

Autoimmune pancreatitis with pancreatic calculi and pseudocyst: a case report

Xiaobing Cui^{1,*} , Wen Xu^{1,*},
Yingchun Zhang¹, Fang Wang¹, Pei Guo² and
Wei Gong¹

Abstract

Autoimmune pancreatitis (AIP) is a unique form of pancreatitis often associated with infiltration of immunoglobulin G4-positive cells, a swollen pancreas, and diffuse narrowing of the pancreatic ducts. Unlike acute pancreatitis, AIP is rarely complicated with pseudocysts. Pancreatic calculi, a feature of ordinary chronic pancreatitis, are unusual during short-term follow-up in patients with AIP. We herein describe a 46-year-old man who initially presented with a submucosal tumor of the stomach. The patient was finally diagnosed with AIP accompanied by a pancreatic tail pseudocyst located in the gastric wall and pancreatic calculi by endoscopic ultrasonography-guided fine-needle aspiration. He underwent endoscopic retrograde cholangiopancreatography, pancreatic duct stent placement, and steroid treatment and achieved good clinical and laboratory responses. Although AIP is a common autoimmune disease that responds well to steroids, pseudocysts and pancreatic calculi are rare manifestations of AIP and should be given special attention, especially in patients with disease relapse.

Keywords

Autoimmune pancreatitis, case report, endoscopic ultrasonography, pancreatic calculus, pancreatic pseudocyst, immunoglobulin G4

Date received: 19 August 2020; accepted: 13 April 2021

¹Department of Digestive Medicine, Shenzhen Hospital of Southern Medical University, Shenzhen, Guangdong, People's Republic of China

²Department of Pathology, Shenzhen Hospital of Southern Medical University, Shenzhen, Guangdong, People's Republic of China

*These authors contributed equally to this work and are considered co-first authors.

Corresponding author:

Wei Gong, Department of Digestive Medicine, Shenzhen Hospital of Southern Medical University, No. 1333 Xinhua Road, Baoan District, Shenzhen, Guangdong 518000, People's Republic of China.
Email: drgwei@foxmail.com



Introduction

Autoimmune pancreatitis (AIP) is a term coined by Yoshida et al.¹ in 1995 to indicate diffuse enlargement of the pancreas and narrowing of the pancreatic ducts related to hyperglobulinemia; it is an autoantibody-positive and steroid-responsive syndrome. The symptoms of AIP include weak or mild abdominal pain, general fatigue, weight loss, jaundice, and various extrapancreatic lesions.² However, pseudocysts, a common complication of acute pancreatitis, rarely develop in patients with AIP.³ Because AIP often responds well to steroid therapy, pancreatic calculi are regarded as an uncommon complication during short-term follow-up.⁴

We herein describe a 46-year-old man who underwent gastroscopy because of a persistent dull pain in his left upper abdomen and was found to have a gastric subepithelial tumor. After further evaluation, he was diagnosed with AIP accompanied by a pseudocyst and pancreatic calculi. He had a good response to steroid treatment after a 2-month follow-up. This is the first reported case of AIP with a simultaneous pancreatic pseudocyst and pancreatic duct calculi.

Case report

A 46-year-old man visited Shenzhen Hospital of Southern Medical University because of a 1-week history of a persistent dull pain in his left upper abdomen. His pain was unrelated to meals or movement. He had no nausea, vomiting, diarrhea, jaundice, chills, or fever. He had no history of chronic disease. He had a history of smoking 7 to 8 cigarettes per day for more than 10 years. He was not an alcohol drinker.

Gastroscopic examination revealed a submucosal mass in the upper gastric body with an obscure boundary and

swollen mucosa (Figure 1(a)). The patient was referred to the inpatient department of digestive medicine for further evaluation and treatment.

Physical examination of the patient's abdomen revealed a soft, nontender spot with no palpable mass and normoactive bowel sounds. His vital signs were within their normal ranges.

