rare tumors

Unexpected diagnosis of rare mesenteric Castleman disease: A case report and literature review

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Abstract

In this report, we present an Asian male patient who was 30 years old and admitted to the hospital due to pancreatitis. While undergoing a CT scan, an isolated mass was unexpectedly discovered in the patient's abdomen. The patient's abdominal pain, which was caused by pancreatitis, had resolved before he underwent surgical resection to remove the mass. Subsequently, the patient was diagnosed with Castleman disease based on pathology. Castleman disease occurring in the mesentery is exceptionally rare. Therefore, we have reviewed the essential information regarding Castleman disease and have found that the crucial part lies in the diagnosis and the consideration of distinct treatment strategies based on different types.

Keywords

Castleman disease, case report, surgery, mesentery, pancreatitis

Date received: 4 July 2023; accepted: 29 April 2024

Introduction

Castleman disease (CD) as known as angiofollicular lymph node hyperplasia (ALNH), was first reported by Benjamin Castleman in 1954. It is a group of lymphoproliferative disorders characterized by lymph node hyperplasia.[1] CD is mainly divided into two types: unicentric CD (UCD), which involves the enlargement of a solitary lymph node or only one region of lymph nodes, and multicentric CD (MCD), which involves multiple lymph node stations and causes constitutional symptoms. Approximately 90% of CD appear as UCD, and the mediastinum is generally involved; on the other hand, the abdomen is rarely involved, let alone the mesentery.[2] In this report, we present a case of a 30-year-old Asian male patient who was accidentally diagnosed with UCD during treatment for acute pancreatitis.

Case report

A 30-year-old Asian male patient presented with sudden abdominal pain lasting for 2 days following overeating. The patient had a medical history of hyperlipidemia and diabetes, both of which were attributed to an unhealthy diet. Laboratory analysis revealed an elevated serum lipase and serum amylase level, leading to the diagnosis of pancreatitis (Table 1). During treatment, a computerized tomography (CT) scan of the abdomen was performed and revealed a sharply demarcated mass measuring 5.5 cm * 6.2 cm in the right upper quadrant, yet this mass was not detected during the physical examination. The mass had branching calcification shadows inside (Figure 1(a)), a slightly enhanced appearance during the arterial phase (Figure 1(b)), and persistent enhancement during the vein phase (Figure 1(c)). As no other enlarged lymph nodes were detected during

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Table 1. Patient's clinical data.

Patient characteristics		
Age	30	
Gender	Male	
Ethnic	Asian	
BMI	31.6	
Laboratory data	At admission	After treatment
White blood cell	$6.13 * 10^9$/L	$5.73 * 10^9$/L
C-reactive protein	46.02 mg/L	27.87 mg/L
Alanine transaminase	40 U/L	67 U/L
Aspartate amino transferase	24 U/L	60 U/L
Alkaline phosphatase	84 U/L	96 U/L
Lipase	174.5 U/L	29.9 U/L
Amylase	130 U/L	29 U/L
Glucose	15.70 mmol/L	8.33 mmol/L
Triglyceride	2.65 mmol/L	2.36 mmol/L
Low density lipoprotein	3.61 mmol/L	2.14 mmol/L

imaging and physical examinations, surgery was performed to remove this single mass after the resolution of pancreatitis.

During the surgery, a spherical mass with a clear margin was observed at the base of the mesentery and was subsequently removed, along with a portion of the jejunum. Macroscopically, the specimen was measured to be 6.9 cm * 5.5 cm * 5.3 cm with a soft texture and a grey-white section peppered with calcifications (Figure 2(a)). Under the microscope, the lymphoid tissue showed hyperplasia, the usual germinal structure was replaced by the mantle zone with an onion skin appearance (Figure 2(b)). Immunohistochemical analysis verified the mass expressed CD20, CD3, Bcl-2, and Ki-67. After these procedures, the patient was diagnosed with hyaline-vascular CD and was safely discharged without any complications. At the most recent follow-up, CT scans indicated the absence of an abdominal mass (Figure 1(d)).

