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Case Presentation

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A Case of Isolated Pancreatic Sarcoidosis with Unprecedented Imaging Findings

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Abstract

Pancreatic involvement in systemic sarcoidosis is infrequently observed, furthermore, isolated pancreatic sarcoidosis is extremely rare. A 47-year-old female presented epigastric and back pain. Contrast-enhanced CT showed diffuse swelling of the pancreas and a thin hypodense area surrounding the pancreas. PET-CT showed FDG accumulation in the whole pancreas, but no obvious abnormal accumulation in other organs. Endoscopic ultrasonography (EUS) showed diffuse pancreatic enlargement, with prominent swelling of the pancreatic head. Hyperechoic foci, strands and

lobularity were observed in the pancreatic parenchyma. Contrast-enhanced harmonic EUS revealed homogeneous enhancement of the pancreatic parenchyma, which persisted continuously. EUS-guided fine needle biopsy was performed and the pathological findings showed noncaseating granulomas. The patient was diagnosed with isolated pancreatic sarcoidosis. The symptoms spontaneously disappeared, therefore steroid therapy was not initiated. Two months after the onset, CT scan showed marked improvement in pancreatic enlargement. In the literatures, pancreatic sarcoidosis predominantly demonstrates hypovascular mass lesions and enlarged lymph nodes on imaging. In contrast, all imaging studies in our case demonstrated diffuse enlargement of the pancreas, resembling autoimmune pancreatitis, with no identifiable pancreatic mass lesion. To the best of our knowledge, such findings have not been reported previously.

Keywords: Pancreatic sarcoidosis; Contrast-enhanced harmonic endoscopic ultrasonography; Endoscopic ultrasound guided fine needle aspiration/biopsy; Noncaseating granulomas; Autoimmune pancreatitis

Introduction

Sarcoidosis is a chronic systemic disease of unknown etiology, characterized by the presence of noncaseating granulomas in affected tissues [1,2]. It primarily affects young and middle-aged adults and can involve multiple organ systems, most commonly the hilar lymph nodes (typically bilaterally), lungs, heart, liver, spleen, eyes, kidneys, lymph nodes, salivary glands, nervous system, muscles, and bones [3,4]. However, involvement of other organs is rare. Pancreatic involvement in sarcoidosis is particularly uncommon and is often identified postmortem. Autopsy studies have reported pancreatic sarcoidosis in 1–5% of patients with systemic sarcoidosis [1,3,5-8], while isolated pancreatic sarcoidosis is exceedingly rare. Due to its infrequent occurrence, the radiological characteristics of pancreatic sarcoidosis remain poorly defined. To date, only a limited number of reports have described its imaging features using Computed Tomography (CT), Magnetic Resonance Imaging (MRI) [9-11], or Endoscopic Ultrasonography (EUS) [7]. Herein, we report a case of isolated pancreatic sarcoidosis with unprecedented imaging findings.

Case Presentation

A 47-year-old woman visited her local doctor because of the onset of epigastric and back pain. Blood tests showed elevated pancreatic enzymes, therefore acute pancreatitis was suspected. Then, the patient was referred to our hospital. Her medical history included sialolithiasis. She smoked a pack of cigarettes and drank occasionally. Her abdomen was flat and soft, without tenderness. Laboratory examinations on admission showed WBC 6430/μL, AMY 269 U/L, lipase 1182U/L, CRP 0.05 mg/dL, IgG4 81 mg/dL, ACE 13.9 U/L, sIL-2R 356 U/mL **(Table 1).** Abdominal ultrasonography revealed diffuse enlargement of pancreas with coarse parenchyma **(Figure 1).** Abdominal Contrast-Enhanced CT (CE-CT) showed diffuse swelling of the pancreas and a thin hypodense area surrounding the pancreas, with a capsule-like structure **(Figure 2).** No lymphadenopathy was observed in other lesions including the hilar lymph nodes. Positron emission tomography CT showed fluorodeoxyglucose accumulation with SUVmax=8.92 in the whole pancreas, but no obvious abnormal accumulation in other organs **(Figure 3).**

