

CASE REPORT

A Case of Non-Swelling Autoimmune Pancreatitis with Multiple Pancreatic Pseudocysts

Hirotsugu Maruyama¹, Kazunari Tominaga¹, Kunihiro Kato¹, Yasuaki Nagami¹, Satoshi Sugimori¹, Masatsugu Shiba¹, Toshio Watanabe¹, Yasuhiro Fujiwara¹, Yuki Kubo¹, Masahiko Ohsawa²

Departments of ¹Gastroenterology and ²Pathology, Osaka City University Graduate School of Medicine, Japan

ABSTRACT

Context Non-swelling autoimmune pancreatitis with multiple pancreatic pseudocysts is very rare. **Case report** A Seventy-five-year-old man was referred to our hospital for further examination of multiple pancreatic cysts with nodules detected by computed tomography. Endoscopic ultrasound examination showed a pancreatic cyst with a nodule (6.3 mm in diameter) in the pancreatic head and another pancreatic cyst with a nodule (8.7 mm in diameter) in the pancreatic tail, and these cysts were connected to the main pancreatic duct. The patient was clinically diagnosed with branch duct type intraductal papillary mucinous neoplasm of the pancreas. The recent international consensus guidelines indicate that a mural nodule indicates high risk for malignancy and recommend surgical resection of branch duct type intraductal papillary mucinous neoplasm with mural nodule. Therefore, pancreatoduodenectomy and pancreatic body tail resection were performed in our hospital. Histopathological findings showed IgG4-positive plasma cells and obstructive phlebitis. Autoimmune pancreatitis associated with multiple pancreatic pseudocysts was the final diagnosis. **Conclusions** We encountered a rare case of autoimmune pancreatitis with pseudocyst but not swollen pancreas nor an increase in serum IgG4 level. The correct diagnosis was very difficult before surgical treatment. In clinical cases with various pancreatic cystic lesions, it is necessary to consider autoimmune pancreatitis in the differential diagnosis.

INTRODUCTION

First reported in 1961, autoimmune pancreatitis (AIP) is a benign disease [1]. The concept of AIP was proposed in Japan in 1995 [2]. A typical case is easily diagnosed by the characteristic imaging features of diffuse or segmental pancreatic enlargement and pancreatic ductal strictures without significant dilation. In addition, the serum IgG4 level is often high in case of AIP [3]. Yoshida *et al.* have also reported that one of the characteristic features of AIP is the absence of a pancreatic cyst [2]. However, only a few cases of AIP with pancreatic cysts have been reported. Most previous reports of AIP with pancreatic cysts described pancreatic enlargement, pancreatic ductal strictures, and elevated serum IgG4 level. The present case did not involve enlargement of the pancreas or an increase in serum IgG4 level. Thus, we report a very rare case of an atypical presentation of AIP.

CASE REPORT

A Seventy-five-year-old man was referred to our hospital for further examination of multiple cystic lesion of the pancreas with nodules detected by computed tomography (CT) at a general medical checkup. The patient had no chief complaint, and habitually consumed alcohol (40mg/day). There was no family history or a past history of liver or pancreatic dysfunction. Physical examination identified no palpable mass in a soft abdomen. All laboratory findings before the admission were within normal ranges: serum amylase 130 IU/L (40–126 IU/L); IgG 702 mg/dL (870–1700 mg/dL); IgG4 36.9 mg/dL (4.8–105 mg/dL). Levels of tumor markers (carcinoembryonic antigen, carbohydrate antigen 19-9, DUPAN-2, and SPAN-1) were all within normal ranges. Contrast enhanced CT examination showed two multilocular cysts 30 mm in diameter in the pancreatic head and tail, and several small cysts in other parts of the pancreas (**Figure 1a & b**). The cyst in the pancreatic head had a contrast-enhanced nodule (**Figure 1c**). No characteristic findings such as swelling of the pancreas were observed in this case (**Figure 1d**). Magnetic resonance imaging (MRI) showed multiple cysts with nodules in the pancreatic head and tail. A low signal intensity was observed in these nodules on T1 and T2 weighted images. On apparent diffusion coefficient map diffusion weighted imaging, the nodules showed a low signal (**Figure 2a**). Magnetic resonance cholangiopancreatography (MRCP)

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Keywords Immunoglobulin G; Pancreatitis; Pancreatic Pseudocyst

Abbreviations AIP Autoimmune pancreatitis; IPMN intraductal papillary mucinous neoplasm;

