

Contents lists available at [ScienceDirect](#)

## International Journal of Surgery Case Reports

journal homepage: [www.casereports.com](http://www.casereports.com)

# Diagnosis of autoimmune pancreatitis with cholesterol granuloma mimicking intraductal papillary-mucinous carcinoma: A case report



Yusuke Takahashi<sup>a,\*</sup>, Naoyuki Yokoyama<sup>a</sup>, Daisuke Sato<sup>a</sup>, Tetsuya Otani<sup>a</sup>, Koko Mitsuma<sup>b</sup>, Hideki Hashidate<sup>b</sup>

<sup>a</sup> Department of Digestive Surgery, Niigata City General Hospital, Niigata, 950-1197, Japan

<sup>b</sup> Department of Pathology, Niigata City General Hospital, Niigata, 950-1197, Japan

## ARTICLE INFO

## Article history:

Received 8 November 2016

Received in revised form 27 February 2017

Accepted 27 February 2017

Available online 1 March 2017

## Keywords:

Pancreatic diseases

Pancreatic neoplasms

Pancreatic cyst

Ductal carcinoma of the pancreas

Case report

## ABSTRACT

**INTRODUCTION:** Pancreatic cysts are often observed incidentally on abdominal computed tomography (CT). For cysts involving intracystic nodules, malignant neoplasms such as intraductal papillary-mucinous carcinoma (IPMC) should be suspected. In contrast, cholesterol granuloma (CG) rarely occurs in the pancreas, and CG-associated autoimmune pancreatitis (AIP) has not yet been reported. To our knowledge, this is the first reported case of AIP with CG mimicking IPMC.

**PRESENTATION OF CASE:** A 56-year-old woman underwent abdominal CT for preoperative breast cancer screening. Asymptomatic polycystic lesions were detected in the pancreatic tail (maximum diameter, 5 cm). Magnetic resonance cholangiopancreatography and endoscopic ultrasonography revealed main pancreatic duct obstruction and a lesion with intracystic nodules (maximum diameter, 10 mm). Serum levels of pancreatic cancer tumor markers and IgG4 were within normal ranges. Because IPMC was suspected, distal pancreatectomy and splenectomy with regional lymphadenectomy were performed after surgery for breast cancer. Pathological examination of the specimen revealed no epithelial neoplasm; however, cholesterol crystals with foreign body giant cells were observed. Moreover, IgG4-positive plasma cells, diffuse lymphocyte infiltration, storiform fibrosis, and obliterative phlebitis were identified in the non-cystic pancreatic parenchyma. The final diagnosis was AIP with CG.

**DISCUSSION:** CG in the pancreas is rare and its pathogenesis remains unclear. The findings of the present case suggest that chronic inflammation due to AIP may cause local bleeding, and that a reaction to the leaked blood cells causes CG.

**CONCLUSIONS:** Although preoperative diagnosis may be difficult, AIP with CG should be considered as a differential diagnosis in pancreatic cysts involving nodular lesions.

© 2017 The Author(s). Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. Introduction

Asymptomatic cystic lesions in the pancreas are often detected incidentally on computed tomography (CT), abdominal ultrasonography, or magnetic resonance imaging (MRI). Candidates for the differential diagnosis of these lesions generally include pseudocysts, true cysts, and various neoplasms. Candidate neoplasms include intraductal papillary-mucinous neoplasms such as intraductal papillary-mucinous carcinoma (IPMC), serous or mucinous cyst neoplasm, and solid pseudopapillary neoplasm [1–3]. From a

clinical perspective, the identification of a malignant neoplasm is particularly important in these cases because of the associated poor prognosis.

Cholesterol granuloma (CG) is a nodule-forming benign disease that is often observed in the middle ear and petrous apex, but rarely occurs in the pancreas [4–6]. CG occurs because of a foreign body reaction to cholesterol crystals, which are derived from the degradation of blood components [4]. The pathogenesis of CG is thought to be related to local chronic inflammation; however, the pathophysiology of pancreatic CG has not been clarified [6,7]. In this case report, we present a surgically treated case of autoimmune pancreatitis (AIP) with CG that mimicked IPMC. This work has been reported in line with the SCARE criteria [8].

