8% (reference range, 9.1%–24.0%). No monoclonal proteins were found in the blood or urine immunofixation electrophoresis. Bone marrow aspiration and biopsy revealed no malignancy. In contrast to hypergammaglobulinemia, hypoalbuminemia with serum albumin of 21 g/L (reference range, 35–52 g/L) was detected, which might result in edema. Our pancreatic CT image showed a swollen pancreatic head, an atrophied pancreatic tail, and an unevenly thickened pancreatic duct and common bile duct with local stenosis (Fig. 1E). Multiple enlarged lymph nodes with elevated metabolism (standardized uptake value [SUV], 7.9), swollen bilateral lacrimal glands and submandibular glands (SUV, 3.3), and enlarged pancreatic head and thickened lower common bile duct (SUV, 3.0) were revealed in the positron emission tomography/CT.

Therefore, the patient was suspected as having possible IgG4-related AIP. Because he refused to undergo lymph node biopsy or pancreatic fine-needle aspiration to exclude malignancy, he was prescribed as prednisone 0.6 mg/kg per day for 1 month as empirical therapy and tapered down to 5 mg/d as maintenance therapy. As a result of the glucocorticoid response, the level of IgG4 decreased from 31.5 g/L to 6.25 g/L, the globulin decreased from 111 g/L to 31 g/L, and the IgG decreased from 91.13 g/L to 17.79 g/L. In the meantime, the albumin level increased, and edema disappeared. The following imaging showed that the enlarged pancreatic head and thickened bile duct normalized (Figs. 1F, G), as well as the enlarged lymph nodes. The patient was, and is still currently, being followed up.

The specific characteristic of our AIP patient is extreme hyperglobulinemia, which is uncommon. In the study by Wang et al³ including 215 patients, the mean levels of IgG and IgG4 were 23.0 and 15.2 g/L, respectively. Based on the previous research,^{4,5} high level of serum IgG4 might be related to hematologic manifestations, good response to glucocorticoid, and a high rate of relapse. According to the study from Kim et al⁶ in 2010, the glucocorticoid dosage for inducing remission was 30 to 40 mg/d for 1 to 2 months, and remission maintenance was needed to prevent relapse with a dosage of 5 to 10 mg/d for at least 6 months in patients who did not achieve complete remission. Furthermore, immunosuppressive agents such as azathioprine could be used for

relapsed patients with AIP. Our patient with high level of serum IgG and IgG4 had good response to glucocorticoid and no evidence of relapse with 5 mg/d prednisone for maintenance of remission.

Another special characteristic is long-time course of disease. Autoimmune pancreatitis is one type of chronic pancreatitis, but it is unknown how long the natural course is. Our patient was 78 years old and was found to have a swollen pancreatic head nearly 10 years before being diagnosed and treated with glucocorticoid. In the study by Lin et al with 118 Chinese AIP patients, the mean age at diagnosis was 53.1 years, and the mean disease duration was 26.8 months.⁷ Therefore, our patient with a 108-month disease course is truly unusual.

From this AIP case, we illustrated that a high level of serum IgG4 might indicate good sensitivity to glucocorticoid, and elderly patients might endure a long course of disease without symptoms. Although this patient has a good condition at present, we still should be aware of the relapse of disease and the risk of hematologic malignancy in the follow-up.

The authors declare no conflict of interest.

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Surgical Treatment of Pancreaticoduodenal Artery Aneurysm Due to Median Arcuate Ligament Syndrome for Which Intraoperative Doppler Ultrasonography Was Beneficial A Case Report

To the Editor:

Although the first case of a pancreaticoduodenal artery aneurysm (PDAA) was reported by Ferguson¹ in 1895, most of the publications since then have been case reports. Pancreaticoduodenal artery aneurysms are rare and account for 2% of all visceral aneurysms.² Almost half of all PDAAAs are associated with celiac axis stenosis (CAS)² and median arcuate