INTERNAL MEDICINE

□ CASE REPORT □

Branch Duct Intraductal Papillary Mucinous Neoplasms of the Pancreas Involving Type 1 Localized Autoimmune Pancreatitis with Normal Serum IgG4 Levels Successfully Diagnosed by Endoscopic Ultrasound-guided Fine-needle Aspiration and Treated without Pancreatic Surgery

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Abstract

We herein report a 68-year-old man with branch duct intraductal papillary mucinous neoplasms of the pancreas (BD-IPMNs) involving type 1 localized autoimmune pancreatitis (AIP) with normal serum IgG4 levels. Although he was referred to our medical center due to suspicion of pancreatic cancer concomitant with BD-IPMNs, endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) revealed a mass suspected of being pancreatic cancer to be type 1 AIP. Steroid administration notably reduced the mass. Although the clinical diagnosis of pancreatic masses in patients with IPMN can be occasionally challenging, performing a pathological examination by EUS-FNA may prevent unnecessary pancreatic surgery in cases of possible AIP.

Key words: autoimmune pancreatitis (AIP), intraductal papillary mucinous neoplasms of the pancreas (IPMN), endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA)

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Introduction

Intraductal papillary mucinous neoplasms of the pancreas (IPMNs) are considered to be a risk factor of pancreatic ductal adenocarcinoma (PDAC) in addition to malignant transformation of IPMNs itself (1, 2). However, there have been some reports regarding the involvement of autoimmune pancreatitis (AIP) in patients with IPMN who underwent surgery following a preoperative diagnosis of suspected invasive carcinoma derived from IPMN or PDAC (3, 4). Interestingly, the possibility of AIP as a paraneoplastic syndrome has recently been reported (5). We herein report a case of branch duct IPMN (BD-IPMN) involving type 1 AIP with normal serum IgG4 levels successfully diagnosed by endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) and treated without pancreatic surgery.

Case Report

A 68-year-old man in whom pancreatic cysts in the pancreatic tail were detected on abdominal ultrasonography by his primary care physician was referred to our medical center. He was diagnosed with suspected BD-IPMNs without malignant findings by magnetic resonance imaging (MRI), resulting in a periodic examination for his pancreatic cysts by his primary physician. Two years later, he was referred to our medical center again due to suspicion of pancreatic cancer in the pancreatic body on contrast-enhanced computed tomography (CECT). The laboratory data on admission were

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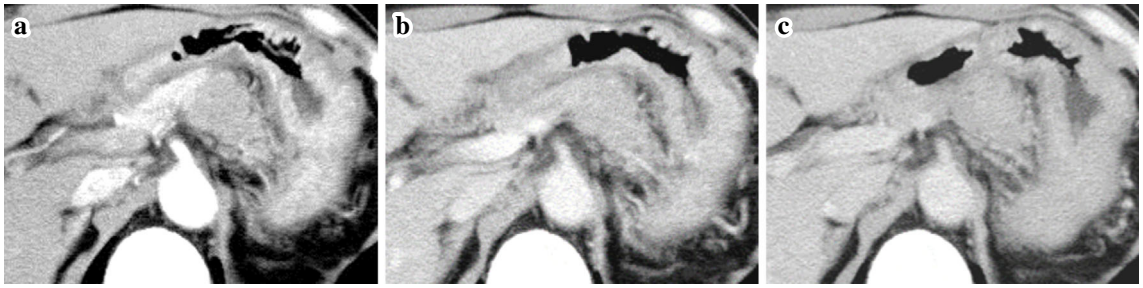

Figure 1. **On CECT (axial) before a steroid trial, a mass lesion about 3 cm in size detected in the pancreatic body showed low density in the early phase (a) and homogenous delayed enhancement in the portal (b) and late (c) phases.**