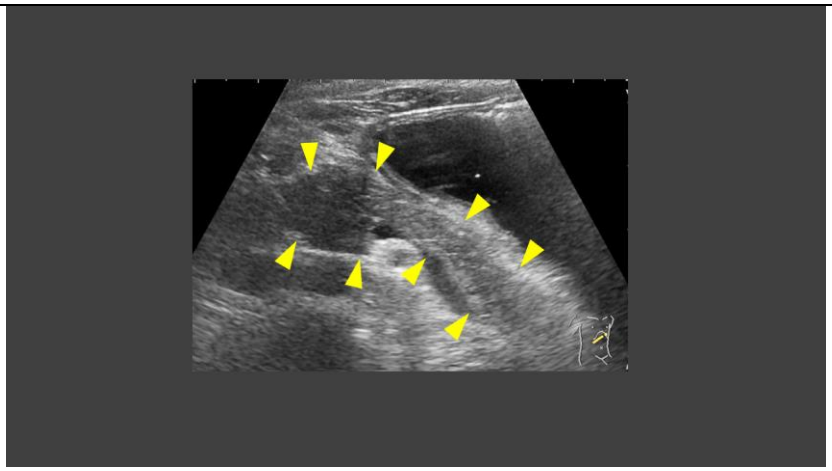

Figure 1: Abdominal ultrasonography revealed diffuse enlargement of pancreas with coarse parenchyma (arrowheads).

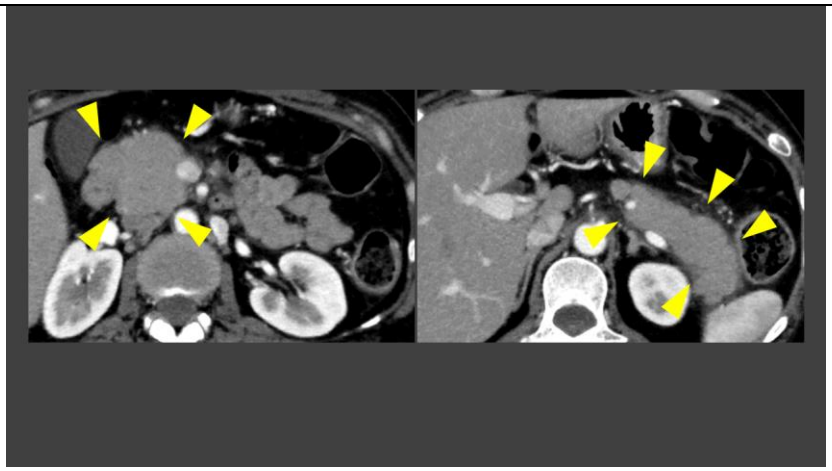

Figure 2: Abdominal contrast-enhanced computed tomography in pancreatic phase showed diffuse swelling of the pancreas (arrowheads) and a thin hypodense area surrounding the pancreas, with a capsule-like structure.

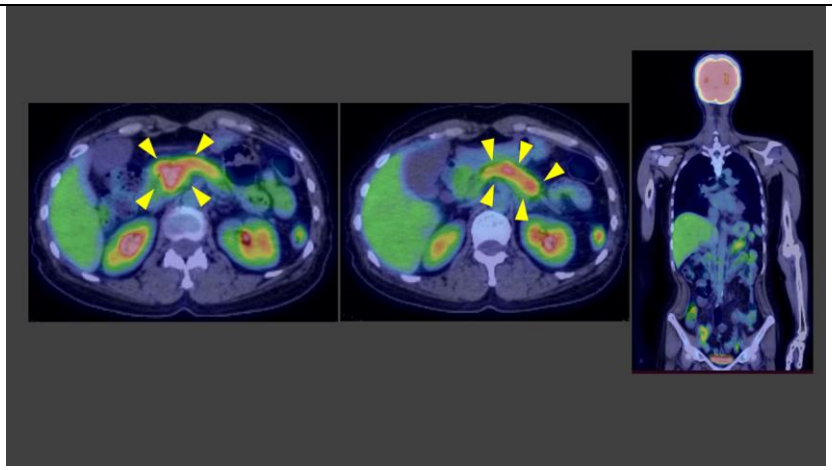

Figure 3: Positron emission tomography computed tomography showed fluorodeoxyglucose accumulation with SUVmax=8.92 in the whole pancreas (arrowheads), whereas no obvious abnormal accumulation in other organs including the hilar lymph nodes.