Contrast-enhanced computed tomography (CT) of the upper abdomen showed a 23- × 17-mm hypodense focus on the fundus (Figure 1(b)). The pancreas exhibited diffuse swelling with partial atrophy (Figure 1(c)), and a 5- × 5-mm hyperdense focus was present in the pancreatic body (Figure 1(d)) with low attenuation of the peripancreatic area. The pancreatic duct showed mild dilation, but the bile duct was normal. Both kidneys showed multiple low-density areas in the parenchyma, indicating immunoglobulin G4 (IgG4)-associated renal involvement (Figure 1(d)). Laboratory test results were as follows: elevated fasting blood glucose (FBG), 6.06 mmol/L (reference range, 4.11–5.89 mmol/L); amylase, 309 U/L (reference range, 30–110 U/L); lipase, 685.5 U/L (reference range, 23–300 U/L); erythrocyte sedimentation rate, 103 mm/hour (reference range, 0–15 mm/hour); IgG, 19.51 g/L (reference range, 7–16 g/L); and IgG4, 15.00 g/L (reference range, 0.03–2.01 g/L). Routine blood tests, liver and renal function tests, and tumor markers [including carbohydrate antigen-199 (CA-199), CA-125, carcinoembryonic antigen, alpha-fetoprotein, and CA-153] were within their reference ranges. Viral marker tests for chronic hepatitis B and C, an anti-human immunodeficiency virus antibody test, a purified protein derivative test, and autoantibody tests were all negative.

We performed endoscopic ultrasonography-guided fine-needle aspiration (EUS-FNA) to attain a final diagnosis. During the procedure, endoscopic

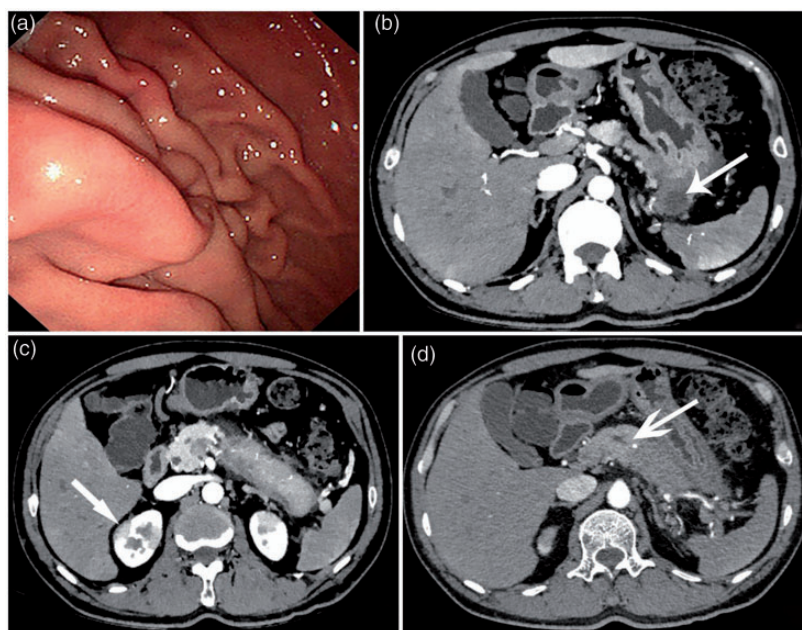


Figure 1. Gastroscopy and computed tomography (CT) findings at the patient's first visit to our hospital. (a) Gastroscopy showed a submucosal mass in the upper gastric body. (b) CT showed a submucosal mass in the fundus (arrow). (c) CT showed a swollen pancreas with partial atrophy and multiple low-density areas in the renal parenchyma (arrow). (d) CT showed calculi in the pancreatic body with pancreatic duct dilation (arrow).

inspection revealed a 27.3×14.9 mm hypoechoic lesion in the gastric fundus with no echo area in the middle, which was in the lamina propria and serosa. After injection of sulfur hexafluoride microbubbles, the hypoechoic area was slightly enhanced and the non-echo area showed no enhancement (Figure 2(a)). A hyperechoic focus of 5.3×4.6 mm (Figure 2(b)) and pancreatic duct dilation in the pancreatic body were observed by EUS (Figure 2(c)). EUS-FNA of the fundic lesion and pancreas was performed with a stylet slow-pull technique using a 19-gauge EUS aspiration needle.

