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CASE REPORT

Unicentric Castleman's disease of hepatic hilum and retroperitoneum: a case report for endoscopic ultrasonography differential diagnosis and a literature review

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Abstract
Castleman's disease (CD) is a highly heterogeneous clinico-pathological entity belonging to the lymphoproliferative disorders. CD can occur in any part of the human body where lymph nodes are present. In addition, very few cases have been reported in hepatic hilum. Here, we present a case of a middle-aged female patient who was presented with abdominal pain and diagnosed as localized Castleman's disease of hepatic hilar and retroperitoneal origin. Diagnosing CD is complex due to its resemblance to many other diseases. EUS and FNA may play a more important role in differential diagnosis of CD and other disease in digestive system.

Keywords Unicentric Castleman's disease · Hepatic hilum and retroperitoneum · Endoscopic ultrasonography · Differential diagnosis

Introduction

Castleman's disease (CD) is a highly heterogeneous clinico-pathological entity belonging to the lymphoproliferative disorders. It can be sub-classified as unicentric Castleman's disease (UCD) or multicentric Castleman's disease (MCD) based on clinical features and the distribution of enlarged lymph nodes with characteristic histopathology [1]. Initially, the disease was most often mistaken for a thymoma and the clinical course was thought to be benign [2]. In 2010, Hakozaki et al. reported that the syndrome appeared to be more common among Asian people especially in Japanese population [3].

Castleman's disease can occur in any part of the human body where lymph nodes are present. In the meta-analysis by Talat et al. the authors indicated the main sites of human body where disease can occur were the chest (29%), neck (23%), abdomen (21%), and retroperitoneum (17%), however, other lymph node groups (axillary, inguinal) and the pelvis were also potential sites of involvement [13]. In addition, very few cases have been reported in hepatic hilum.

Hereby, we present a case of a middle-aged female patient who was presented with abdominal pain in our hospital and diagnosed as localized Castleman's disease of hepatic hilar and retroperitoneal origin.

Case report

A female patient, 53 years old, presented in our hospital with upper abdominal pain since 7 days which was not subsided by painkillers. Patient had no abdominal distention or fever and had normal bowel and bladder habit. Patient had history of Hepatitis B since 32 years not under medication. Physical examination on admission revealed no obvious abnormality in cardiac, pulmonary and abdomen system and no local lymph nodes palpable. Contrast-enhanced CT examination (CECT) from another hospital revealed multiple cysts in liver (largest being 2*2 cm), multiple soft tissue-like density on right posterior side of pancreatic head (largest being 2.6 cm*3.5 cm*3.9 cm) and retroperitoneal lymphadenopathy.

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On further examination, complete blood count showed increased monocyte level and decreased lymphocyte count. Liver function test, renal function test, and tumor markers were normal. Contrast MRI of abdomen was done in our hospital which revealed: (1) multiple lymph nodes in hepatic hilar area, retroperitoneum and around major blood vessels, some being enlarged, and (2) multiple cysts in liver. CT of head, spinal cord and chest showed no obvious lymph node enlargement or masses. Upper endoscopy revealed chronic gastritis and colonoscopy revealed inflammation of ileum. Endoscopic ultrasonography (EUS) revealed mass in right posterior side of pancreatic head of size 3.3 cm*2.8 cm, hard in consistency. Fine-needle aspiration (FNA) biopsy by 22G EUS-FNA (Olympus, NA-220H-8022) was sent to pathologic evaluation which revealed "hemorrhagic cellulose exudation, showed a small amount of extruded lymphoid cell aggregation and a small amount of mucosal columnar epithelial cell fragments". Then the primary diagnosis of "metastatic tumor or lymphoma" was made and referred to Surgery department for further evaluation and treatment. Then, patient underwent surgery for "retroperitoneal mass" and was treated with antibiotics, proton-pump inhibitor, analgesic and fluid supplement. No obvious complications were noted during surgery and post-surgery. Post-surgical pathological diagnosis confirmed the diagnosis of "Castleman's disease", hyaline-vascular type. Immunohistochemistry report suggested: CD20 (B precursor +); CD21 (dendritic cell network +); Ki 67 (germinal center +) (Fig. 1). Hence, the final diagnosis of Unicentric Castleman's disease of hepatic hilum and retroperitoneum was made. The patient did not have any symptoms and recurrence in 3 months and 6 months follow-up period.