EUS showed diffuse pancreatic enlargement, with prominent swelling of the pancreatic head **(Figure 4).** Hyperechoic foci and strands, as well as lobularity, were observed in the pancreatic parenchyma. Contrast-enhanced harmonic EUS (CH-EUS) using an ultrasound contrast agent (Sonazoid®; Daiichi-Sankyo, Tokyo, Japan) revealed homogeneous enhancement of the pancreatic parenchyma, which persisted continuously **(Figure 5).** EUS-guided fine needle biopsy (EUS-FNB) using a disposable 19-gauge needle (SharkCore, Covidien, Japan Inc.) was performed **(Figure 6).** The pathological findings showed that multiple nodular granulomas composed of epithelioid cells were diffusely distributed throughout the specimen **(Figure7).** Immunostaining revealed CD68 positivity, clearly highlighting the

epithelioid granulomas **(Figure 8).** Additionally, negative. IgG4, Ziehl-Neelsen, and D-PAS staining were

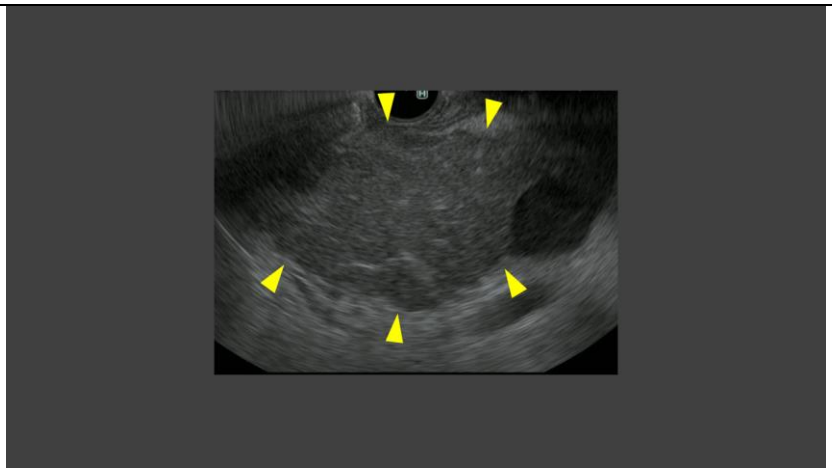

Figure 4: Endoscopic ultrasonography showed diffuse pancreatic enlargement, with prominent swelling of the pancreatic head (arrowheads). Hyperechoic foci and strands, as well as lobularity, were observed in the pancreatic parenchyma.