The EUS-FNA histopathological findings revealed inflammatory cells and spindle-shaped macrophages in biopsy samples of the pancreas (Figure 3(a)). Immunohistochemistry showed scattered IgG4- and IgG-positive inflammatory

cells in the samples (Figure 3(b), (c)). Inflammatory cells and epithelial cells were observed in samples of the fundic lesion (Figure 3(d)). Based on the serum IgG4 elevation, endoscopic and CT imaging findings, and exclusion of neoplasia, the patient was finally diagnosed with IgG4-related AIP complicated by a pseudocyst localized in the gastric wall and pancreatic calculi. However, because of the lack of unbroken tissue, the pathological findings were only a reference and could not be used as a basis for diagnosis.

Therefore, the patient underwent endoscopic retrograde cholangiopancreatography along with endoscopic sphincterotomy and pancreatic duct stent placement for pancreatic drainage (Figure 2(d), (e)). Outpatient oral prednisone treatment was started at a dosage of 70 mg/day, which

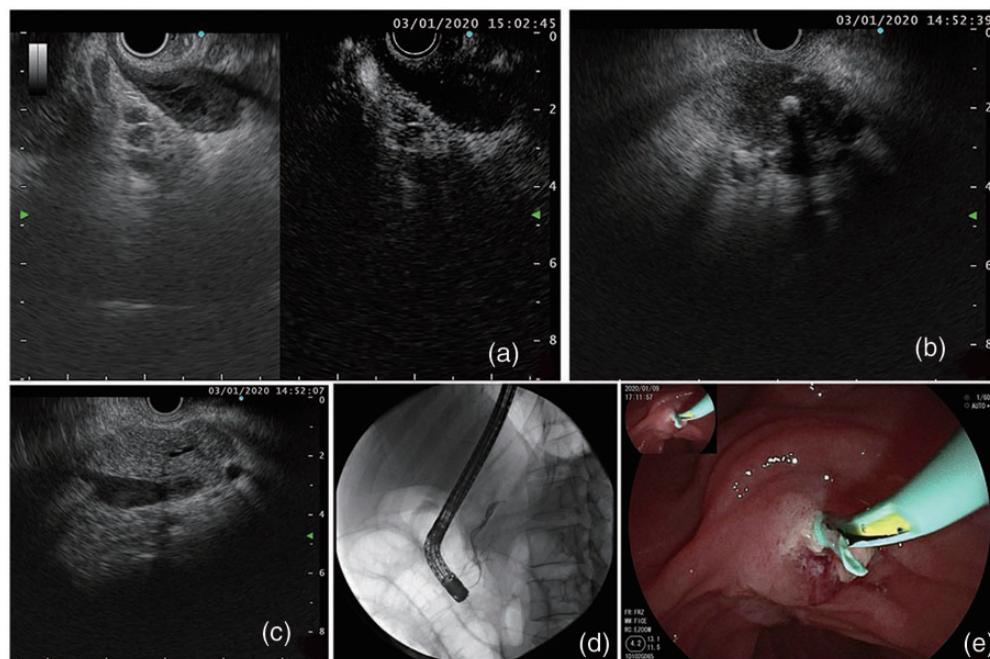


Figure 2. Endoscopic ultrasound (EUS) and endoscopic retrograde cholangiopancreatography findings of the patient. (a) EUS showed a gastric abscess with surrounding enhancement after injection of sulfur hexafluoride microbubbles. EUS showed (b) calculi and (c) pancreatic duct dilation in the pancreatic body. (d) Endoscopic retrograde cholangiopancreatography showed pancreatic duct dilation. (e) Pancreatic duct stent placement was performed.