Correspondence Kazunari Tominaga

Department of Gastroenterology

Osaka City University Graduate School of Medicine

1-4-3, Asahimachi, Abeno-ku

Osaka, 545-8585, Japan

Tel +81-6-6645-3811

Fax +81-6-6645-3813

E-mail tomy@med.osaka-cu.ac.jp

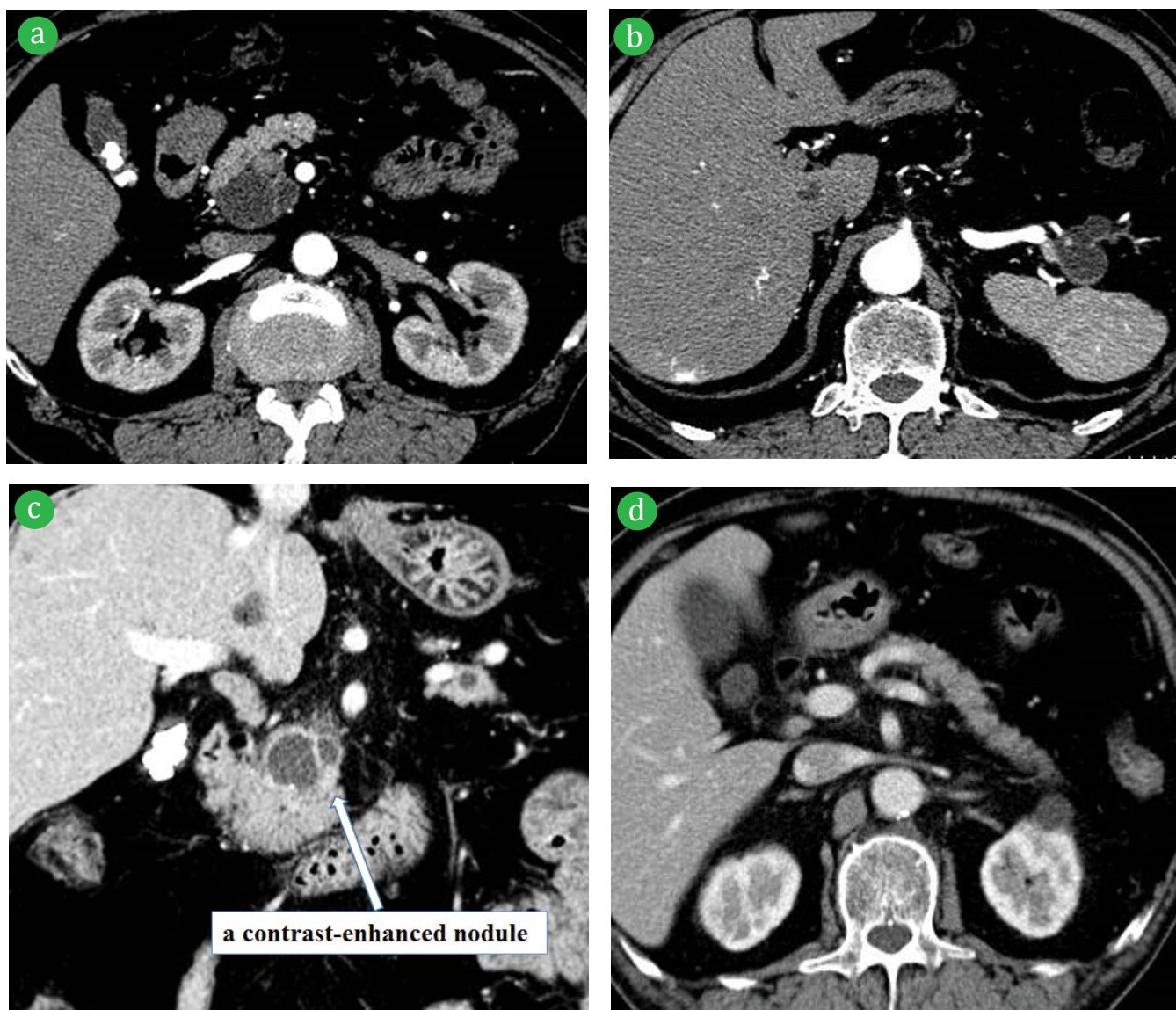


Figure 1. Contrast enhanced computed tomography images. Two multilocular cysts 30 mm in diameter in the (a). pancreatic head and (b). tail. (c). The cyst in the pancreatic head had a contrast-enhanced nodule. (d). The image showed no swelling of the pancreas.