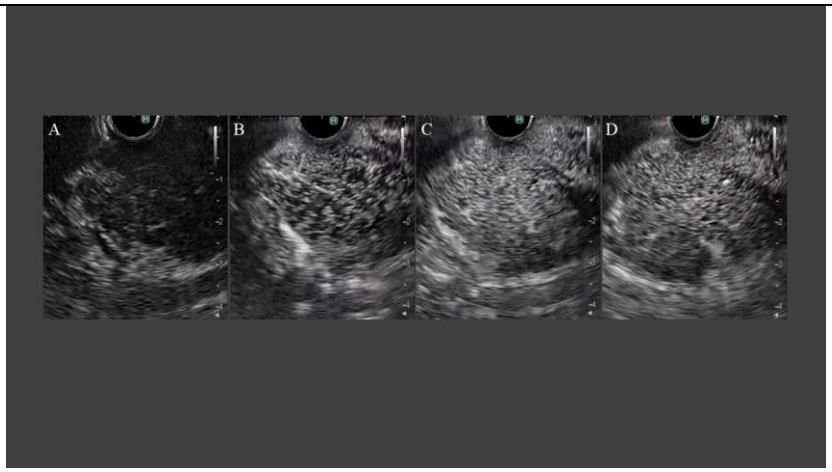

Figure 5: A) Pre-contrast, B) 20 seconds after contrast injection, C) 40 seconds after contrast injection, D) 60 seconds after contrast injection. Contrast-enhanced harmonic endoscopic ultrasonography using an ultrasound contrast agent (Sonazoid®; Daiichi-Sankyo, Tokyo, Japan) demonstrated homogeneous enhancement of the pancreatic parenchyma from approximately 20 seconds after contrast injection, which persisted beyond 60 seconds after injection.

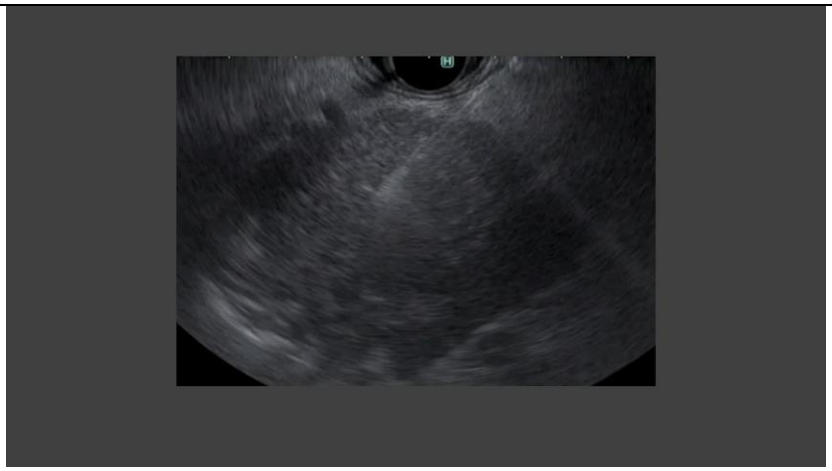

Figure 6: Endoscopic ultrasound guided fine needle biopsy was performed, and the pancreatic head was punctured from the stomach using a disposable 19-gauge needle (SharkCore, Covidien, Japan Inc.).

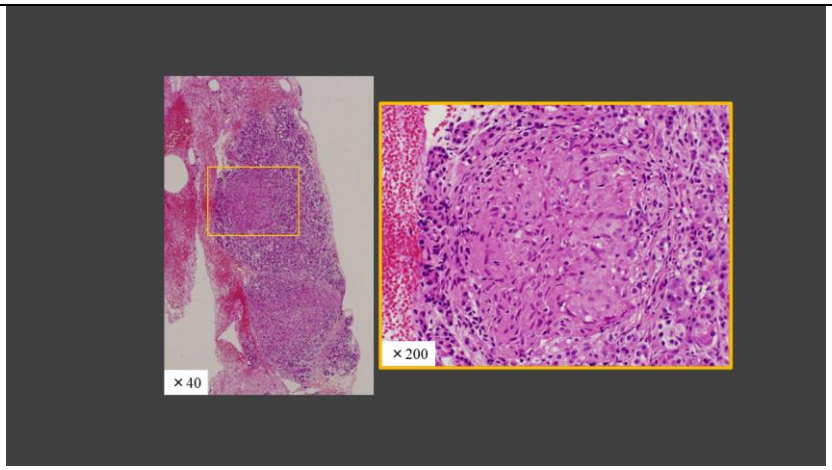

Figure 7: Histopathological findings. Hematoxylin and Eosin staining was performed. Multiple nodular granulomas composed of epithelioid cells were diffusely distributed throughout the specimen.