was reduced by 10 mg every 2 weeks. After 2 months of steroid treatment, the patient's abdominal pain was completely relieved. CT (Figure 4(a), (b)) and EUS (Figure 4 (c), (d)) revealed an improvement in the diffuse pancreatic swelling, disappearance of kidney involvement, and complete resolution of the pseudocyst. However, EUS also revealed that the pancreatic stent had spontaneously fallen off and that multiple hyperechoic foci remained in the pancreatic body, the largest of which measured 6.2×5.1 mm (Figure 4(d)). Laboratory tests showed elevated FBG (6.82 mmol/L), improved IgG4 (4.68 g/L) and IgG (10.1 g/L) levels, and normalization of amylase (57 U/L), lipase (40.6 U/L), and the erythrocyte sedimentation rate (10 mm/hour). At the time of this writing, the patient was

being treated with a gradual reduction of prednisone and was still undergoing outpatient follow-up.

Discussion

AIP is a unique form of pancreatitis categorized into types 1 and 2. Type 1 presents as lymphoplasmacytic sclerosing pancreatitis with IgG4 infiltration and serum IgG4 elevation. Type 2 presents as idiopathic duct-centric pancreatitis and lacks IgG4 elevation.⁵ In the present case, although the pancreatic histology did not meet the diagnostic criteria² (>10 cells/HPF of IgG4-positive cells) because of the lack of unbroken tissue, another important purpose of EUS-FNA was to exclude pancreatic carcinoma before steroid treatment.

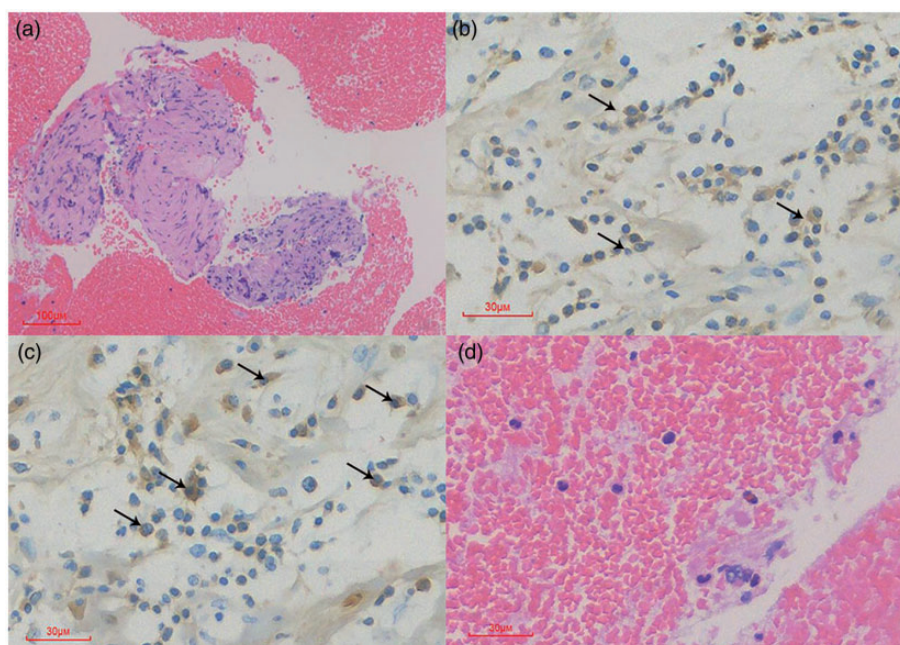


Figure 3. Pathologic findings of the samples obtained by endoscopic ultrasound-guided fine-needle aspiration. (a) Microscopic view showed staining of inflammatory cells and spindle-shaped macrophages in biopsy samples of the pancreas (hematoxylin–eosin staining, $\times 100$). Immunohistochemistry showed (b) scattered IgG-positive cells (3/HPF) and (c) IgG4-positive cells (5/HPF) in biopsy samples of the pancreas ($\times 400$) (arrow). (d) Microscopic view showed inflammatory cells and blood clots in biopsy samples of the gastric lesion (hematoxylin–eosin staining, $\times 400$).