did not show the irregular narrowing of the pancreatic duct (**Figure 2b**). Endoscopic ultrasound (EUS) showed 22×25 mm multilocular cyst in the pancreatic head and 30×28 mm multilocular cyst in the pancreatic tail, and several small cysts in the pancreatic body. These multilocular cysts had the nodules. The size of the nodules were 6.3 mm (head) and 8.7 mm (tail) in diameter, respectively (**Figure 3a, b**), and were connected to the main pancreatic duct (**Figure 3c**). The clinical diagnosis was branch duct type intraductal papillary mucinous neoplasm of the pancreas (IPMN) because the cysts were multiple and multilocular and connected to the pancreatic duct. The recent international consensus guidelines indicate that a mural nodule in branch duct type IPMN is a sign of malignant transformation and an indication for surgery. The patient underwent pancreatoduodenectomy and pancreatic body tail resection. Macroscopic findings revealed necrotic tissue with multilocular cysts of 30 mm in diameter in the pancreatic head and tail, respectively. Macroscopic findings showed a protruding pancreatic tissues growing toward the cyst in the pancreatic head

(**Figure 4a**) and no nodule in the cyst of the pancreatic tail (**Figure 4b**). Histopathological findings revealed the abundant of collagen fibers, infiltration of plasma cells, and eosinophils in the protruding pancreatic tissues. We think that the nodule of the pancreatic head was diagnosed as a histological thickness associated with AIP itself and necrotic tissue in the pancreatic tail, respectively (**Figure 4c, d**). These findings indicated storiform fibrosis (**Figure 5a**) and obstructive phlebitis (**Figure 5b**). CD38, a marker of plasma cells, was co-expressed with strong immunoreactivity for IgG4 in the plasma cells (**Figure 6a, b**). The ratio of IgG4 positive cells to total IgG positive cells was 83% (136/163) (**Figure 6c**). Thick fibrosis and inflammation and a few pancreatic duct epithelium in the cystic wall were histologically confirmed (**Figure 7a, b**). The presence of pancreatic duct epithelium suggested to connection to the main pancreatic duct. There was no granulocytic epithelial lesion in the wall. The final diagnosis was lymphoplasmacytic sclerosing pancreatitis associated with multiple pancreatic pseudocysts. After the operation, pancreatic fistula and abscess formation

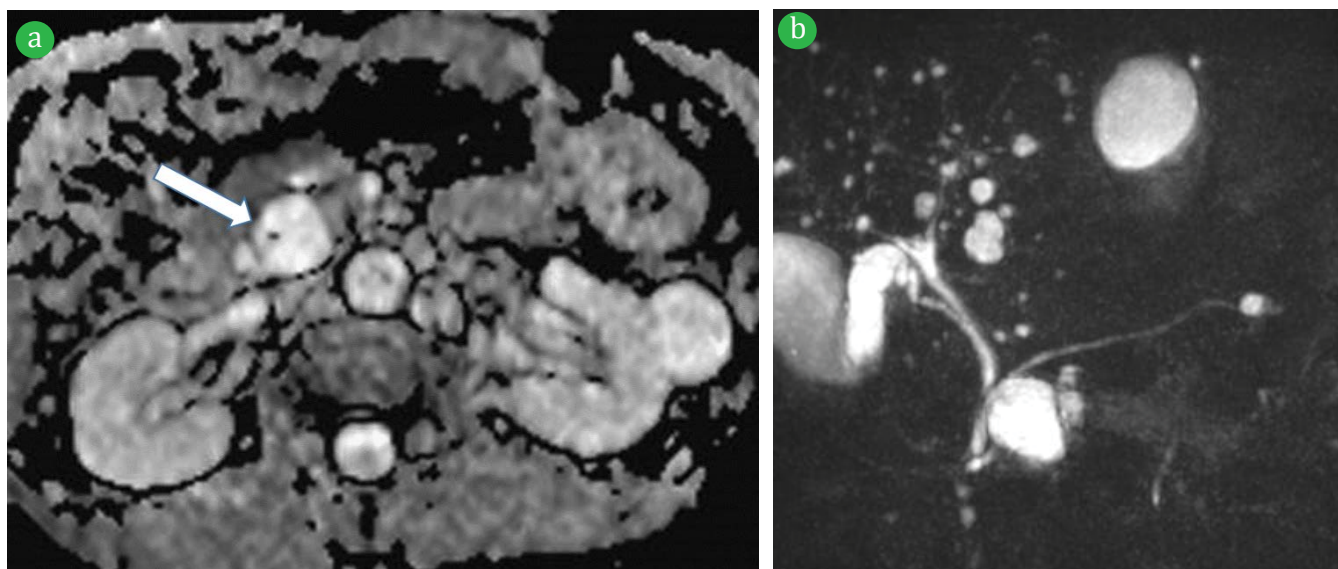


Figure 2. Magnetic resonance imaging. **(a).** The nodule had the low signal on apparent diffusion coefficient map. **(b).** Magnetic resonance cholangiopancreatography did not show the irregular narrowing of the pancreatic duct.