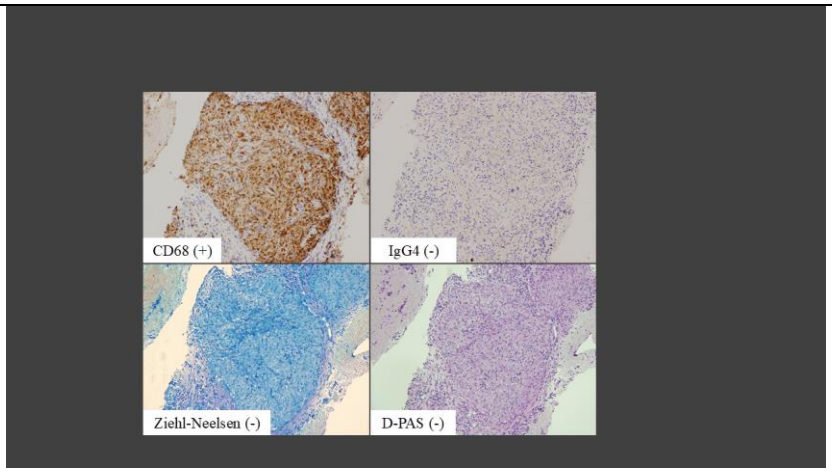

Figure 8: Immunostaining revealed CD68 positivity, clearly highlighting the epithelioid granulomas. Additionally, IgG4, Ziehl-Neelsen, and D-PAS staining were negative.

Based on these findings, we diagnosed the patient with pancreatic sarcoidosis. The electrocardiogram and echocardiography revealed no abnormality and no eye lesions were identified. Therefore, we diagnosed the case as isolated pancreatic sarcoidosis. Steroid therapy was considered due to the symptoms of epigastric and back pain, however, the MRI immediately prior to treatment showed that the pancreatic swelling was improving **(Figure 9).** Therefore, the patient was administered only an oral proteolytic enzyme inhibitor and a digestive enzyme supplement pancrelipase. Two months after the onset of symptoms, epigastric and back pain disappeared, and blood tests showed that pancreatic enzymes had normalized. CT scan also showed marked improvement in pancreatic enlargement **(Figure 10).** The patient has been followed up since then, and no relapse has been observed after 4 years.

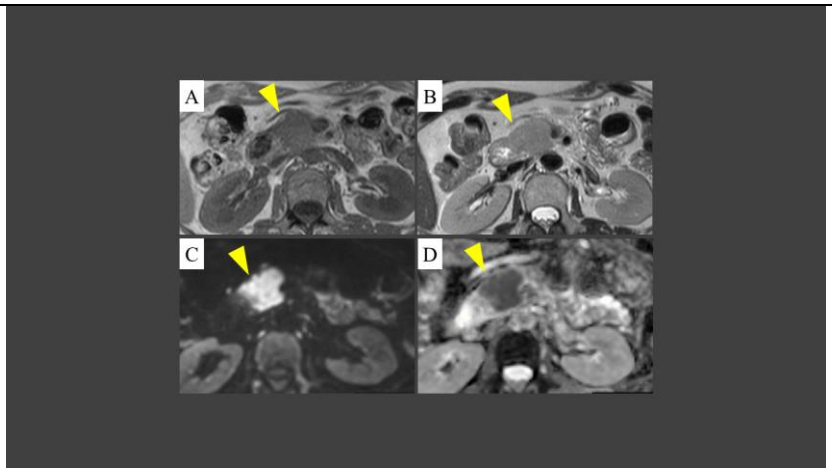

Figure 9: A) T1 weighted image, B) T2 weighted image, C) Diffusion-weighted image (b=1000), D) Apparent diffusion coefficient map. Magnetic resonance imaging showed the pancreatic swelling was improving (arrowheads).