Discussion

CD is not well-known among clinicians due to its low incidence of 21–25 cases per million person-years.[3] As aforementioned, CD can be divided into two types: UCD and MCD. From an etiological and pathogenic perspective, MCD is subdivided into three types: (1) Human Herpesvirus 8 (HHV8)-associated MCD (HHV8-MCD); (2) Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy, and Skin changes syndrome (POEMS)-associated MCD (POEMS-MCD); and (3) idiopathic MCD (iMCD) including iMCD with thrombocytopenia, anasarca, fever, reticulin fibrosis, and organomegaly (TAFRO) and iMCD not otherwise specified (NOS).[4] Since UCD often does not have any symptoms except for incidentally detected masses, while MCD is characterized by nonspecific clinical features such as fever, inappetence, nausea and vomiting, weight loss, weakness or fatigue, anemia and enlarged peripheral lymph nodes,[5] CD is inconspicuous and can be difficult to diagnose. Therefore, clinicians should conduct a scrupulous system review and physical examination to determine the diagnosis of CD.

Laboratory studies such as whole blood cell analysis, serum biochemical tests, urinalysis, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), direct antiglobulin test (DAT), serum protein electrophoresis (with immunofixation if a monoclonal band is seen) and IgG subclasses, and serology for HIV, are necessary, especially for suspected patients with MCD. Ultrasonography, CT, and MRI, these imaging examinations are considered to be helpful diagnostic tools, as UCD displays characteristic imaging features, such as well-defined, homogeneous, solid, and hypervascular masses.[6] The latest evidence suggests that the median Standardized Uptake Value (SUV)-max of CD in PET-CT fluctuates between 3 and 8, which is lower than that of lymphoma. This differentiation could assist in distinguishing between the two conditions.[7]

A subsequent lymph node biopsy or complete excision is highly recommended to establish the histopathological diagnosis. There are three conventional histopathologic classifications: hyaline-vascular or hypervascular (HV), plasma cell or plasmacytic (PC) types, and mixed type. The Hyaline-vascular histologic variant, which mostly occurs in UCD, is characterized by increased follicles, atrophic germinal centers and concentrically arranged broadened mantle zones forming an onion-skin appearance.[8] In iMCD-TAFRO, the hypervascular variant mainly exhibits the same features mentioned above but also displays a distinct absence of follicular sinuses and gives a lollipop appearance with proliferated vessels penetrating the atretic follicles.[4] The features of the PC type manifest as hyperplastic plasma cells in the interfollicular zone.[9] PC histopathology is most commonly observed in HHV8-MCD, iMCD, and POEMS-MCD, but is rare in UCD. In some cases of MCD, there may be histologic features of both the hypervascular variant and the plasmacytic variant, known as the mixed variant. The borders between these three histopathologic classifications are quite ambiguous. Besides, thymomas, angioimmunoblastic T cell lymphoma, and advanced stages of HIV-related lymphadenopathy exhibit similar pathological features to the HV variant, whereas infections, autoimmune diseases, primary or acquired immunodeficiencies, and malignancies share similarities with the PC variant.[10] This serves as a reminder that further differential diagnosis is necessary if lymph node biopsy results are consistnet with CD.

