A Patient with Pancreatic Castleman’s Disease Arising around the Main Pancreatic Duct

Takaaki Matsumoto, Kosuke Okuwaki, Mitsuhiro Kida, Shi-Xu Jiang, Hiroshi Imaizumi, Hiroshi Yamauchi, Shiro Miyazawa, Tomohisa Iwai, Miyoko Takezawa, Hiroshi Tajima and Wasaburo Koizumi

Abstract

Castleman’s disease of the pancreas is extremely rare. To the best of our knowledge, Castleman’s disease arising around the main pancreatic duct has not been previously reported. The patient was a 74-year-old man. Abdominal ultrasonography performed at a health check-up revealed a dilated main pancreatic duct. Pancreatic cancer was strongly suspected on various imaging studies. However, the results of a cytological examination of the pancreatic juice were negative for malignancy. The patient did not want to undergo a histological diagnosis by endoscopic ultrasound-guided fine-needle aspiration, thus pylorus-preserving pancreatoduodenectomy was performed. Pancreatic Castleman’s disease arising around the main pancreatic was diagnosed by the histopathological examination.

Key words: Castleman’s disease, pancreas, EUS

(Intern Med 54: 2007-2012, 2015)
(DOI: 10.2169/internalmedicine.54.4665)

Introduction

In 1956, Castleman et al. in the United States first reported Castleman’s disease, a lymphoproliferative disease associated with localized or multicentric lymph node hyperplasia (1). Castleman’s disease can be classified into hyaline-vascular (HV) type, plasma cell (PC) type, and mixed type (2) based on the histological features. Clinically, Castleman’s disease can be divided into unicentric (localized) or multicentric disease. The most common site of the soft tissue mass associated with Castleman’s disease is the mediastinum. To the best of our knowledge, only 24 cases of Castleman’s disease of the pancreas have been reported. Pancreatic Castleman’s disease is thus extremely rare. We herein describe a case of Castleman’s disease arising around the main pancreatic duct that presented with imaging findings similar to those of pancreatic cancer. A systematic literature search indicated that similar cases have not yet been reported, making this case very interesting.

Case Report

The patient was a 74-year-old man in whom abdominal ultrasonography performed during a health check-up revealed dilatation of the main pancreatic duct at the body and tail of the pancreas. Contrast-enhanced computed tomography (CT) of the abdomen was performed for further evaluation, and a mass 12 mm in diameter was found in the head of the pancreas. Cancer of the head of the pancreas was suspected, and the patient was referred to our hospital.

The medical history and the family history were irrelevant to the current disorder. As for lifestyle, the patient had smoked 20 cigarettes per day for 34 years and drank 44 g of alcohol per day for 54 years. Blood tests showed no distinct abnormalities, and the results of the tests were negative for carcinoembryonic antigen, cancer antigen 19-9, DUPAN-2, and SPan-1. The interleukin-6 levels were not measured. Contrast-enhanced CT of the abdomen showed a poorly demarcated mass lesion with slight enhancement of the pan-
A contrast-enhanced CT scan of the abdomen showing low enhancement of the pancreatic head as compared with that of the pancreatic parenchyma in the early phase (A). A poorly demarcated area showing mild enhancement was seen in the late phase (B).

Endoscopic ultrasonography showed a well-demarcated, ischemic, hypoechoic area, 15×15 mm in size, at the head of the pancreas (A, B). The main pancreatic duct distal to the same site was dilated to approximately 4 mm (C).

Endoscopic retrograde pancreatography showed a severe stricture in the main pancreatic duct at the head of the pancreas and mild dilation of the pancreatic duct near the tail of the pancreas.

The imaging findings most strongly suggested cancer of the head of the pancreas. The differential diagnosis included pancreatic neuroendocrine neoplasm, acinar cell carcinoma, serous cystic neoplasm (solid type), and chronic pancreatitis. The results of a cytological examination of a sample of the pancreatic juice obtained by aspiration were negative for malignancy. We recommended that the patient undergo endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) for a definitive diagnosis. However, the patient wanted to undergo surgery without any histopathological evidence. Therefore, pylorus-preserving pancreatoduodenectomy, PD-II reconstruction, and D2 lymph-node dissection were performed.