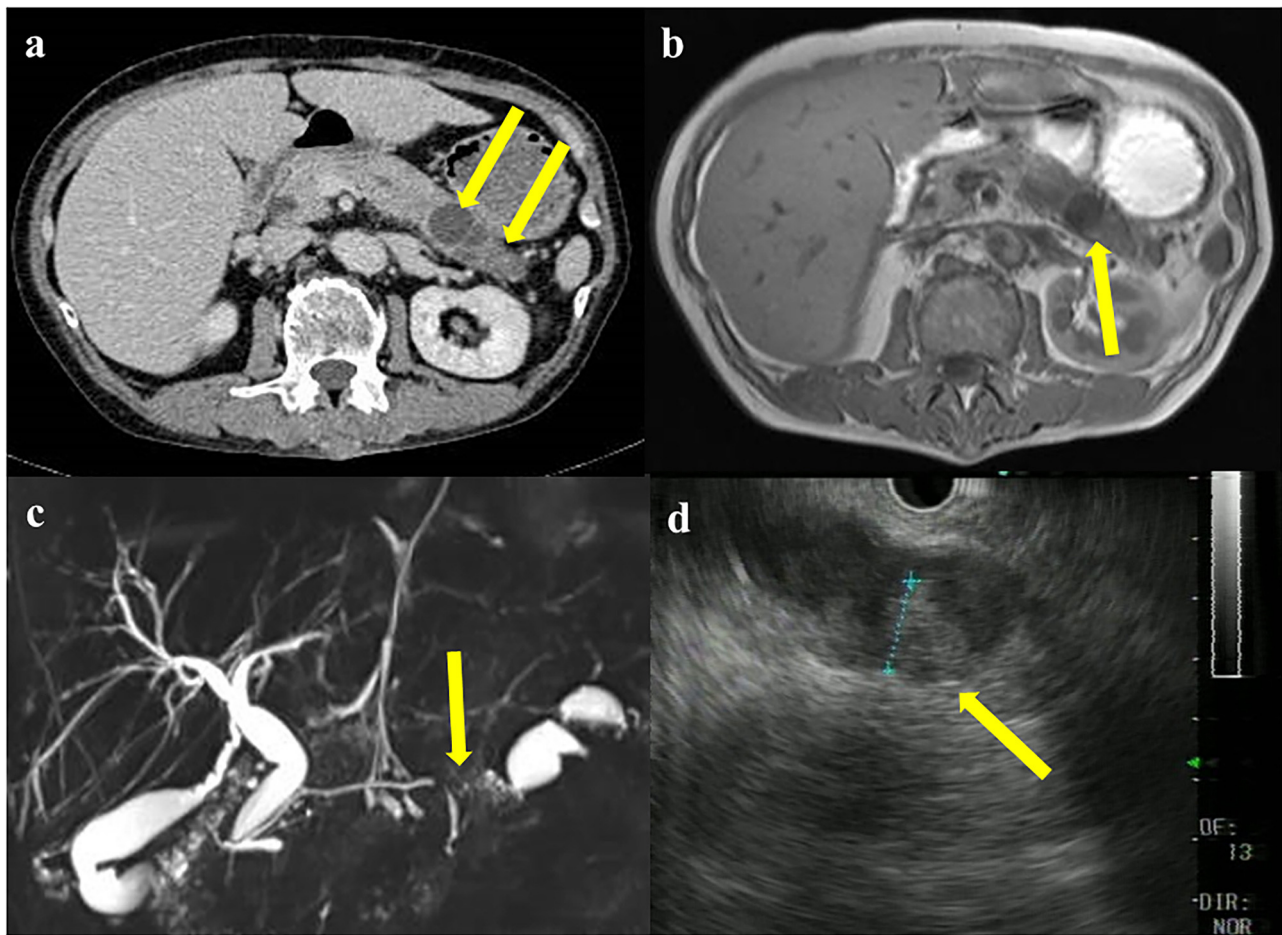
**Abbreviations:** AIP, autoimmune pancreatitis; CG, cholesterol granuloma; CT, computed tomography; IgG4, immunoglobulin G4; IPMC, intraductal papillary-mucinous carcinoma; MRI, magnetic resonance imaging.

