Castleman disease mimicked pancreatic carcinoma: report of two cases

Hua Guo1,2,3, Yan Shen1,2,3, Wei-Lin Wang1,2,3, Min Zhang1,2,3, Hong Li1,2,3, Ying-Sheng Wu1,2,3, Sheng Yan1,2,3, Xiao Xu1,2,3, Jian Wu1,2,3 and Shu-Sen Zheng1,2,3*

Abstract
Castleman disease (CD) is an uncommon benign lymphoproliferative disorder, which usually presents as solitary or multiple masses in the mediastinum. Peripancreatic CD was rarely reported. Herein, we report two cases of unicentric peripancreatic CD from our center. A 43-year-old man and a 58-year-old woman were detected to have a pancreatic mass in the routine medical examinations. Both of them were asymptomatic. The computed tomography and ultrasonographic examination revealed a mild enhancing solitary mass at the pancreatic head/neck. No definite preoperative diagnosis was established and Whipple operations were originally planned. The intraoperative frozen section diagnosis of both patients revealed lymphoproliferation. Then the local excisions of mass were performed. Histological examination revealed features of CD of hyaline-vascular type. No recurrence was found during the follow-up period. CD should be included in the differential diagnosis of pancreatic tumors. Local excision is a suitable surgical choice.

Keywords: Castleman disease, Peripancreatic tumor, Hyaline-vascular type

Background
Castleman disease (CD) is an uncommon benign lymphoproliferative disorder of unknown etiology. It was first described by Castleman in 1956 [1]. There are three pathologic variants: hyaline vascular CD, plasma cell CD, and mixed type of CD is characterized that a patient had features of both hyaline vascular and plasma cell types of CD [2]. Plasmablastic variant of CD, which was considered as a subvariant of plasma cell type, occurs predominantly in immunosuppressed patients and human immunodeficiency virus (HIV)-positive patients [3]. Clinically, CD may present in the forms of unicentric and multicentric. The unicentric variant of CD (UCD) is the most common form of the disease, which is confined to a single lymph-node chain or area, with hyaline vascular type. It is often asymptomatic and curable by surgical excision of the mass. The multicentric variant of CD (MCD) is a less common but more aggressive form. Its corresponding histological pattern is usually the plasma cell and mixed type [3]. Unicentric peripancreatic CD was rarely reported in the published literature. Herein, we report two cases of unicentric peripancreatic CD of hyaline vascular type from our center.

Case presentation
Case 1: a 43-year-old man visited to us with an abdominal mass detected by ultrasonographic examination in a routine medical examination. He had a history of IgA nephropathy for 1 year. The preoperative serum creatinine was slightly elevated. The patient was asymptomatic with a normal appetite, no vomiting, no abdominal pain, no jaundice, and no weight loss. The tumor markers CEA, AFP, and CA125 were normal, the CA 19-9 was 54.8 U/mL(normal range, 0–37 U/mL). Chest X-ray was normal. As the serum creatinine was slightly elevated, the unenhanced computed tomography (CT) and contrast-enhanced ultrasonography were performed, the result showed a 3 × 2.1 cm, well-demarcated, mass at the pancreatic head (Figure 1).

Case 2: a 58-year-old woman with no remarkable medical history visited our hospital with a mass detected by ultrasonographic examination in a routine examination.

*Correspondence: shusenzheng@zjue.edu.cn
1Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery
First Affiliated Hospital,School of Medicine, Zhejiang University, 79 Qingchun Street, Zhejiang Province, Hangzhou 310003, China
2Key laboratory of Combined Multi-organ Transplantation, Ministry of Public Health, 79 Qingchun Street, Zhejiang Province, Hangzhou 310003, China
Full list of author information is available at the end of the article

© 2012 Guo et al; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/2.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.
This patient was also asymptomatic. Laboratory data were within normal limits and a chest X-ray was normal. Tumor markers CEA, AFP, and CA125 were normal, the CA 19–9 was 46.4 U/mL. Contrast-enhanced CT showed a 4 × 2.7 cm, well-demarcated, mild enhancing mass at the pancreatic neck (Figure 2).

Both patients were asymptomatic. The image findings revealed a mass in pancreas, preoperative tumor marker CA 19–9 were slightly elevated. Both were mimicked carcinoma of pancreas, and Whipple operations were planned before the operation. Intraoperatively, the masses were found closely adhere to pancreas. The masses were encapsulated and well demarcated from the attached pancreatic tissue. Thorough exploration revealed no intra-abdominal lymphadenopathy or any visceral abnormalities. The intraoperative frozen section diagnosis of both patients revealed lymphoproliferation. Then the original plan was changed, the local excisions of the masses were performed to avoid a more morbidity manner of the Whipple operation. The postoperative
histological examination revealed typical features of the hyaline-vascular type of CD. Hematoxylin-eosin (HE) stains showed typical paracortical expansion with mixed inflammatory cells, and a prominent proliferation of blood vessels. High-power photomicrograph of one area showed a germinal center with the classic ‘onionskin’ appearance (Figure 3). The tumor markers were re-examined 1 month after the operation, and the CA 19–9 in both patients were within normal range.