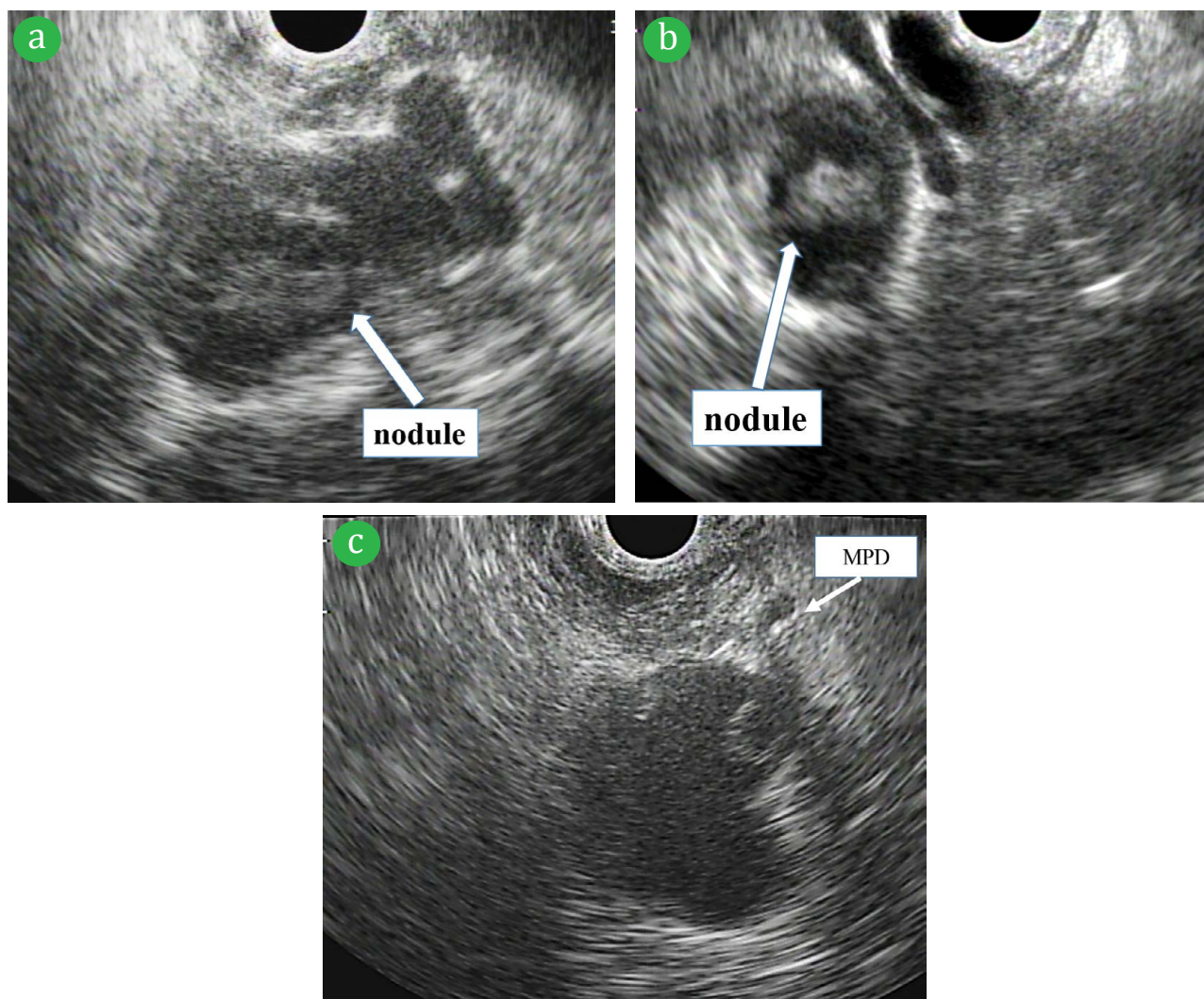


Figure 3. Endoscopic ultrasound image. The size of the nodules was **(a).** 6.3 mm (head) and **(b).** 8.7 mm (tail) in diameter, respectively and **(c).** were connected to the main pancreatic duct.

occurred, which was managed with antibacterial agents and CT-guided percutaneous drainage, respectively. The patient was discharged on the 58th hospital day and no significant post-treatment problems have occurred.