So there are several points worth noting when making a formal diagnosis of Castleman disease. Lymphomas typically present with a single enlarged lymph node that exhibits
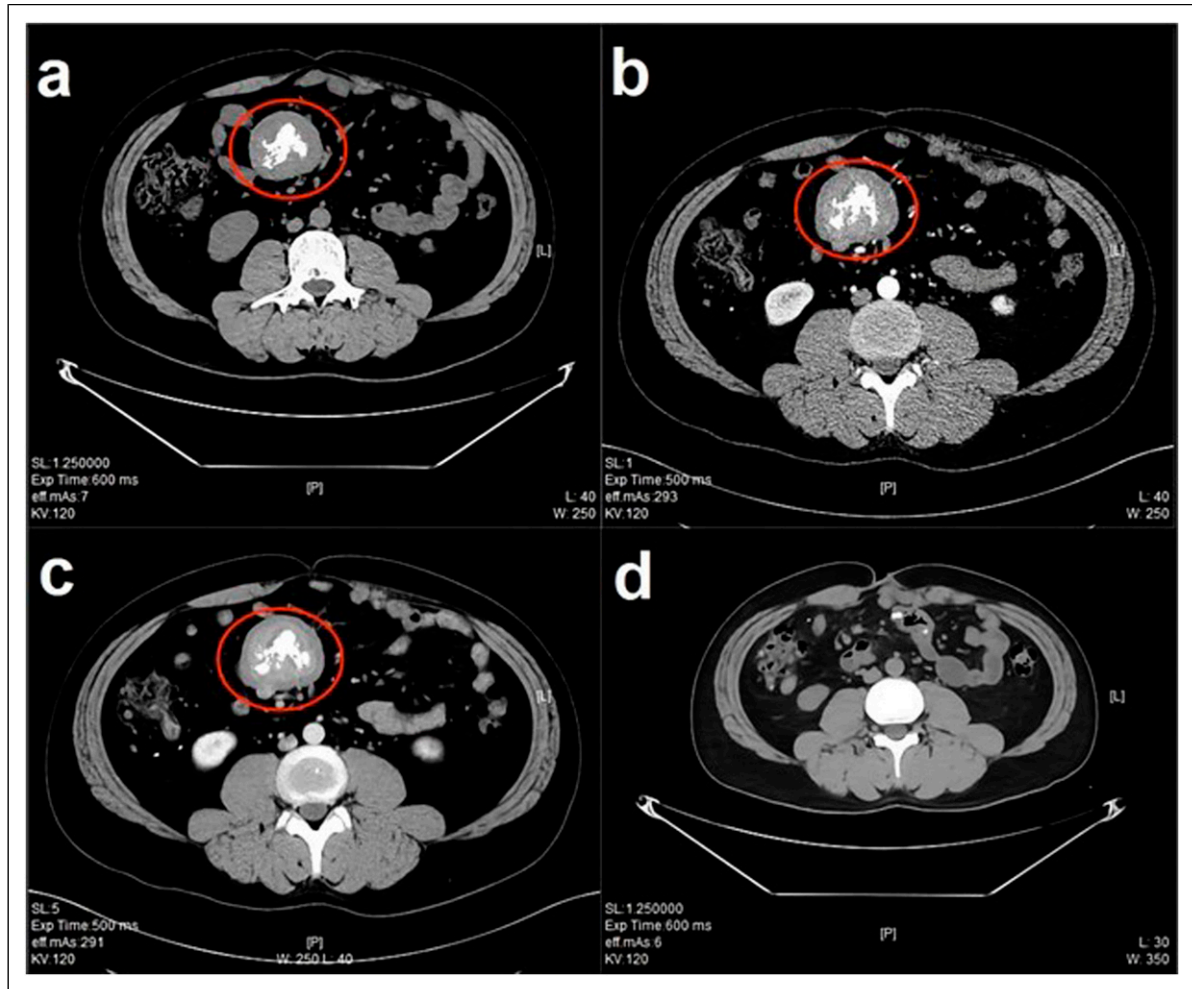
Figure 1. The computed tomography (CT) imaging of the patient. (a) The CT scan shows a sharply demarcated mass with branching calcification shadows inside. (b) Slight enhancement at the arterial phase. (c) Persistent enhancement at the vein phase. (d) CT re-examination after 2 years showed no enlarged mass or lymph nodes.
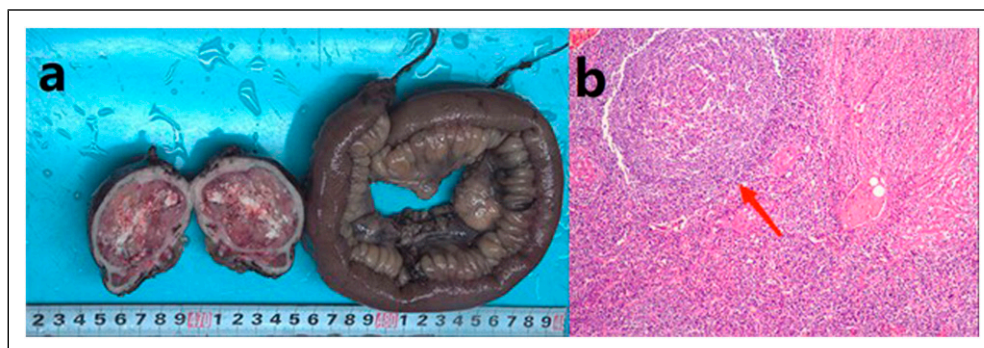