Discussion
The etiology and pathophysiologic basis of CD remains unclear until now. The chronic inflammation, immuno-deficiency state, and autoimmune disorders (such as viral infection involving the human herpes virus 8, the Epstein-Barr virus, or autoimmune hemolytic anemia) are considered to be the possible causal factors of CD. The dysregulation of inflammatory mediators, particularly interleukin-6 (IL-6) secretion has become the leading theory explaining constitutional symptoms and laboratory abnormalities [4,5]. Of the two patients, case1 was diagnosed as IgA nephropathy which considered an autoimmune disease, and received steroid treatment, but case2 had no inflammatory or autoimmunity disorder. Komatsuda et al. [6] reported a patient who developed UCD during the course of immunosuppressive therapy for IgA nephropathy associated with cutaneous nodules, the symptoms and abnormal laboratory findings were improved after anti-interleukin-6 receptor antibody administration. Whether case1 with peripancratic CD was associated with IgA nephropathy or immunosuppressive therapy was uncertain.

Clinically, CD is usually divided into unicentric and multicentric types. The UCD is most common with Hyaline vascular type. The mass is usually asymptomatic and localized, and is discovered incidentally, although some patients present with fever, fatigue, and localized pressure symptoms from the mass. The histological findings are of a multiple germinal center surrounded by circumferentially arranged layers in an onionskin pattern, of small lymphocytes, with a prominent vascular stroma and occasional plasma cells, which are characteristic of hyaline-vascular disease.

The preoperative diagnosis of the CD is very difficult. CD most commonly presents as a solitary mass. The classic CT appearance of hyaline vascular CD is that of a solitary enlarged lymph node or localized nodal mass that demonstrate homogeneous intense enhancement after contrast material administration. Diagnostic image sometimes mimics malignancy and CD cannot be identified because of the lack of disease specific signs. Some case reports had introduced an endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) to establish the diagnosis of CD preoperatively [7,8], however, the sensitivity and specificity of this manner still had not been confirmed by large sample random clinical trial. The diagnosis of CD was still mostly dependent on the postoperative histological examination. Our two patients were both mimicked as carcinoma of pancreas so the preoperative cytologic examinations were not performed.
Surgery, radiotherapy, steroids, immunotherapy (interferon-α or anti-IL-6 antibodies), and combination chemotherapy have all been used to manage the disease [4]. Complete surgical excision remains the most used treatment strategy for unicentric CD, which confers a cure rate approaching 100% [9]. When the lesion is completely removed the prognosis is always perfect. If complete resection is difficult, partial resection may also be helpful, the recurrence rate after subtotal resection is also low [10]. Recurrence of CD after surgical excisions is rarely reported, even if the patients show recurrence, the disease remains progression-free after a repeat resection [11]. Extended surgery, which might cause more morbidity, is not required because CD was considered as a benign procedure. Radiotherapy or chemotherapy may be helpful, but it is not curative and the results vary [12]. Neoadjuvant use of rituximab [13] and neoadjuvant radiotherapy [14] have been reported in the treatment of irresectable unicentric CD to reduce tumor size and vascularity to allow for a less morbid surgical resection. In the two patients, during the intraoperative exploration, the occupation was found solitary, and the masses were encapsulated and well demarcated from the attached pancreatic tissue. The intraoperative frozen section diagnosis revealed lymphoproliferation. So the original surgical plans were changed, the Whipple resection given up, and the mild morbidity local excisions were performed, respectively. When the pathology results were available, chest CT scan and neck ultrasound scan were tested to confirm the tumors were unicentric. The postoperative courses were uneventful. No recurrence was found during the follow-up period. Interestingly, preoperative CA 19–9 of the two patients were slightly elevated, and the CA 19–9 levels were reduced to normal range after the tumor excision. Whether the elevation of serum CA 19–9 level correlated with the CD needs more evidences.

Conclusions
In conclusion, CD should be included in the differential diagnosis of pancreatic tumors. Preoperative and intraoperative differential diagnosis of CD is important. The less morbidity local excision is a suitable surgical choice.

Consent
Written informed consent was obtained from the patients for publication of this report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interest
The authors declare that they have no competing interests.