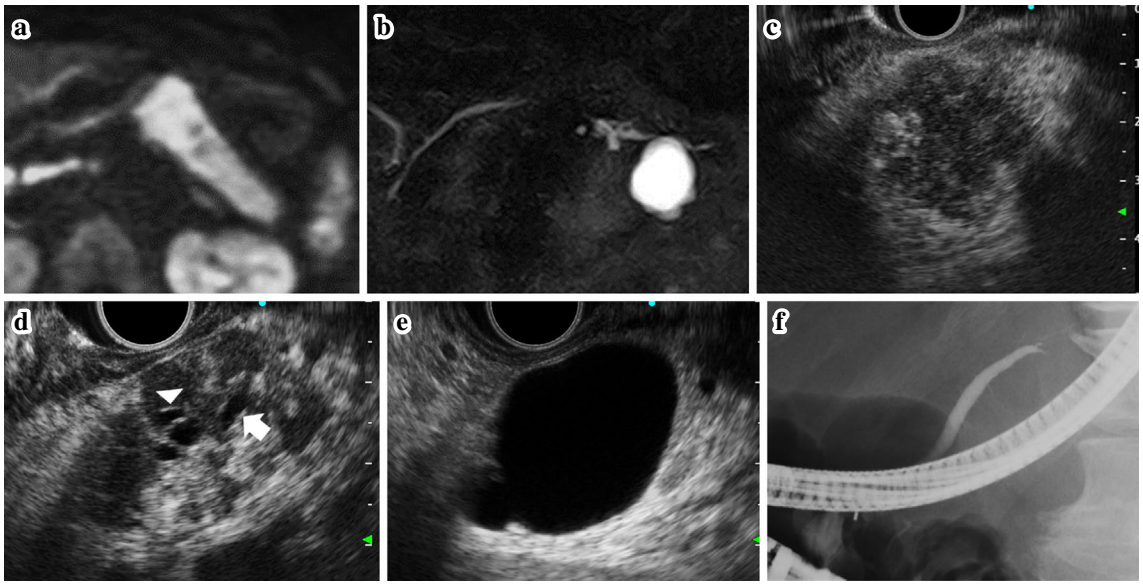

Figure 2. **The findings of imaging studies before a steroid trial were as follows: a: On diffusion-weighted images, the mass lesion in the pancreatic body showed a high signal. b: MRCP showed stenosis of the MPD in the pancreatic body, upstream MPD dilation 3 mm in diameter, and multiple pancreatic cysts considered to be BD-IPMNs in the pancreatic tail. c: EUS visualized a 3-cm-diameter low echoic mass with a heterogeneous internal echo structure in the body of the pancreas. d, e: On EUS, suspected BD-IPMNs were also detected in the pancreatic body and tail apart from the mass lesion. d shows small pancreatic cysts in the pancreatic body (arrowhead, cyst; arrow, main pancreatic duct) and e shows a multilocular pancreatic cyst more than 30 mm in size without a mural nodule in the pancreatic tail. f: On ERP, obstruction of the MPD in the pancreatic body was detected, and the upstream MPD could not be visualized.**

as follows: tumor markers such as serum carbohydrate antigen 19-9 (CA19-9) and carcinoembryonic antigen (CEA) levels were within normal ranges. The serum IgG4 level was also normal (46.5 mg/dL), whereas the levels of pancreatic enzymes such as serum amylase and lipase were elevated (181 and 384.8 U/mL, respectively). On CECT, a mass lesion about 3 cm in size detected in the pancreatic body showed low density in the early phase and homogenous delayed enhancement in the portal and late phases (Fig. 1). On MRI, this mass lesion showed a low signal in both T1- and T2-weighted images and a high signal in the diffusion-weighted image (Fig. 2a). Magnetic resonance cholangiopancreatography (MRCP) showed a stenosis of the main pancreatic duct (MPD) in the pancreatic body, upstream MPD dilation 3 mm in diameter, and multiple pancreatic cysts a maximum of 3 cm in diameter considered to be BD-IPMNs in the pancreatic body and tail (Fig. 2b). Endoscopic ultrasonography (EUS) visualized a 3-cm low echoic mass with a heterogeneous internal echo structure in the body of the pancreas (Fig. 2c). In addition, apart from this mass lesion, suspected BD-IPMNs 30 mm in maximum size without mural nodules were detected in the tail side of the pancreas (Fig. 2d and e). On endoscopic retrograde pancreatography (ERP), obstruction of the MPD in the pancreatic body was detected, and the upstream portion of the MPD was not visualized (Fig. 2f).