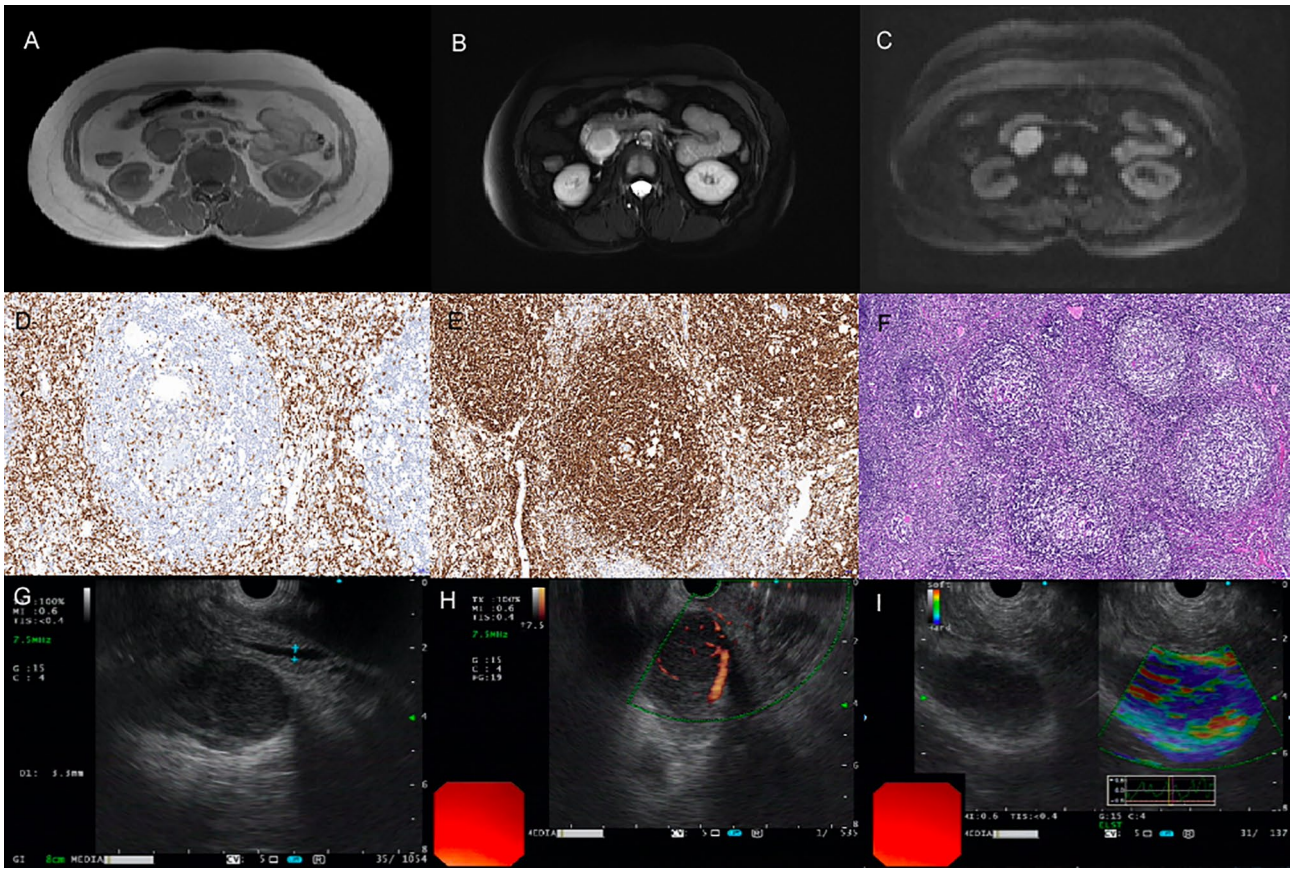

Fig. 1 The diagnostic examination results and post-surgical pathology of Castleman's disease patient. **a–c** The MRI image of hyperintense, well-circumscribed mass of Castleman's disease. T1WI (**a**) and T2WI (**b**) and DWI (**c**) image showed hypointense localized retroperitoneal mass of about 3.8*2.9*3.9 cm. **d–f** The pathology of mass in Castleman's disease patient. **d** Positive staining of CD3 (×200). **e** Positive staining of CD20 (×200). **f** The pathology specimens showed the histologic "onion skin appearance" round mass with encapsulation surrounded by concentrically arranged small lymphocytes (HE, ×100). **g** EUS illustrated the hypoechoic, well-demarcated mass of 3.3*2.8 cm in Castleman's disease. **h** Ultrasonic elastography illustrated the stiffness of the tissue, blue color denotes hard consistency and green color denotes soft consistency, stiffness scale 3–4. **i** EUS illustrated the increased vascularity in Castleman's disease

Discussion

Histologically, Castleman's disease is classified into two major types according to pathological findings: the hyaline-vascular type and the plasma cell type, and third the mixed variant types [1, 4]. Hyaline vascular UCD is the most common type, accounting for approximately 76–91% of patients with Castleman's disease. It may involve a single node or a localized group of nodes. It affects both genders equally. The median age reported lies in the fourth decade [5, 6].