No malignant cells were observed in the tissue samples obtained; however, the patient presented with a diffuse swollen pancreas, serum IgG4 elevation ($>2\times$ upper limit of reference range), kidney involvement, CA-199 within the reference range, and a good steroid response. Therefore, we excluded pancreatic carcinoma and finally diagnosed the patient with type 1 AIP.

Pseudocysts are common in acute pancreatitis but are rarely reported in AIP. The formation of a pseudocyst in a patient with AIP might be related to the activation of inflammatory processes and pancreatic ductal disruption along with leakage of pancreatic juice.⁶ Therefore, in the present case, we performed endoscopic retrograde cholangiopancreatography and pancreatic

duct stent placement to drain the pancreatic juice. Steroid treatment is clinically, radiologically, and serologically effective for AIP.⁶ According to current reports, small pseudocysts (<3 cm) respond well to steroid treatment whereas large pseudocysts (>3 cm) do not; instead, the latter require endoscopic or surgical intervention.³ In this case, the subepithelial tumor in the gastric fundus was finally diagnosed as a pancreatic tail pseudocyst, and the patient recovered well after pancreatic juice drainage and steroid treatment. This outcome indicates that comprehensive therapy is necessary for patients with AIP according to their situation.

AIP was historically considered a non-progressive disease that did not lead to pancreatic calculi formation or chronic

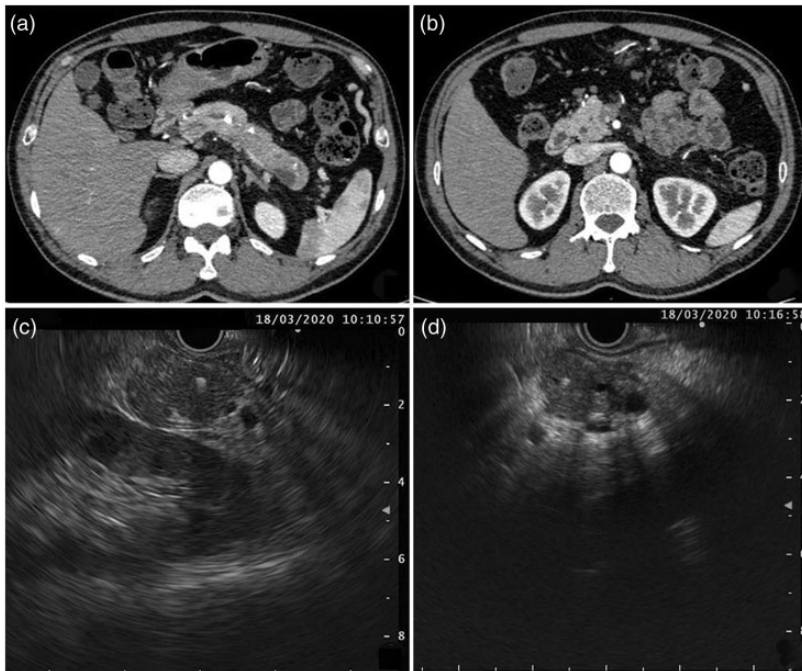


Figure 4. Computed tomography and endoscopic ultrasound (EUS) findings at the patient's follow-up visit after steroid treatment. (a) Follow-up computed tomography showed alleviation of the swollen pancreas and (b) disappearance of low-density areas in the renal parenchyma. (c) EUS showed that pancreatic calculi remained in the pancreatic body. (d) EUS showed complete resolution of the pseudocyst and the new appearance of pancreatic calculi in the pancreatic tail.

pancreatitis because it responded well to steroid treatment.¹ However, more recent research has revealed that some patients with relapse of AIP develop pancreatic calculi formation, pancreatic atrophy, exocrine or endocrine dysfunction, and/or pancreatic duct dilation over the long term,^{7,8} which meet the diagnostic criteria for chronic pancreatitis.⁹ Pancreatic juice stasis secondary to narrowing of the duct of Wirsung and duct of Santorini results in increased intrapancreatic duct pressure and eventually leads to calculi development;^{7,10} therefore, we performed pancreatic duct stent placement and endoscopic sphincterotomy to drain the pancreatic juice in an attempt to eliminate the calculi. However, although the patient's disease course was short, the patient presented

with continuous FBG elevation, focal pancreatic body atrophy, upstream pancreatic duct dilation, and increased pancreatic calculi formation even after pancreatic juice drainage. These findings indicate that AIP may progress to a chronic stage. In future follow-up studies, we should consider the possibility of relapse, exocrine or endocrine dysfunction, and even the potential of malignancy.