Authors’ contributions
Guo H had the idea of case report and wrote the main manuscript. Wang WL, Shen Y, and Zhang M performed the operations. Wu YS, Yan S, Xu X, and Wu J collected the patients’ data and follow-up radiological images. Li H participated in the manuscript preparation. Zheng SS revised the manuscript for important intellectual content, and gave the final approval for the version to be submitted for publication. All authors read and approve the final manuscript.

Acknowledgements
This work was supported by Projects of Ministry of Public Health (No.2010022015). We thank all the pathologists, particularly Professor ZM Wang, in our hospital for their work on the pathology.

Author details
1Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, First Affiliated Hospital, School of Medicine, Zhejiang University, 79 Qingchun Street, Zhejiang Province, Hangzhou 310003, China. 2Key laboratory of Combined Multi-organ Transplantation, Ministry of Public Health, 79 Qingchun Street, Zhejiang Province, Hangzhou 310003, China. 3Key laboratory of Organ Transplantation of Zhejiang Province, 79 Qingchun Street, Zhejiang Province, Hangzhou 310003, China.

Received: 27 April 2012 Accepted: 6 July 2012 Published: 23 July 2012

References
1. Castleman B, Verson L, Menendez VP: Localized mediastinal lymphnode hyperplasia resembling thymoma. Cancer 1956, 9:822–830.
2. Cronin DM, Wamke RA: Castleman disease: an update on classification and the spectrum of associated lesions. Adv Anat Pathol 2009, 16:236–246.
3. Casper C: The aetiology and management of Castleman disease at 50 years: translating pathophysiology to patient care. Br J Haematol 2005, 129:5–17.
4. El-Osta HA, Kurzrock R: Castleman’s disease: from basic mechanisms to molecular therapeutics. Oncologist 2011, 16:497–511.
5. Powles T, Stebbing J, Bazies J, Hatzimichael E, Mandala S, Nelson M, Gazzard B, Bower M: The role of immune suppression and HIV-V in the increasing incidence of HIV-associated multicentric Castleman’s disease. Ann Oncol 2009, 20:775–779.
6. Komatsu A, Wakai H, Togashi M, Sawada K: IgA nephropathy associated with Castleman disease with cutaneous involvement. Am J Med Sci 2010, 339:486–490.
7. Yasufuku K, Chiyo M, Seike Y, Chihajed PN, Shibuya K, Iizasa T, Fujisawa T: Real-time endobronchial ultrasound-guided transbronchial needle aspiration of mediastinal and hilar lymph nodes. Chest 2004, 126:122–128.
8. Kashab MA, Canto MI, Singh VR, Ali S2, Fishman EK, Edli BH, Giday S: A rare case of peripancreatic Castleman’s disease diagnosed preoperatively by endoscopic ultrasound-guided fine needle aspiration. Endoscopy 2011, 43(suppl 2 UCTN):E128–E130.
9. Chen CH, Liu HC, Tung KY, Lee JJ, Liu CL, Liu TP: Surgical outcome of superficial and deep Castleman disease. ANZ J Surg 2007, 77:339–343.
10. Bowne WB, Lewis JJ, Filippa DA, Nesvold R, Brooks AD, Burt ME, Brennan MF: The management of unicentric and multicentric Castleman’s disease: a report of 16 cases and a review of the literature. Cancer 1999, 85:706–717.
11. Kim MH, Hwang S, Choi YB, Oh ST, Kim SC, Choi GM, Ahn CS, Kim KH, Moon DB, Ha TY, Song GW, Jung DH, Yu ES, Lee SG: Castleman disease of the abdomen–single-center experience of 13 surgically treated patients over 11 years. Hepatogastroenterology 2010, 57:1060–1063.
12. Baek HI, Kook H, Han DK, Shin MG, Kim HS, Hwang TJ: Unicentric Castleman disease relapsed after rituximab-CHOP chemotherapy or radiation therapy in an adolescent. J Pediatr Hematol Oncol 2012, 34(5): e206–e208. PMID:22258344.
13. Bandiera B, Ainsworth C, Shikle J, Rupard E, Roach M: Treatment of unicentric Castleman disease with neoadjuvant rituximab. Chest 2010, 138(1):1239–1241.
14. de Vries IA, van Acht MM, Demeyere TB, Lybeer ML, de Zoete JP, Nieuwenhuijzen GA: Neoadjuvant radiotherapy of primary inersectable unicentric Castleman’s disease: a case report and review of the literature. Radiat Oncol 2010, 5:7.

doi:10.1186/1477-7819-10-154

Cite this article as: Guo et al.: Castleman disease mimicked pancreatic carcinoma: report of two cases. World Journal of Surgical Oncology 2012 10:154.