\* Corresponding author at: Niigata City General Hospital, Department of Digestive Surgery, 7-463 Shumoku, Chuo-ku Niigata City, 950-1197, Japan.

E-mail address: [niigata.takahashi@hosp.niigata.niigata.jp](mailto:niigata.takahashi@hosp.niigata.niigata.jp) (Y. Takahashi).

<http://dx.doi.org/10.1016/j.ijscr.2017.02.053>

2210-2612/© 2017 The Author(s). Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



**Fig. 1.** Preoperative images. a) Enhanced abdominal computed tomography showing polycystic lesions in the pancreatic tail (arrows). b) The cystic lesion in the pancreas appearing as a low-intensity area on T1-weighted magnetic resonance imaging (arrow). c) Magnetic resonance cholangiopancreatography showing obstruction of the main pancreatic duct in the proximity of the cystic lesions (arrow). d) Endoscopic ultrasonography showing several nodules (maximum diameter, 10 mm) in the cystic lesion (arrow) in the pancreas.

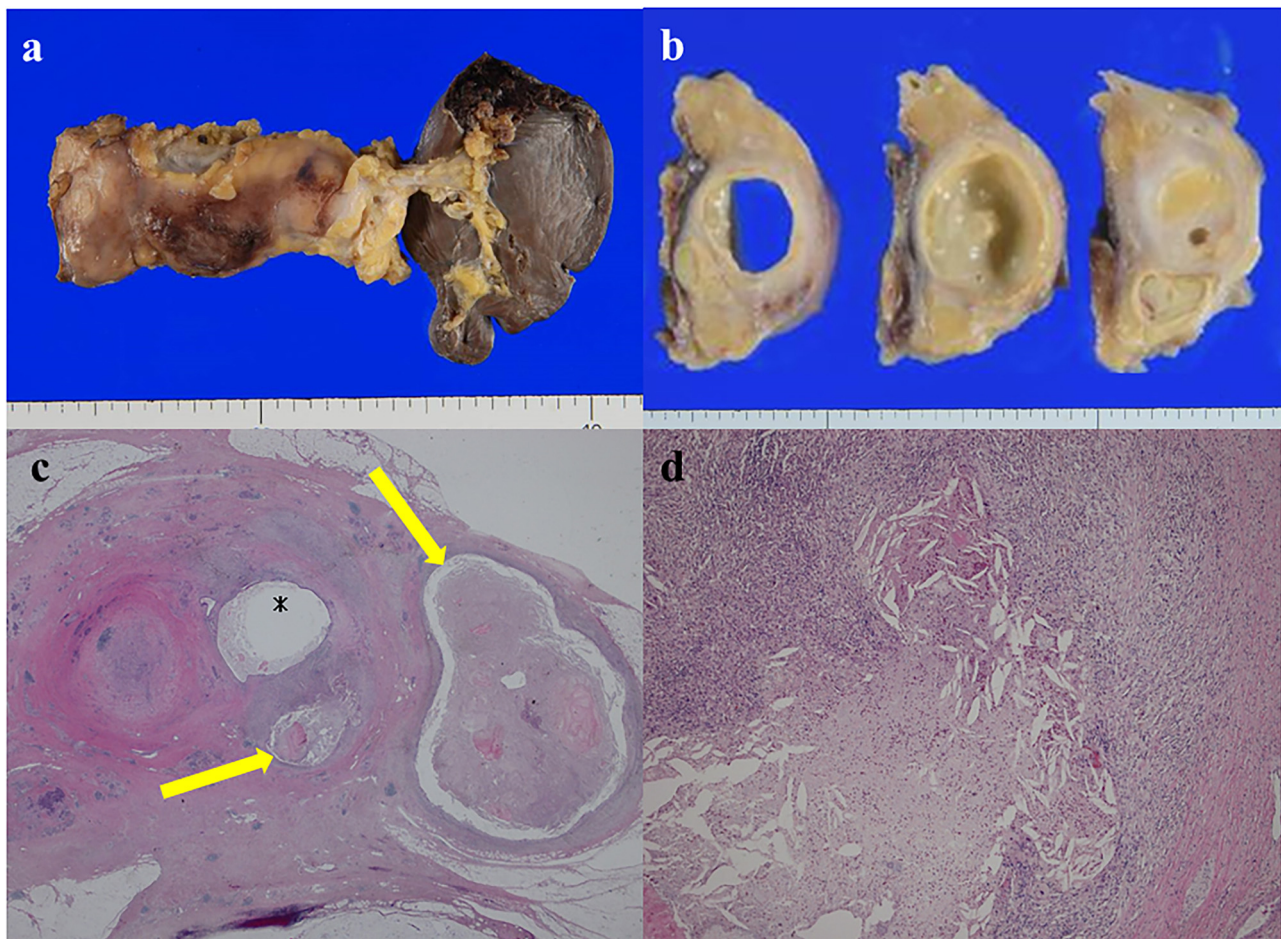
## 2. Presentation of case

A 56-year-old woman with no abdominal symptoms underwent abdominal-enhanced CT as part of a preoperative examination for left breast cancer. The CT showed polycystic lesions (maximum diameter, 5 cm) in the pancreatic tail and no indications of chronic pancreatitis, such as parenchymal atrophy or calcification (Fig. 1a). She had no history of acute pancreatitis, abdominal trauma, or other related conditions. The pancreatic cysts appeared as low- and high-intensity areas on T1- and T2-weighted MRI, respectively (Fig. 1b). Magnetic resonance cholangiopancreatography revealed obstruction of the main pancreatic duct in the proximity of the cystic lesions (Fig. 1c). Intracystic nodules (maximum diameter, 10 mm) were detected using endoscopic ultrasonography (Fig. 1d). Endoscopic retrograde pancreatography could not be performed because cannulating the pancreatic duct was infeasible. Serum levels of immunoglobulin G4 (IgG4) were within the normal limits, as were serum levels of the tumor markers carcinoembryonic antigen, carbohydrate antigen/cancer antigen 19-9, DUPAN-2, and s-pancreas-1 antigen. On the basis of these findings, we suspected IPMC and planned surgical treatment. Gross examination during surgery revealed a hard-cystic tumor at the pancreatic tail that compressed nearby organs. However, neither local invasion, nor distal metastases were found. On dissecting the pancreas, milky white pancreatic juice drained from the main pancreatic duct. Distal pancreatectomy and splenectomy with regional