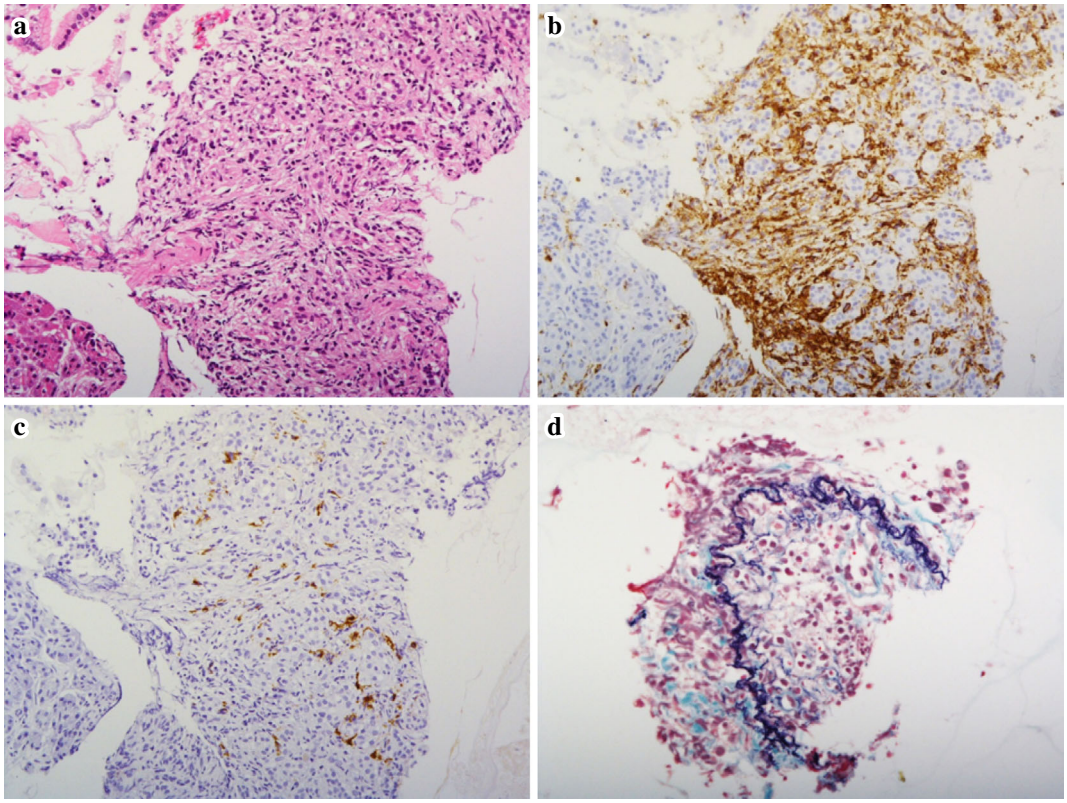

Figure 3. **a: Hematoxylin and Eosin staining (40×). The specimen was fibrotic with infiltration of many lymphocytes and plasmacytes. b: LCA staining (40×). Many LCA-positive cells diffusely infiltrated the fibrotic lesion of the specimen. c: IgG4 staining (40×). Infiltration of abundant (≥10 cells/HPF) IgG4-positive cells in the fibrotic lesion of the specimen was detected. d: Elastica-Masson staining (100×). Obliterative phlebitis was detected.**