The pathological findings of the resected specimen are shown in Fig. 4. Macroscopically, the mass was a greyish-white, poorly demarcated nodular lesion, 15 mm in diameter, located in the head of the pancreas. A histological ex-
amination revealed that the lesion consisted of lymphoid tissue, which surrounded the main pancreatic duct and its branches. There was no obvious mucosal destruction due to lymphocytic infiltration in the pancreatic duct. Lymphoid follicles were scattered throughout the lesion, some of which contained mildly hyalinized small vessels. Vascular prolif-
Table. Summary of Pancreatic Castleman’s Disease (HV Type).

| Year | Reference | Age (years) / Sex | Site of tumor | Size (mm) | Symptoms | Treatment |
|------|-----------|------------------|---------------|-----------|----------|-----------|
| 1982 |           | 71/Female        | Body and tail | 50        | No symptoms | STP       |
| 1989 |           | 64/Female        | Tail          | 35        | Back pain   | DP        |
| 1993 |           | 34/Female        | Peripancreatic | 60        | Abdominal pain | Excision |
| 1994 |           | 36/Female        | Peripancreatic | 40        | No symptoms   | Excision |
| 2004 |           | 56/Female        | Head          | 25        | Abdominal pain | PD        |
| 2005 |           | 53/Male          | Tail          | 46        | No symptoms   | DP        |
| 2007 |           | 58/Male          | Head          | 40        | No symptoms   | PD        |
| 2007 |           | 49/Female        | Body          | 35        | No symptoms   | Excision |
| 2007 |           | 23/Female        | Body and tail | 80        | Abdominal pain | DP        |
| 2008 |           | 50/Female        | Body          | 39        | No symptoms   | Excision |
| 2012 |           | 64/Male          | Head and body | 61        | Systemic     | Enucleation |
| 2013 |           | 48/Female        | Peripancreatic | 38        | Abdominal pain | DP        |
| 2015 | Present case | 74/Male        | Head          | 15        | No symptoms   | PD        |

DP: Distal pancreatectomy, STP: Subtotal pancreatectomy, PD: Pancreatoduodenectomy

**Discussion**

Castleman’s disease can be classified into HV type, PC type, and mixed type based on the histological features. Clinically, Castleman’s disease can be divided into unicentric (localized) or multicentric disease. Most cases of unicentric Castleman’s disease are HV type (3). PC type is characterized by chronic inflammatory symptoms due to the excessive production of interleukin-6 by enlarged lymph nodes, which is associated with various laboratory abnormalities such as gammaglobulinemia, elevated C-reactive protein levels, and the appearance of various autoantibodies. PC type can be associated with interstitial pneumonia, glomerulonephritis, and secondary amyloidosis. In contrast, unicentric Castleman’s disease (most commonly HV type) is often asymptomatic early in the disease course, with no characteristic findings on the blood tests. Therefore, the disease is generally detected accidentally based on symptoms associated with tumor growth or the results of imaging studies. Surgical resection is the treatment of choice, and the outcomes after curative resection are normally good. The most common site of the soft tissue mass associated with Castleman’s disease is the mediastinum. We systematically searched the PubMed/MEDLINE and Embase databases and found only 24 reported cases of Castleman’s disease of the pancreas (4-25). Thirteen patients had HV type, the same histologic type as our patient (4, 5, 7, 8, 13-15, 18-20, 23-25). The characteristics of these patients are summarized in Table. The median age was 50 years (range, 23 to 71 years). There were 4 men and 9 women. HV type Castleman’s disease arose in the head of the pancreas in 2 patients, the body of the pancreas in 2, the tail of the pancreas in 3, the head and body of the pancreas in 1, the body and tail of the pancreas in 2, and was peripancreatic in 3. The median tumor diameter was 40 mm (range, 35 to 80 mm). The initial symptoms were abdominal pain in 4 patients, back pain in 1, systemic in 1, and absent in 7. As for treatment, pancreaticoduodenectomy was performed in 2 patients, distal pancreatectomy in 5, subtotal pancreatectomy in 1, excision in 4, and enucleation in 1. None of the 24 previously reported patients showed changes involving the main pancreatic duct. Pancreatic Castleman’s disease arising around the main pancreatic duct, such as in our patient, is thus considered extremely rare.

In the present patient, Castleman’s disease involved the main pancreatic duct. A severe stricture had developed in the main pancreatic duct at the site of the mass. Dilatation of the pancreatic duct was therefore present at the tail of pancreas, suggesting pancreatic cancer. A differential diagnosis from pancreatic cancer was thus challenging. In addi-
tion to pancreatic cancer, the differential diagnosis included pancreatic neuroendocrine neoplasm, acinar-cell carcinoma, serous cystic neoplasm (solid type), chronic pancreatitis, and follicular pancreatitis.