lymphadenectomy were performed. The operative time and blood loss were 183 min and 3010 g, respectively.

On the surface, the resected pancreas showed nodular and cystic changes (Fig. 2a). The cut section revealed cystic lesions containing milky fluid, which was found to contain cholesterol crystals when examined microscopically (Fig. 2b). Based on gross appearance alone, it was difficult to determine whether the lesion was a malignant neoplasm (such as an IPMC or mucinous cyst neoplasm) or a benign lesion. Histological analysis revealed that the cystic lesion consisted of a dilated main pancreatic duct and cavities of degenerated granulomas containing cholesterol crystals that were surrounded by foreign body giant cells (Fig. 2c and d). In addition, the rest of the pancreatic tissue around the lesion showed prominent lymphocyte infiltration, storiform fibrosis, obliterative phlebitis, and IgG4-positive plasma cells, meeting the pathological diagnostic criteria of AIP, as revised by the Japan Pancreas Society in 2011 (Fig. 3). No neoplastic epithelium was observed in the main or branched pancreatic ducts. On the basis of these findings, we ultimately diagnosed the lesion as AIP with CG. The postoperative course was uneventful and the patient was discharged from our hospital 10 days after the surgery. During the 4-year follow-up period after surgery, she had remnant pancreatitis twice. Her remnant pancreatitis was suspected to be drug-induced, rather than AIP. It was thought to have resulted from drugs (eldecalcitol and/or letrozole) that she was prescribed after surgery for breast cancer,





**Fig. 2.** Resected specimen and findings of cholesterol granuloma. a) It was impossible to distinguish the cholesterol granuloma from a malignant neoplasm based on macroscopic examination of the resected specimen. b) The cut surface of the cystic lesions showed milky fluid. c) Granulomatous and cystic lesions (arrows) surrounded the main pancreatic duct (\*) (H&E, 5× magnification). d) Cholesterol crystals with inflammatory cells and foreign body giant cells were observed (H&E, 40× magnification). H&E: hematoxylin-eosin stain.

and has not occurred again following adjustments to the drugs she was receiving.