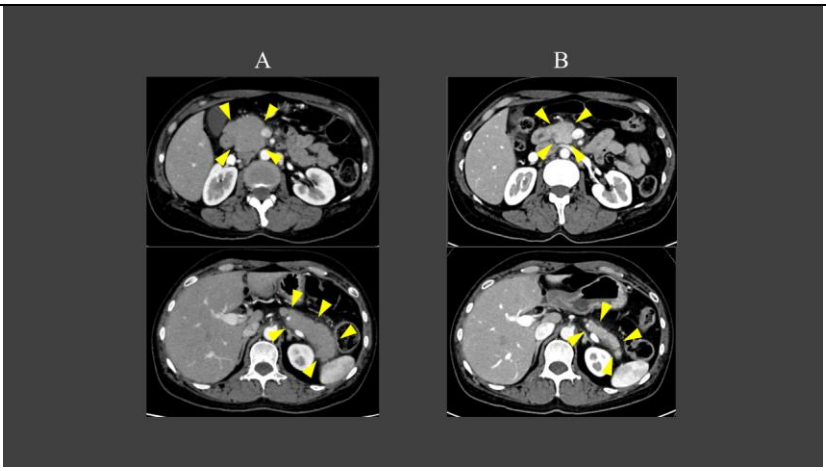

Figure 10: A) contrast-enhanced computed tomography (CE-CT) at the initial visit, B) CE-CT two months later. CT scan showed marked improvement in pancreatic enlargement (arrowheads).

Discussion

Pancreatic involvement in systemic sarcoidosis is infrequently observed. Furthermore, isolated pancreatic sarcoidosis is extremely rare; to date, approximately only 40 cases have been reported in the literature. In reported 25 cases with pancreatic sarcoidosis, patients presented with abdominal pain (66%), weight loss (45%), obstructive jaundice (29%) and nausea/emesis (20%), pruritus (12%), fever (8%), diarrhea (4%), abdominal distention (4%) and ascites (4%), while 16% of patients were asymptomatic **[12]**. Furthermore, 35% had elevated amylase, 62% had elevated Angiotensin-converting enzyme and 26% had bilateral hilar lymphadenopathy **[12].** Generally, corticosteroids are the treatment of choice for sarcoidosis. While the overall prognosis varies, mild pancreatic involvement usually has a good outcome, with a high rate of spontaneous remission **[1,6,13].** Corticosteroids may help relieve abdominal pain and lower elevated serum amylase and lipase levels **[14].** In previous reports, 18 patients with pancreatic sarcoidosis were followed up. Six improved without treatment, whereas, and 10 improved with corticosteroids **[1,12].** In the present case, although corticosteroid therapy was considered due to epigastric and back pain resembling symptoms of acute pancreatitis, imaging findings showed improvement in pancreatic enlargement. Therefore, the patient was treated only with an oral proteolytic enzyme inhibitor and the digestive enzyme supplement pancrelipase, after which the symptoms resolved.

In the literatures, pancreatic sarcoidosis demonstrates

solid mass lesions located in the head of the pancreas, or multiple nodule lesion in the whole pancreas [15]. Therefore, it may mimic pancreatic malignancies. Varieties of differential diagnoses are considered for a pancreatic mass, for instance, pancreatic adenocarcinoma, primary pancreatic lymphoma, pancreatic neuroendocrine neoplasm, Autoimmune Pancreatitis (AIP), metastasis other primary sites, and rare diseases such as pancreatic tuberculosis or pancreatic sarcoidosis. So far, there is no specific diagnostic imaging for pancreatic sarcoidosis. Although CE-CT is a useful modality for detecting pancreatic masses, it is not specific for diagnosing pancreatic sarcoidosis. Pancreatic sarcoidosis lesions detected on CE-CT showed a lower density than the pancreatic parenchyma. Essentially, an ill-defined pancreatic head mass, narrowing and dilatation of the common bile duct with or without pancreatic duct dilatation, and enlarged lymph nodes are the most common CT findings reported in the literatures [10,16-21]. MRI findings in pancreatic sarcoidosis have been described in the literature. MRI findings of a patient with pancreatic sarcoidosis revealed pancreatic masses with slight hyperintensity on T2-weighted images and delayed progressive enhancement after administration of gadolinium, becoming isointense to the rest of the pancreas on the portal venous and delayed venous phases [10,22]. EUS findings in pancreatic sarcoidosis are limited so far. Previous reports described that pancreatic sarcoidosis was hypoechoic mass lesion on EUS, which was similar to the appearance of pancreatic cancer [23-25]. CH-EUS findings in pancreatic sarcoidosis are crucially limited. It is reported that CH-EUS visualized isoenhancement or hypo-enhancement relative to the surrounding pancreatic parenchyma [23,25]. Until recently, the differentiation of pancreatic sarcoidosis from pancreatic cancer was difficult in most cases, therefore, with diagnostic or therapeutic intent, surgical intervention was needed. However, since 2016, the number of reports describing the diagnosis of pancreatic sarcoidosis by EUS-guided Fine Needle Aspiration/Biopsy (EUS-FNA/B) has increased. EUS-FNA/B is a safe and minimally invasive procedure with high diagnostic performance [26].