In conclusion, type 1 AIP is a pancreatic manifestation of IgG4-related disease and often responds well to steroid treatment. However, special and infrequent complications of AIP such as pseudocysts and pancreatic calculi should be considered over the long term, especially in patients with disease relapse. Endoscopic intervention should be personalized for accurate diagnosis and

effective treatment. Further studies of the long-term follow-up and prognosis of AIP are required.

Acknowledgment

We thank Edanz Group China (www.liwenbianji.cn/ac) for editing the English text of a draft of this manuscript.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Ethics

Written informed consent was obtained from the patient described in this case report. The requirement for ethics approval was waived because of the nature of the study (case report). The patient's privacy has been protected.

Funding

This work was supported by the Medical Scientific Research Foundation of Guangdong Province of China (A2019564) and by the Research Foundation of Shenzhen Hospital of Southern Medical University (PT2018KY01).

ORCID iD

Xiaobing Cui  <https://orcid.org/0000-0002-5200-6960>

References

1. Yoshida K, Toki F, Takeuchi T, et al. Chronic pancreatitis caused by an autoimmune abnormality. Proposal of the concept of autoimmune pancreatitis. *Dig Dis Sci* 1995; 40: 1561–1568. DOI: 10.1007/bf02285209.
2. 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: 352–358. DOI: 10.1097/MPA.0b013e3182142fd2.
3. Donet JA, Barkin JA, Keihanian T, et al. Pancreatic pseudocysts and parenchymal necrosis in patients with autoimmune pancreatitis: a systematic review. *Pancreas* 2018; 47: 952–957. DOI: 10.1097/mpa.0000000000001121.
4. Ikeura T, Miyoshi H, Shimatani M, et al. Long-term outcomes of autoimmune pancreatitis. *World J Gastroenterol* 2016; 22: 7760–7766. DOI: 10.3748/wjg.v22.i34.7760.
5. Proctor RD, Rofe CJ, Bryant TJ, et al. Autoimmune pancreatitis: an illustrated guide to diagnosis. *Clin Radiol* 2013; 68: 422–432. DOI: 10.1016/j.crad.2012.08.016.
6. Sohn JW, Cho CM, Jung MK, et al. A case of autoimmune pancreatitis manifested by a pseudocyst and IgG4-associated cholangitis. *Gut Liver* 2012; 6: 132–135. DOI: 10.5009/gnl.2012.6.1.132.
7. Ito T, Kawa S, Matsumoto A, et al. Risk factors for pancreatic stone formation in type 1 autoimmune pancreatitis: a long-term Japanese multicenter analysis of 624 patients. *Pancreas* 2019; 48: 49–54. DOI: 10.1097/mpa.0000000000001210.
8. Maruyama M, Watanabe T, Kanai K, et al. Autoimmune pancreatitis can develop into chronic pancreatitis. *Orphanet J Rare Dis* 2014; 9: 77. DOI: 10.1186/1750-1172-9-77.
9. Shimosegawa T, Kataoka K, Kamisawa T, et al. The revised Japanese clinical diagnostic criteria for chronic pancreatitis. *J Gastroenterol* 2010; 45: 584–591. DOI: 10.1007/s00535-010-0242-4.
10. Maruyama M, Arakura N, Ozaki Y, et al. Risk factors for pancreatic stone formation in autoimmune pancreatitis over a long-term course. *J Gastroenterol* 2012; 47: 553–560. DOI: 10.1007/s00535-011-0510-y.