DISCUSSION

AIP is a benign disease that was firstly reported in 1961 [1]. Its characteristic clinicopathologic features are irregular narrowing of the pancreatic duct, swelling of

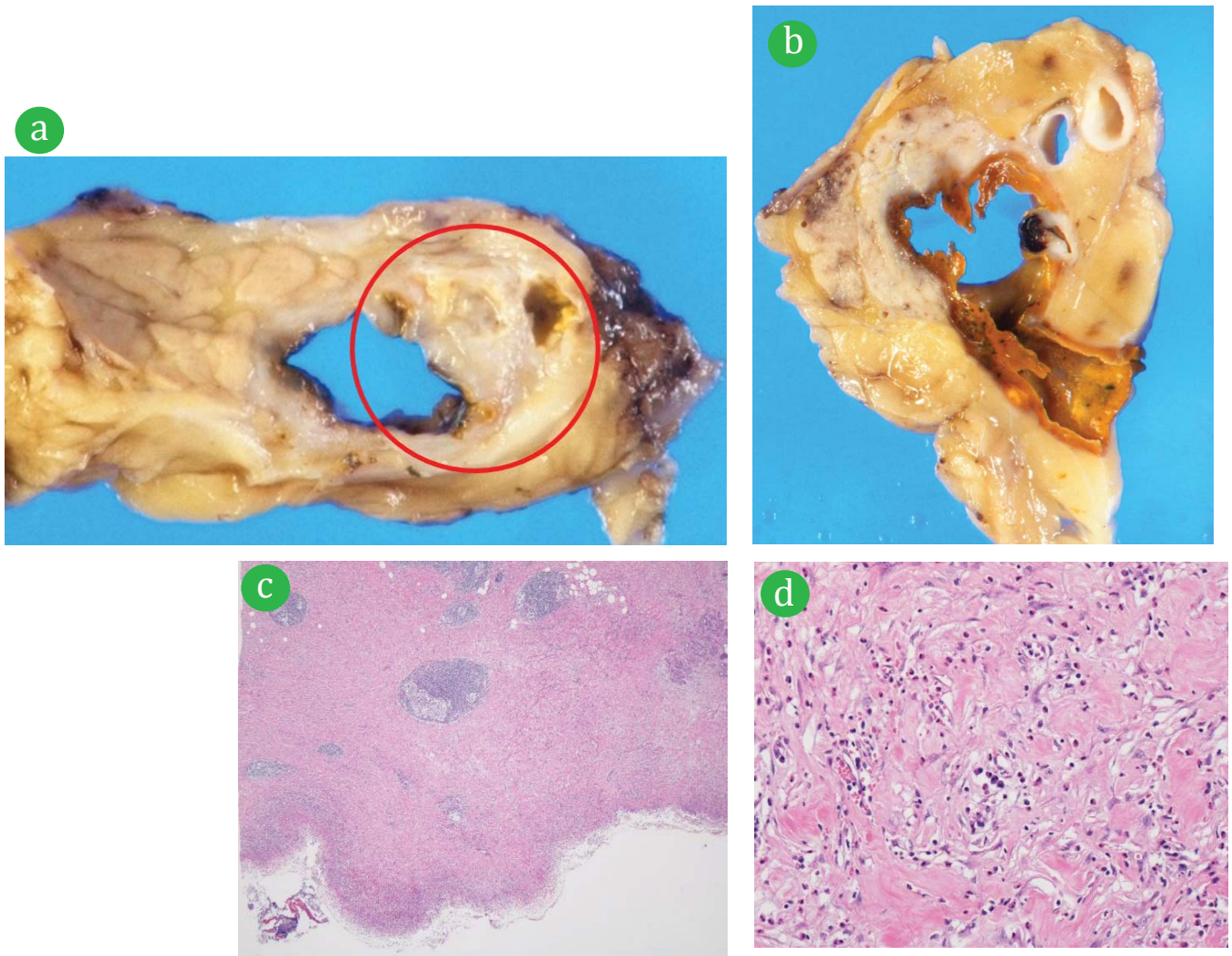


Figure 4. Macroscopic & pathological findings of the resected pancreatic tumor. **(a).** The pancreatic tissue was protruded toward the cyst in the pancreatic head (area of red circle). A part of the protruded pancreatic tissues was diagnosed as a nodule. **(b).** The pancreatic tail cyst had no nodule in the cyst. The pathology of the area of red circle showed the abundant of collagen fibers, infiltration of plasma cells, and eosinophils. hematoxylin and eosin staining; original magnification **(c).** $\times 20$, **(d).** $\times 100$.