Although PDAC concomitant with BD-IPMNs was clinically suspected, localized autoimmune pancreatitis (AIP) could not be excluded as a differential diagnosis due to several findings by imaging studies, such as homogenous delayed enhancement on CECT and only slight dilation of the upstream MPD on MRCP. Therefore, EUS-FNA for the mass lesion in the pancreatic body using a 22-G needle (Expect™, Boston Scientific, Marlboro, MA, USA) was performed in order to obtain pathological evidence. The specimen collected by EUS-FNA was processed with the cell-block method (6) and subjected to Hematoxylin and Eosin (H&E) staining, Elastica-Masson staining, and immunostaining. The specimen was histopathologically fibrotic with infiltration of many lymphocytes and plasmacytes, and obliterative phlebitis was also detected (Fig. 3). Immunostaining revealed diffuse infiltration of many leukocyte common antigen (LCA)-positive cells and an abundance of IgG4-positive cells (≥10 cells/high-power field) in the fibrotic lesion of the specimen. These pathological findings met the definition of Level 1 lymphoplasmacytic sclerosing pancreatitis (LPSP) by the international consensus diagnostic criteria (ICDC) (7), resulting in a diagnosis of type 1 AIP for this mass lesion.

In order to confirm this diagnosis, a steroid trial by administration of 30 mg/day prednisolone for 2 weeks was performed. Two weeks after the initial administration of prednisolone, CECT revealed the mass lesion in the pancreatic body to be notably reduced in size, and the enhancement patterns of this mass lesion on CECT returned to those of the normal pancreas five months after the initial administration of prednisolone (Fig. 4a-c). ERP three weeks after the initial administration of prednisolone showed improvement of the MPD obstruction in the pancreatic body, visualization of the MPD up to the pancreatic tail, and communication of the MPD with the 30-mm BD-IPMN in the pancreatic tail (Fig. 4d), which definitively revealed this pancreatic cyst to be BD-IPMN.

Discussion

An occurrence of PDAC as well as carcinogenesis of IPMN itself is considered to be an important issue in patients with IPMN (1, 2). However, there have recently been two case reports (3, 4) and a pathological study (8) regarding the involvement of AIP in patients with IPMN. Of the two case reports, one is a report on a patient with multiple BD-IPMNs in the pancreatic uncus who suffered from obstructive jaundice with diffuse enlargement of the pancreas (3). The other is a report on a patient in whom mass lesions in the pancreatic head were detected during a follow-up (4). Both patients underwent pancreatic surgery due to the diagnosis of suspected invasive carcinoma derived from