### 3. Discussion

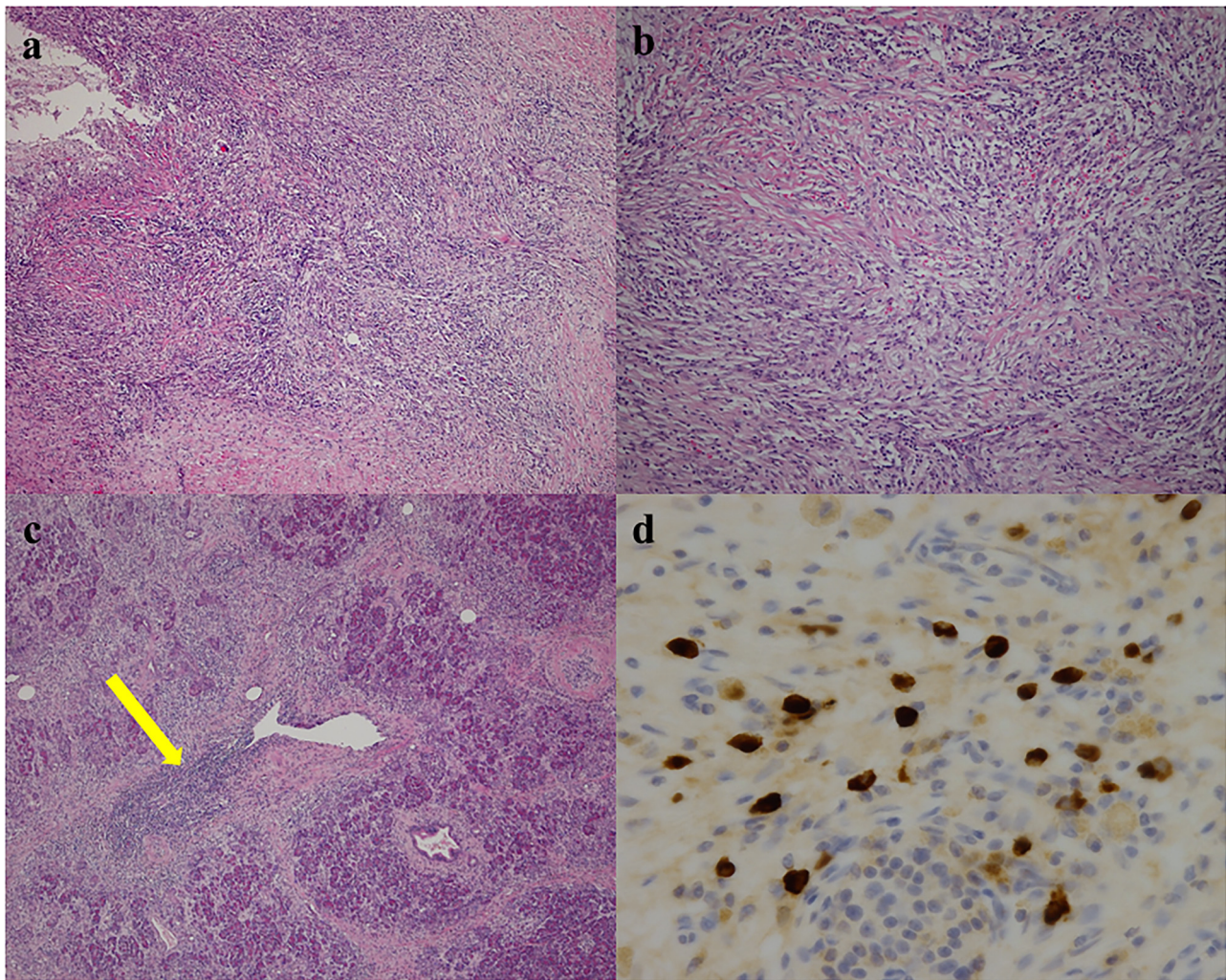
In this report, we have described a novel case of pancreatic CG development, which was suspected to be related to AIP. Although this condition is quite rare, the radiographic and pathologic findings of the present case have important clinical implications for the treatment of cystic diseases of the pancreas.