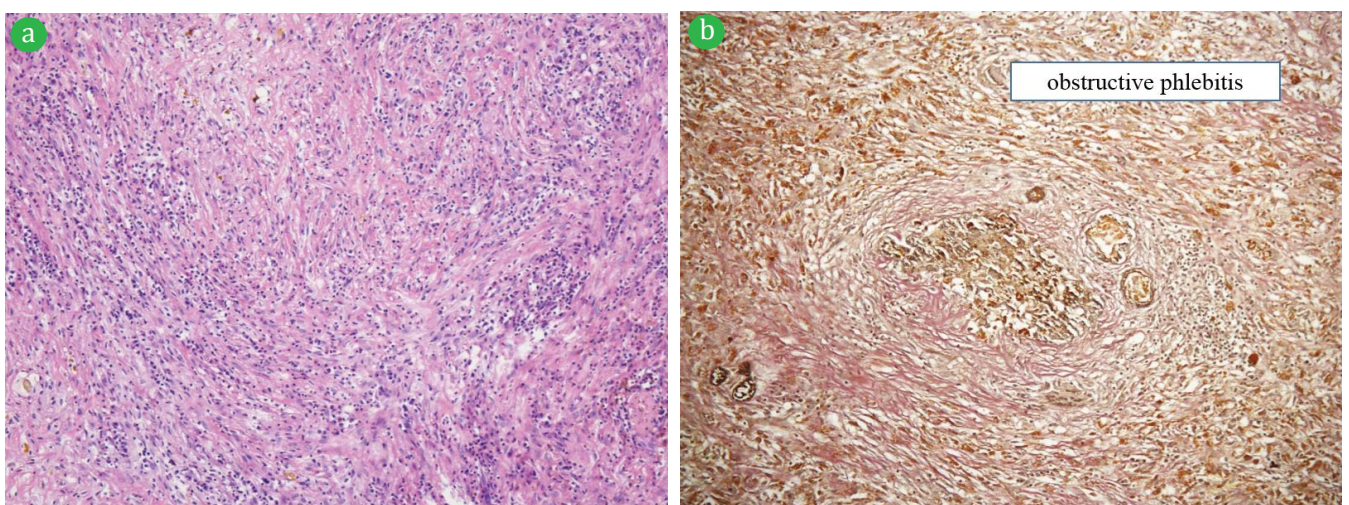


Figure 5. Pathological findings of the resected pancreatic tumor. **(a).** Storiform fibrosis is visible in the pancreatic tissue (hematoxylin and eosin staining; original magnification $\times 100$). **(b).** Obstructive phlebitis Elastic-van Gieson staining; original magnification: $\times 400$.

the pancreas, lymphoplasmacytic infiltration and fibrosis, and a favorable response to corticosteroid. Furthermore, serological elevation of IgG4 level is essential for a correct diagnosis of AIP [4]. Yoshida *et al.* have also reported that one of the characteristic features of AIP is an absence of

pancreatic cyst [2]. In general, most previous reports of AIP have also showed the absence of pseudocysts in the pancreas. Findings such as diffuse pancreatic enlargement with delayed enhancement and pancreatic ductal strictures without significant dilation detected using dynamic CT