Castleman’s disease is characterized by a well-demarcated, homogeneous, parenchymal, hypoechoic mass on abdominal ultrasonography. Calcification in the lesion is present in some cases (19). The findings on EUS are considered similar to those on abdominal ultrasonography. On contrast-enhanced CT, the lesions are generally visualized as markedly enhanced, well-demarcated parenchymal masses in the relatively early phase. Lesions less than 5 cm in diameter are usually homogeneously and markedly enhanced, whereas those 5 cm or more in diameter may show heterogeneous enhancement, reflecting the presence of fibrosis or necrosis in the lesion (19). One study described a patient who underwent contrast-enhanced ultrasonography using microbubble contrast agents. The lesion was markedly enhanced in the arterial phase, with gradual washout during the venous phase, consistent with the findings on contrast-enhanced CT (19). However, many other pancreatic tumors present with similar imaging findings. Currently, imaging findings specific to Castleman’s disease remain to be established. In particular, Castleman’s disease may be difficult to diagnose solely on the basis of imaging studies in patients with small lesions, similar to the present case. Therefore, a histopathological examination is essential for the diagnosis of Castleman’s disease. A correct diagnosis requires an assessment of the overall structure of lymph nodes. A needle biopsy or other procedures for partial biopsy may therefore be inappropriate. In fact, EUS-FNA was performed in 2 previous patients, but did not lead to a definitive diagnosis in either patient (14, 15). Castleman’s disease of the pancreas was successfully diagnosed preoperatively in only 1 patient. EUS-guided Trucut biopsy (EUS-TCB) using a 19-gauge Tru-Cut needle was performed for the diagnosis (20). As compared with FNA, TCB can obtain a sufficient tissue volume, which may have led to the correct diagnosis. In our patient, however, the tumor size was only 15 mm in diameter, and TCB was not feasible. A definitive diagnosis would also have been difficult to obtain on EUS-FNA, even if informed consent had been obtained from the patient. Conversely, Torrez et al. reported that even small specimens obtained by FNA may be useful for the differential diagnosis of malignant tumors of the pancreas (23). However, we have frequently encountered difficulty in the detailed examination, including immunostaining, of small specimens. Therefore, we believe that the differential diagnosis is difficult.

According to a histopathological examination of the lesion in our patient, atypia was low-grade despite the presence of lymphocyte proliferation at the lesion site. Moreover, the lesion was well demarcated from the normal tissue and only compressed the main pancreatic duct with no signs of invasion. These findings suggested non-tumorous lymphoproliferative disease. The differential diagnosis of non-tumorous lymphoproliferative disease included IgG4-related sclerosing disease and mucosa-associated lymphoid-tissue (MALT) lymphoma. The presence of virtually no IgG4-positive cells on immunostaining ruled out IgG4-related sclerosing disease. A polymerase chain reaction revealed no distinct immunoglobulin heavy chain gene rearrangements. The k/λ ratio was not abnormal, ruling out monoclonal immunoglobulinemia. There was also no evidence supporting a diagnosis of MALT lymphoma. The disease concept of “follicular pancreatitis” was proposed by Zen et al. (26). This disease is very similar to Castleman’s disease because lymphoid follicles are formed in the pancreatic parenchyma. Histopathologically, however, our patient showed many hyalinized small blood vessels coursing from outside the lymphoid follicles to a germinal center, a finding that is consistent with the hyaline-vascular type of Castleman’s disease. Because the present case sporadically showed characteristic findings of HV type Castleman’s disease, such as hyalinized small blood vessels entering a germinal center from an extralymphatic site, we made a diagnosis of Castleman’s disease.

We herein described our experience with a patient who had pancreatic Castleman’s disease involving the main pancreatic duct. Castleman’s disease of the pancreas is extremely rare. To the best of our knowledge, however, pancreatic Castleman’s disease arising around the main pancreatic duct has not been reported previously. Because our patient showed changes of the main pancreatic duct on the imaging studies, a differential diagnosis from pancreatic cancer was challenging.