The clinical manifestation of AIP varies considerably. It is occasionally difficult to distinguish pancreatic duct stenosis due to AIP from that caused by invasive ductal adenocarcinoma. However, AIP mimicking mucin-producing cystic neoplasm is not common [9]. According to both the diagnostic criteria for AIP that were proposed by the Japanese Pancreatic Society and the diagnostic criteria for type 1 AIP that were proposed by the International Consensus Group, all characteristic pathological findings of AIP were confirmed in the present case [10–12]. Patients with AIP usually exhibit clinical signs such as elevated serum IgG4 levels and extra-pancreatic lesions, apparently because AIP is an IgG4-related disease. However, in our case, no clinical signs were observed other than the pathological findings in the resected pancreas. From this perspective, our case was quite unusual in comparison with typical AIP cases. In practice, the unusual features of the case made it difficult to suspect a benign lesion and rule out the neoplas-

tic differential diagnoses based on preoperative findings. AIP is a benign disease, and seldom requires surgery because it responds well to steroids. Owing to a lack of previous literature regarding this entity, detail pathophysiology and mechanism of AIP with CG are unknown; this case report provides new insights into these aspects. Moreover, interestingly, in our patient, the postoperative clinical course is also unusual, because she currently has no AIP- or IgG4-related symptoms without steroid administration after surgery, excluding drug-induced pancreatitis. To elucidate pathophysiology and the clinical significance of AIP with CG, further case reports will be necessary. Consequently, it is important to distinguish this disease from malignant neoplasms of the pancreas, such as IPMC. In our case, CG might have been caused by focal bleeding due to autoimmune pancreatitis. Moreover, pancreatitis might also have been responsible for the obstruction of the main pancreatic duct that was detected on magnetic resonance cholangiopancreatography.

High-intensity areas in both T1- and T2-weighted images and other distinctive MRI features are reportedly characteristic of CG in the middle ear and other organs, including the pancreas [4,5]. In the present case, the pancreatic cysts lacked these distinctive features. Moreover, owing to the absence of characteristic clinical features of AIP, such as diffuse or segmental pancreatic enlargement on CT and elevated serum IgG4 levels, a preoperative definitive diagnosis of AIP seemed to be impossible in this case. Generally, if polycystic lesions that involve nodules are detected in the pancreas, a malign-





**Fig. 3.** Pathological findings that met the diagnostic criteria of autoimmune pancreatitis. a) Prominent lymphocyte and plasma cell infiltration (H&E, 40× magnification). b) Storiform fibrosis (H&E, 100× magnification). c) Obliterative phlebitis (arrow) (H&E, 40× magnification). d) Immunohistochemical staining for IgG4, showing >10 IgG4-positive plasma cells per high-power field (400× magnification). H&E: hematoxylin-eosin stain.

nant neoplasm should be suspected (especially IPMC) and surgical management should be considered despite normal levels of serum tumor markers related to pancreatic cancer [3].

#### 4. Conclusion

AIP with CG is a potentially benign disease. Therefore, to avoid unnecessary surgeries, the differential diagnosis of pancreatic cystic lesions should include AIP with CG mimicking IPMC.

#### Conflicts of interest

None.

#### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

#### Ethical approval

Ethical approval was not obtained for this case report.

#### Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying figures. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

#### Author contributions

Yusuke Takahashi, Naoyuki Yokoyama, Daisuke Sato, Tetsuya Otani, Koko Mitsuma, and Hashidate Hideki contributed to the case report conception and design, and also drafted the manuscript. Naoyuki Yokoyama and Tetsuya Otani participated in the treatment of the patient. Koko Mitsuma and Hideki Hashidate diagnosed this disease pathologically and provided special comments about specimen findings. Naoyuki Yokoyama revised the manuscript critically. All authors read and approved the final manuscript.