In our case, CE-CT showed diffuse swelling of the pancreas and a thin hypodense area surrounding the pancreas, similar to a capsule-like rim in AIP. Other imaging tests similarly showed diffuse enlargement of the pancreas, resembling AIP. No pancreatic mass lesion was found. These findings have never been

reported in the pancreatic sarcoidosis. Therefore, these findings are highly characteristic of our case. Pathological examination via EUS-FNB demonstrated multiple epithelioid granulomas, which allowed for the diagnosis of pancreatic sarcoidosis. IgG4 immunostaining was negative. Since serum IgG4 was negative and immunohistochemical staining of the pathological specimen was also negative for IgG4, type 1 AIP was ruled out. Furthermore, as granulocytic epithelial lesion was not observed in the histological examination, type 2 AIP was excluded.

In the present case, the reason why diffuse pancreatic enlargement was observed remains unclear. However, both sarcoidosis and AIP are systemic inflammatory diseases, therefore, the occurrence of pancreatic sarcoidosis in such imaging findings is considered possible. While pancreatic sarcoidosis is extremely rare, it should be included in the differential diagnosis if diffuse pancreatic enlargement is detected.

Table 1: Laboratory Examinations.

<Peripheral blood count>		<Blood chemistry>		Na	139 mEq/L
WBC	6800 /μL	TP	7.1 g/dL	K	4.6 mEq/L
RBC	457×10^4 /μL	ALB	4.2 g/dL	Cl	109 mEq/L
Hb	9.2 g/dL	AST	15 IU/L	CRP	0.02 mg/dL
Hct	30.10%	ALT	13 IU/L	CEA	11.2 ng/mL
Plt	$47.4\times10^{4/\mu L}$	ALP	54 IU/L	CA19-9	15.9 U/mL
		LD	175 IU/L	Span-1	13.8 U/mL
<Coagulation>		γ-GTP	21 IU/L	Erastase1	3858 ng/dL
PT %	89.50%	AMY	221 IU/L		
PT-INR	1.07	Lipase	980 IU/L	<Immunology>	
		Cre	0.65 mg/dL	IgG	1175 mg/dL
		BUN	7.7 mg/dL	IgG4	81 mg/dL
		Glu	99 mg/dL	ANA	<40 titer
		HbA1c	6.10%	sIL-2R	356 U/mL
		T-BIL	0.4 mg/dL	ACE	13.9 U/L

WBC: White blood cell, RBC: Red blood cell, Hb: Hemoglobin, Hct: Hematocrit, Plt: Platelet, PT: Prothrombin time, PT-INR: Prothrombin time-international normalized ratio, TP: Total protein, ALB: Albumin, AST:

Aspartate aminotransferase, ALT: Alanine amino-transferase, ALP: Alkaline phosphatase, LD: Lactate dehydrogenase, γ-GTP: γ-Glutamyl transpeptidase, AMY: Amylase, Cre: Creatinine, BUN: Blood urea nitrogen, Glu: Blood glucose, T-Bil: Total bilirubin, CRP: C-reactive protein, CEA: Carcinoembryonic antigen, CA19-9: Carbohydrate antigen 19-9, Span-1: S-pancreas-1antigen, IgG: Immunoglobulin G, ANA: Antinuclear antibody, sIL-2R: Soluble interleukin-2 receptor, ACE: Angiotensin-converting enzyme

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