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

References

1. Castleman B, Iversion L, Menendez VP. Localized mediastinal lymph node hyperplasia resembling Thymoma. Cancer 9: 822-830, 1956.
2. Keller AR, Hochholzer L, Castleman B. Hyaline-vascular and plasma-cell types of giant lymph node hyperplasia of the mediastinum and other locations. Cancer 29: 670-683, 1972.
3. Frizzera G. Castleman’s disease and related disorders. Semin Diagn Pathol 5: 346-364, 1988.
4. Lepke RA, Pagani JJ. Pancreatic Castleman disease simulating pancreatic carcinoma on computed tomography. J Comp Assist Tomogr 6: 1193-1195, 1982.
5. LeVan T, Clifford S, Staren ED. Castleman’s tumour masquerading as a pancreatic neoplasm. Surgery 106: 884-887, 1989.
6. Brossard G, Ollivier S, Pellegrin JL, Barbeau P, De Mascarel A, Leng B. Pancreatic Castleman’s tumour revealed by prolonged fever. Presse Med 21: 86, 1992.
7. Corbisier F, Ollier JC, Adloff M. Pancreatic localization of a Castleman’s tumour. Acta Chir Belg 93: 227-229, 1993.
8. Baikovas S, Glenn D, Stanton A, Vonhethoff L, Morris DL. Castleman disease: an usual cause of a peripancreatic hilar mass. Aust N Z J Surg 64: 219-221, 1994.
9. Chaulin B, Pontais C, Laurent F, De Mascarel A, Drouillard J. Pancreatic Castleman disease: CT finding. Abdom Imaging 19: 160-161, 1994.
10. Le Borgne J, Joubert M, Emam N, et al. Pancreatic localization of a Castleman’s tumour. Gastroenterol Clin Biol 23: 536-538, 1999.
11. Soler R, Rodriguez E, Bello MJ, Alvarez M. Pancreatic Castleman’s disease: MR findings. Eur Radiol 13: 48-50, 2003.
12. Erkan N, Yildirim M, Selek E, Sayhan S. Peripancreatic Castleman disease. J Pancreas 5: 491-494, 2004.
13. Yilmaz R, Ersin S, Makay O, Akgun E, Yuce G, Elmas N. Pancreatic Castleman’s tumor: an unusual case. Acta Chir Belg 104: 354-356, 2004.
14. Goetze O, Banasch M, Junker K, Schmidt WE, Szymanski C. Unicentric Castleman’s disease of the pancreas with massive central calcifications. World J Gastroenterol 11: 6725-6727, 2005.
15. Wang H, Wieczorek RL, Zenilman ME, Desoto-Lapaix F, Ghosh BC, Bowne WB. Castleman’s disease in the head of the pancreas: report of a rare clinical entity and current perspective on diagnosis, treatment, and outcome. World J Surg Oncol 5: 133, 2007.
16. Wasielica-Berger J, Kaniewska M, Cepowicz D, Wereszczynska-Siemiatkowska U, Kebr a B, Dabrowski A. Castleman disease imitating pancreatic tumor presenting with pericardial and pleural effusion. Pancreas 35: 382-384, 2007.
17. Maithel SK, Pratt W, Kelleher T, et al. Autoimmune pancreatitis in the setting of Castleman disease. Pancreas 35: 384-387, 2007.
18. Tunru-Dinh VW, Ghani A, Tom YD. Rare case of Castleman disease involving the pancreas. Am Surg 73: 1284-1287, 2007.
19. Mangini M, Aiani L, Bertolotti E, et al. Parapancreatic Castleman disease: contrast-enhanced sonography and CT features. J Clin Ultrasound 35: 207-211, 2007.
20. Rhee KH, Lee SS, Huh JR. Endoscopic ultrasonography-guided trucut biopsy for the preoperative diagnosis of peripancreatic Castleman’s disease: a case report. World J Gastroenterol 14: 2115-2117, 2008.
21. Caralabopoulos A, Misiakos EP, Foukas P, et al. Localized peripancreatic plasma cell Castleman disease. Am J Surg 199: e51-e53, 2010.
22. Campa D, Farina EC, Resegotti A, et al. Castleman disease in differential diagnosis of a pancreatic mass. Eur J Surg 168: 744-746, 2002.
23. Apodaca-Torrez FR, Filho BH, Beron RJ, Goldenberg A, Goldman SM, Lobo EJ. Castleman’s disease mimicking pancreatic tumor. J Pancreas 13: 94-97, 2012.
24. Fu L, Wang XL, Babu SR, et al. Pancreatic Castleman’s disease: studies of three cases and a cumulative review of the literature. Indian J Surg 75: 34-38, 2013.
25. Cecka F, Ferko A, Jon B, Subrt Z, Kasparova P, Repak R. Pancreatic Castleman disease treated with laparoscopic distal pancreatectomy. Hepatobiliary Pancreat Dis Int 12: 332-334, 2013.
26. Zen Y, Ishikawa A, Ogiso S, Heaton N, Portmann B. Follicular cholangitis and pancreatitis—clinicopathological features and differential diagnosis of an under-recognized entity. Histopathology 60: 261-269, 2012.

© 2015 The Japanese Society of Internal Medicine
http://www.naika.or.jp/imonline/index.html