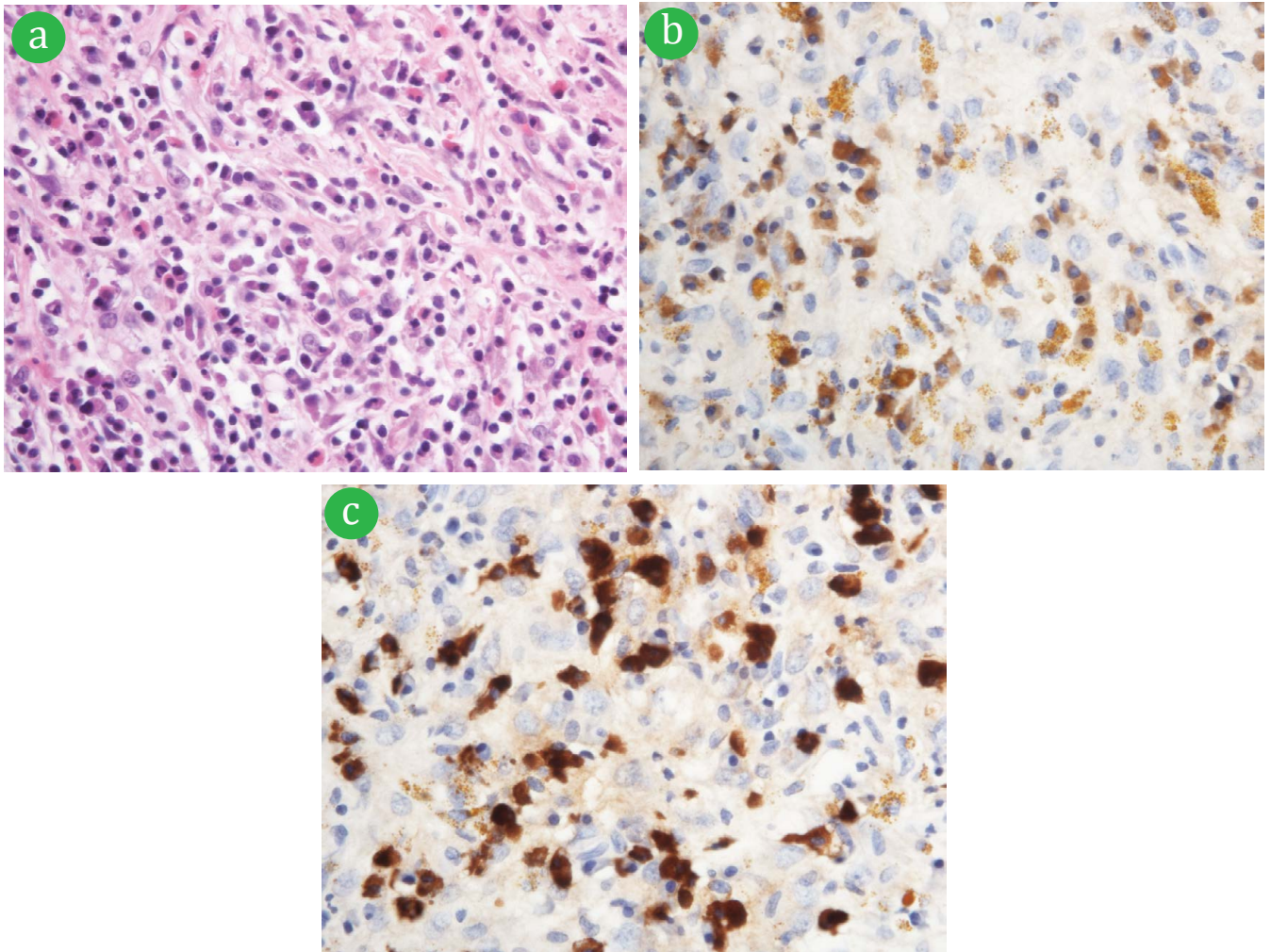


Figure 6. Immunostaining with the IgG4 antibody. **(a).** Abundant plasma cells are observed in the inflammatory cells. **(b).** hematoxylin and eosin staining, original magnification $\times 400$, **(c).** Strong immunoreactivities for IgG and IgG4 are observed in the plasma cells (original magnification $\times 400$).

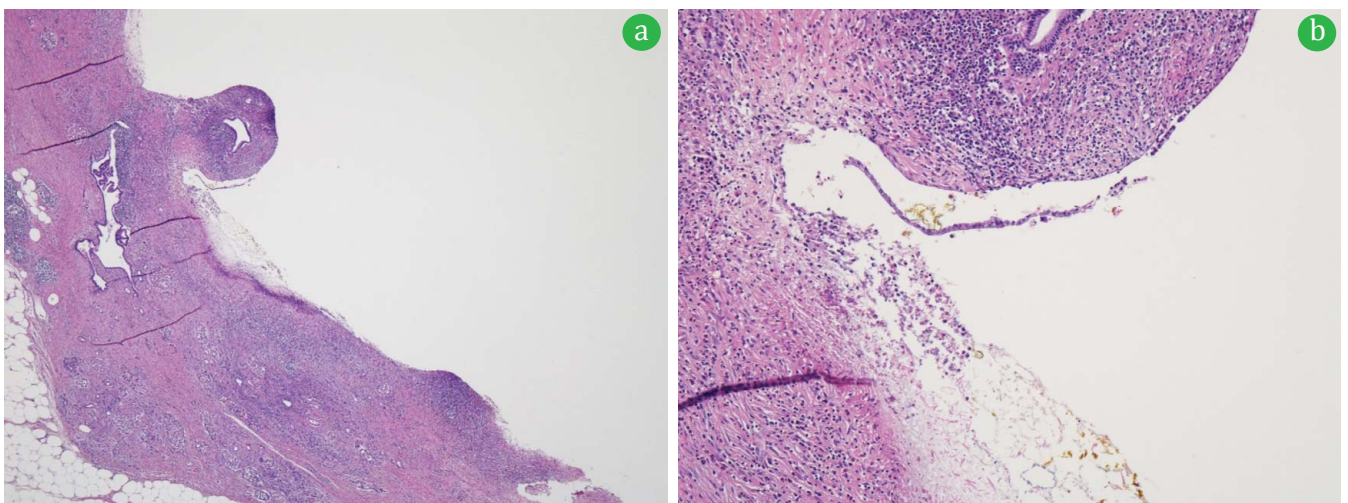


Figure 7. Pathological findings of the resected cystic wall. Thick fibrosis, inflammation, and a few of pancreatic duct epithelium in the cystic wall were confirmed. hematoxylin and eosin staining, original magnification **(a).** $\times 20$, **(b).** $\times 100$.

and/or MRI and elevated serum IgG4 levels can lead to a definitive clinical diagnosis of AIP [5]. Therefore, non-swelling of the pancreas with pseudocysts as in the present AIP case may be very rare, although there is one report of 26 cases of AIP with pancreatic pseudocysts.