#### Registration of research studies

This case report was not registered in a publicly accessible database.

### Guarantor

Yusuke Takahashi accepts full responsibility for the work and the conduct of the case report, had access to the data, and controlled the decision to publish.

### Acknowledgment

None.

### References

- [1] B. Buerke, C. Schülke, Cystic lesions of the pancreas, *Radiologe* 55 (2015) 145–156 (quiz 157. [Article in German]).
- [2] B. Kalb, J.M. Sarmiento, D.A. Kooby, N.V. Adsay, D.R. Martin, MR imaging of cystic lesions of the pancreas, *Radiographics* 29 (2009) 1749–1765.
- [3] A. Stark, T.R. Donahue, H.A. Reber, O.J. Hines, Pancreatic cyst disease: a review, *JAMA* 315 (2016) 1882–1893.
- [4] N. Julien, O. Sterkers, N. Martin, G. Kharsa, F. Paquelin, Cholesterol granuloma of the middle ear. Apropos of 3 cases, *Ann Otolaryngol Chir Cervicofac* 106 (1989) 145–151 (Article in French).
- [5] C. Morales Angulo, A. del Valle Zapico, G. Paternina, M.L. Diéz Lizuain, I. González Rodilla, J. Rama Quintela, Cholesterol granuloma of the petrous apex, *Acta Otorrinolaringol. Esp.* 45 (1994) 203–205 (Article in Spanish).
- [6] H. Imai, S. Osada, Y. Sasaki, A. Ikawa, Y. Tanaka, N. Okumura, et al., Cholesterol granuloma in the pancreas accompanied by peritoneal disseminated lesions, *Pancreas* 40 (2011) 795–796.
- [7] K. Sakai, K. Nakano, S. Matsuda, H. Tsujigiwa, T. Ochiai, M. Shoumura, et al., Pathological analysis of cell differentiation in cholesterol granulomas experimentally induced in mice, *Int. J. Med. Sci.* 13 (2016) 220–224.
- [8] SCARE Group R.A. Agha, A.J. Fowler, A. Saetta, I. Barai, S. Rajmohan, D.P. Orgill, The SCARE Statement: Consensus-based surgical case report guidelines, *Int. J. Surg.* 34 (2016) 180–186.
- [9] A. Kraemer, M. Lewin, P. Balladur, N. Mourra, E. Turet, F. Paye, Autoimmune pancreatitis mimicking an intra-ductal papillary mucinous neoplasm of the pancreas: an original case, *Gastroenterol. Clin. Biol.* 32 (2008) 635–639 (Article in French).
- [10] K. Okazaki, S. Kawa, T. Kamisawa, T. Ito, K. Inui, H. Irie, et al., Working committee of the Japan pancreas society and the research committee for intractable pancreatic disease supported by the ministry of health, labour and welfare of Japan. Amendment of the Japanese consensus guidelines for autoimmune pancreatitis, 2013 I. Concept and diagnosis of autoimmune pancreatitis, *J. Gastroenterol.* 49 (2014) 567–588.
- [11] T. Shimosegawa, S.T. Chari, L. Frulloni, T. Kamisawa, S. Kawa, M. Mino-Kenudson, et al., International Association of Pancreatology: international consensus diagnostic criteria for autoimmune pancreatitis: guidelines of the International Association of Pancreatology, *Pancreas* 40 (2011) 352–358.
- [12] L. Zhang, S. Chari, T.C. Smyrk, V. Deshpande, G. Klöppel, M. Kojima, et al., Autoimmune pancreatitis (AIP) type 1 and type 2: an international consensus study on histopathologic diagnostic criteria, *Pancreas* 40 (2011) 1172–1179.

### Open Access

This article is published Open Access at [sciedirect.com](http://sciedirect.com). It is distributed under the [IJSCR Supplemental terms and conditions](#), which permits unrestricted non commercial use, distribution, and reproduction in any medium, provided the original authors and source are credited.