The usual presentation for UCD is a single enlarged lymph node or widened mediastinum, often asymptomatic, not typically associated with HIV or HHV-8 infection as in MCD and has a high cure rate with surgical excision of the enlarged lymph node [7]. Patients with MCD have significant lymphadenopathy and an aggressive, sometimes fatal, clinical course [8]. Clinically, Castleman's disease can be classified into either localized or systemic forms. Localized Castleman's disease of the hyaline-vascular type is usually asymptomatic, whereas patients with the plasma cell variant often have systemic manifestations. The diverse presentations of the disease make its diagnosis complicated. Other clinical entities may accompany Castleman's disease, such as lymphoid neoplasms, POEMS syndrome, amyloidosis, and osteosclerotic myeloma [5, 11]. Diagnosis is made when the features of enlarged lymph nodes are seemed to have correlated with histopathologic and clinical features of Castleman's lymph nodes and all other infectious, autoimmune, and neoplastic diseases known to demonstrate resembling features have been systematically excluded.

Basically, as reported by many literatures, the common site to occur Castleman's disease is thorax. Other sites involve cervical area and retroperitoneum. As per our best knowledge, few cases of CD have been reported in hepatic hilum [9–13] among which Robert L. Cirillo Jr et al. reported the first case in 1998 [14]. In addition, in our case, the patient presented with localized enlarged lymph nodes in hepatic hilar area, retroperitoneum and surrounding major blood vessels. The patient was surgically treated with no recurrent complains on 6-month follow-up period. In our case, after the manifestation of well-circumscribed mass in hilar and retroperitoneum in CT and MRI, EUS-FNA via 22-gauge needle (Olympus, NA-220H-8022) was done to confirm the morphology and consistency of the mass. EUS showed hypoechoic, well-demarcated mass of 3.3*2.8 cm with tissue stiffness score of 4. Spectral Doppler showed increased vascularity in the mass (Fig. 1). Our EUS findings were concomitant with the characteristics of UCD-hyaline variant type concluded by Lv et al. in case series study [15]. In EUS examination, similar features can also be seen in lymphoma as a relationship between Hodgkin's lymphoma (HL) and Castleman's disease has been well documented, specially, plasma cell variant. In our center, another patient whose CT showed a mass with mild enhancement in hilar area of liver was admitted. Then EUS-FNA was done. EUS showed a hypoechoic mass of 3.8*2.9*3.9 cm near to duodenum. Ultrasonic elastography revealed the hard consistency of the tissue and Doppler revealed diminished vascularity (Fig. 2).

Many existing literatures have emphasized on differentiating Castleman's disease with lymphoma as both give very resembling features which can easily be misdiagnosed. In 2014, Deepa et al. reported a case of a female with mediastinal mass which was initially presumed as lymphoma but later diagnosed as Castleman's disease [12]. In another case reported by Filliatre-Clement et al. a rare case of Castleman's disease associated with HL in axillary lymphadenopathy was described [13]. Therefore, we can conclude that the precise examination should be performed to identify both diseases correctly. EUS has some distinguishing features between Castleman's disease and lymphoma. Although EUS showed hypoechoic, well-demarcated mass in both Castleman's disease and lymphoma, ultrasonic elastography revealed the hard consistency of the tissue in lymphoma than in Castleman's disease and Doppler showed the increased vascularity in Castleman's disease and diminished vascularity in lymphoma. Therefore, EUS-FNA is one of the very important diagnostic modality in terms of analysis of morphology, origin and consistency of the masses specially in abdominal cavity which also has advantage of its feasibility in taking biopsy specimens for further histopathological confirmation.

Talat N et al. also discussed complete surgical resection is curative for UCD, leading to excellent long-term outcomes with 10-year overall survival rates in excess of 95%. However, death within 10 years due to Castleman's disease was found significantly more common ($P < 0.05$) when the disease was located in the retroperitoneum, mediastinum, or abdomen and pelvis. In a retrospective study by Lu Zhang et al. for UCD patients, the 1-year and 5-year survival rates were 98.5% and 97.0% after treatment [16]. It is also very essential to differentiate Castleman's disease from lymphoma and to identify unicentric or multicentric disease at a clinical level in a stepwise approach as both need varying treatment modalities. Geramizadeh et al. have discussed the recurrence of Castleman's disease that mimicked lymphonodular hyperplasia or association of these two diseases in their case report [10]. However, recurrences of UCD has been rarely reported and are usually related to incomplete initial resection or missed lymph nodes at the initial evaluation, though not all UCD recurrences are in the same anatomical location. Many literatures have discussed radiotherapy to be a reasonable