Recent studies have shown that serum IgG4 levels are not elevated in about 20% of AIP patients [6], and the sensitivity of serum IgG4 elevation for diagnosing

AIP varies from 68% [7] to 81% [8]. The detection rate of diffuse and/or segmental pancreatic enlargement and irregular narrowing of pancreatic ducts using CT and/or MRI was 92.9% and 89.6%, respectively. The frequency of cystic formation in AIP is reported to be 7% [5, 9]. In the present case, the serum IgG4 level was not elevated. Considering these simultaneous atypical findings of a non-swelling pancreas, cyst formation, and no increase in serum IgG4 level, the present case must be rare.

In the present case, fibrosis and lymphoplasmacytic infiltration of IgG4 positive cells into the pancreatic tissue surrounding the cysts were histologically confirmed. Cyst formation in AIP is associated with a highly active state of inflammation and severe narrowing of the branched pancreatic ducts. Recently, Miki *et al.* have reported indicated that the mechanism(s) of pancreatic pseudocyst formation associated with AIP are due to the stricture of the main pancreatic duct followed by obstructive pancreatitis [9]. The cyst formation in the histopathological findings may occur by the similar mechanism(s). However, no past history of chronic pancreatitis and pancreatic enlargement were observed in the present case. Furthermore, apparent communication between the multilocular cyst with nodules and the pancreatic duct was confirmed on MRI and EUS. Thus, we could not clearly identify the detailed mechanism(s) of pancreatic pseudocyst formation associated with AIP in this case. However, we did achieve the correct diagnosis after surgery. We experienced a rare case of AIP with pseudocyst but not swelling of the pancreas or increase in serum IgG4 levels. It was very difficult to obtain a correct diagnosis without surgical specimens. In clinical practice, when evaluating patients with various pancreatic cystic lesions, the possibility of AIP should be considered during the differential diagnosis.

Conflict of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

References

1. Sarles H, Sarles JC, Muratore R, Guien C. Chronic inflammatory sclerosis of the pancreas-an autoimmune pancreatic disease? *Am J Dig Dis* 1961; 6:688-98. [PMID: 13746542]
2. Yoshida K, Toki F, Takeuchi T, Watanabe S, Shiratori K, Hayashi N. Chronic pancreatitis caused by an autoimmune abnormality. Proposal of the concept of autoimmune pancreatitis. *Dig Dis Sci* 1995; 40:1561-8. [PMID: 7628283]
3. Hamano H, Kawa S, Horiuchi A, Unno H, Furuya N, Akamatsu T, Fukushima M, et al. High serum IgG4 concentrations in patients with sclerosing pancreatitis. *N Engl J Med* 2001; 344:732-8. [PMID: 11236777]
4. Chang KA, Kim TN, Lee SH. Autoimmune pancreatitis complicated by an infected pseudocyst. *Clin J Gastroenterol* 2010; 3:168-73. [PMID: 26190126]
5. Kanno A, Masamune A, Shimosegawa T. Nationwide epidemiological survey of autoimmune pancreatitis in Japan. *Japan Pancreas Society*. 2015; 30:54-61.
6. Kamisawa T, Takuma K, Tabata T, Inaba Y, Egawa N, Tsuruta K, Hishima T, et al. Serum IgG4-negative autoimmune pancreatitis. *J Gastroenterol* 2011; 46:108-16. [PMID: 20824290]
7. Ryu JK, Chung JB, Park SW, Lee JK, Lee KT, Lee WJ, Moon JH, et al. Review of 67 patients with autoimmune pancreatitis in Korea. A multicenter nationwide study. *Pancreas* 2008; 37:377-85. [PMID: 18953249]
8. Chari ST, Takahashi N, Levy MJ, Smyrk TC, Clain JE, Pearson RK, Petersen BT, et al. A diagnostic strategy to distinguish autoimmune pancreatitis from pancreatic cancer. *Clin Gastroenterol Hepatol* 2009; 10:1097-103. [PMID: 19410017]
9. Miki M, Lee L, Igarashi H, Niina Y, Hijioka M, Ueda K, Fujiyama T, et al. Formation mechanism of pancreatic pseudocyst associated with autoimmune pancreatitis and efficacy of corticosteroid therapy: Considerations from 12 cases. *Japan Pancreas Society* 2014; 29:711-20.