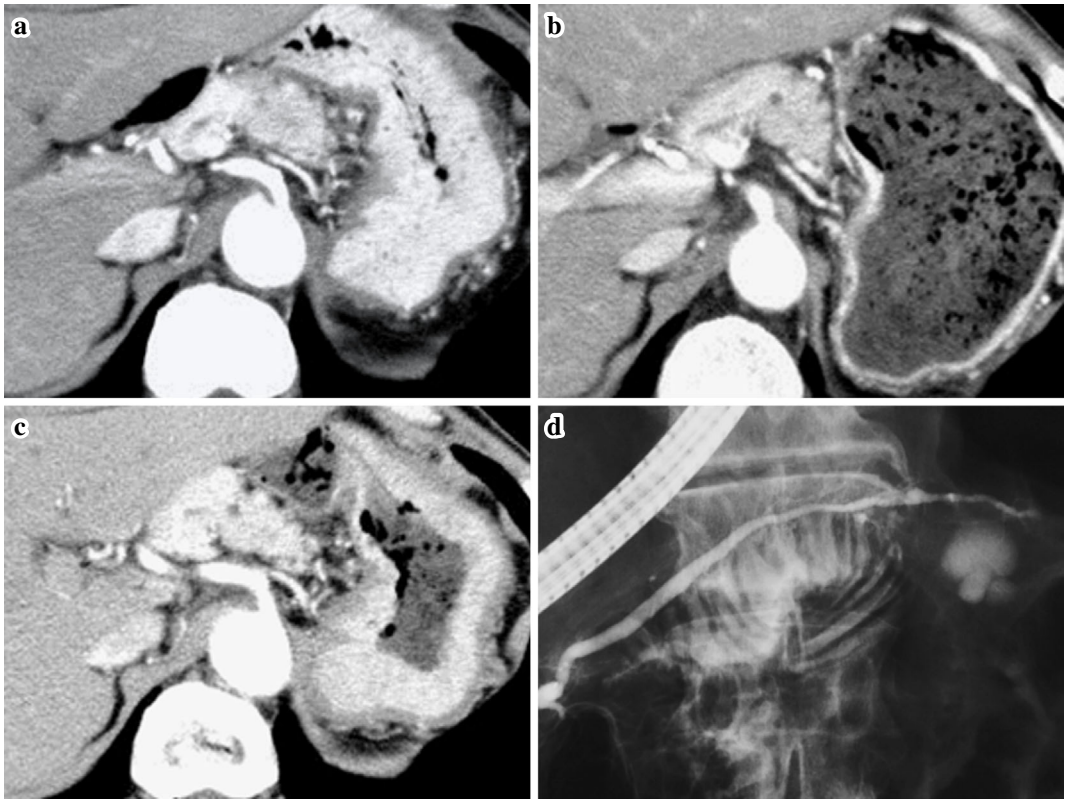

Figure 4. **a-c: CECT (axial) after the initial administration of prednisolone (a: 2 weeks after, b: 2 months after, c: 5 months after) showed the mass lesion in the pancreatic body to be notably reduced in size, and the enhancement patterns of this mass lesion on CECT returned to those of the normal pancreas. d: ERP after a steroid trial revealed improvement of the MPD obstruction in the pancreatic body, visualization of the MPD up to the pancreatic tail and communication of the MPD with the 30-mm BD-IPMN in the pancreatic tail.**

IPMN or PDAC, resulting in a pathological diagnosis of AIP. The pathological study reported cases of fibrotic lesions infiltrated by IgG4-positive cells adjacent to IPMNs (8). Although such coexistence in these reports may be coincidental, it may also suggest that IPMNs contribute to the pathogenesis of some AIPs. In addition, Shiokawa et al. implied the possibility of AIP as a paraneoplastic syndrome because of the high rate of concomitant neoplasia (5), which may support the above-mentioned possibility regarding a pathogenic correlation between IPMN and AIP.

For patients with IPMN, we should not only pay careful attention to the occurrence of concomitant PDAC but also recognize the possible involvement of AIP, although the occurrence of AIP in patients with IPMN may be rare and the pathogenic relationship between IPMN and AIP has not yet been clarified. It is clinically important to discriminate AIP from PDAC because an appropriate diagnosis of AIP can prevent unnecessary surgery. However, when AIP shows a localized structure on imaging studies and the serum IgG4 levels are normal, the clinical discrimination from PDAC can be extremely difficult (9, 10). In such cases, the appropriate diagnosis of AIP depends on whether or not the possibility of AIP can be considered based on imaging study findings. In the present case - in which a pancreatic mass lesion and BD-IPMNs coexisted, the serum IgG4 levels were normal, and ERP showed obstruction of MPD in the pancreatic body - PDAC should have first been taken into consideration. However, homogenous delayed enhancement on CECT and only slight dilation of the upstream MPD on MRCP introduced the possibility of AIP (11) and led to the performance of EUS-FNA, which allowed us to avoid an unnecessary operation.

Recently, two multicenter prospective studies on the diagnostic ability of EUS-FNA using a 22-G needle for patients with suspected AIP have been reported (12, 13). In the report of Kanno et al. (12), the percentage of the diagnostic ability of EUS-FNA for Level 1 LPSP and level 1 or 2 LPSP was 41% (32/78) and 57.7% (45/78) in 78 cases of suspected AIP, respectively, while in the report of Morishima et al. (13), these respective values were 7.9% (3/38) and 65.8% (25/38) in 38 cases of definitive AIP. These findings indicate that level 2 or more LPSP can be diagnosed in almost 60% of patients with AIP in whom EUS-FNA has been performed, and that EUS-FNA can improve the diagnostic ability for AIP for many patients with AIP.

Although the clinical diagnosis of pancreatic mass lesions in patients with IPMN can be challenging, performing a pathological examination by EUS-FNA may prevent unnecessary pancreatic surgery in cases of possible AIP.

The authors state that they have no Conflict of Interest (COI).

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