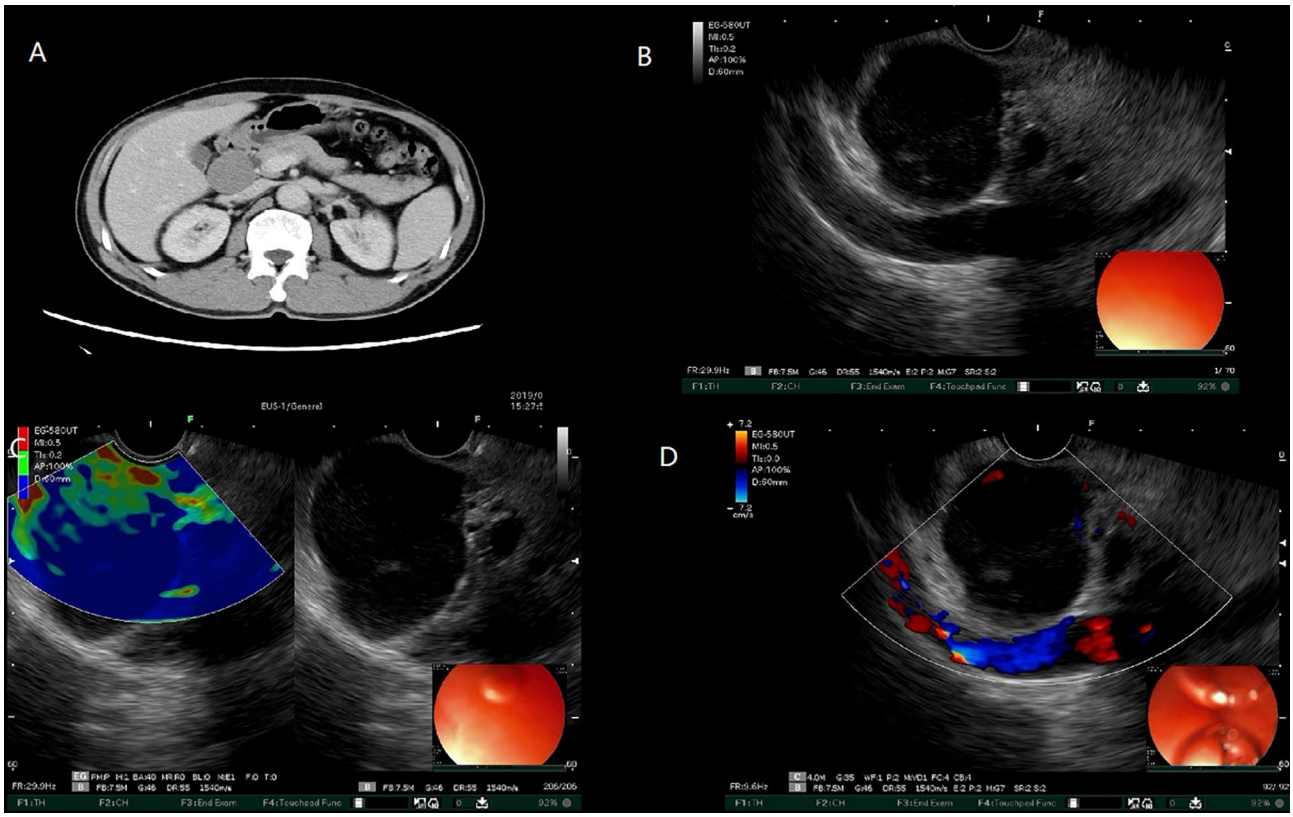

Fig. 2 The examination result of lymphoma patient. **a** CT showed a mass with mild enhancement in hilar area of liver. **b** EUS illustrated the hypoechoic, well-demarcated mass of 3.6*3.2 cm in lymphoma. **c** Ultrasonic elastography illustrates the stiffness of the tissue, blue color denotes hard consistency and green color denotes soft consistency, consistency scale 4. **d** EUS illustrated diminished vascularity in lymphoma

alternative treatment option in unresectable cases of UCD [14–21]. For UCD, complete resective surgery has the best survival prognosis with very low recurrence rate; however, radiotherapy can be considered alternative option for unresectable cases.

Diagnosing Castleman's disease is complex due to its resemblance to many other diseases. It requires careful assessment of clinical, biochemical, radiographic, and histological features. Histopathological assessment is the gold standard for diagnosing Castleman's disease. EUS and FNA may play a more important role in differential diagnosis of Castleman's disease and other disease in digestive system. But further clinical researches are needed to support it.

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Declarations

Conflict of interest There is no conflict of all the authors in financial interests or connections, direct or indirect, or other situations that might raise the question of bias in the work reported or the conclusions, implications, or opinions stated.

Informed consent The patient has provided informed consent for publication of the case, and the Ethics Review Board of Zhongda Hospital of Nanjing City approved the study.

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