Figure 2. The surgical specimens and pathological of the patient. (a) Complete excised mesenteric mass. (b) Concentrically arranged broadened mantle zones form an onion-skin appearance (pointed by the arrow).

histopathological features similar to those seen in UCD. However, these CD-like features are usually limited in scope and do not fully involve the lymph node as they would in true Castleman disease. Positive diagnostic biomarkers, like HHV8 in HHV8-MCD and an M-protein in POEMS-MCD, help establishes the diagnosis in a patient with multicentric lymphadenopathy and CD histopathology.[11] iMCD, especially iMCD NOS, often presents with polyclonal hyper-gammaglobulinemia, commonly accompanied by moderately increased IgG4 levels.[12] To diagnose iMCD, one must not only meet the criteria, which include characteristic lymph node histopathology and multicentric lymphadenopathy, but also exclude all reactive and/or secondary mimics, including autoimmune diseases and infections.[4]

In our case, UCD was found located in the mesentery during treatment for acute pancreatitis. We found that there there exists a limited association between between UCD and the pancreas or pancreatitis. There are several UCD cases involving the pancreas,[13,14] while only Wu et al. reported a case of Castleman's disease presenting as acute pancreatitis and its pathological type was MCD.[15] Although we speculated that the patient's pancreatitis was caused by hyper-lipidemia, the extent of blood lipid elevation appears insufficient to solely induce pancreatitis. Therefore, the relationship between UCD and pancreatitis is still uncertain. Similarly, TAFRO-iMCD, is often associated with adrenalitis and adrenal necrosis, particularly in Asian patients, while remains poorly understood.[16,17]

Finally, we opted for complete resection as a form of treatment. Surgery is widely acknowledged as the most effective treatment for UCD.[18] This conclusion is particularly applicable to mesenteric Castleman disease. Mesenteric Castleman disease is mostly asymptomatic but sometimes causes localized abdominal symptoms such as pain or distension when the mesenteric masses compress the intestines or mesenteric vessels. Complete resection can resolve these symptoms. Mesenteric Castleman disease is primarily associated with the HV type. However, there is a rare case where the histologic variant of this mesenteric Castleman disease, which is associated with trigeminal neuropathy, is of the plasma cell type.[19] This reminds surgeons that mesenteric Castleman disease may not always be UCD, and if it is the MCD or PC type, transferring the patient to the hematology department and administering systemic therapy is crucial.

Besides surgery, radiation therapy can also be considered an appropriate option to UCD.[20] In a systematic review conducted by Talat et al., it was discovered that 11 patients with unresectable UCD remained stable long-term through active surveillance without any form of therapy.[21] UCD seems quite an indolent disease, but we cannot disregard the risk of developing follicular dendritic cell sarcomas, both Hodgkin and non-Hodgkin lymphoma,[22] as well as associated paraneoplastic conditions such as paraneoplastic

pemphigus (PNP) and obliterative bronchiolitis. Notably, UCD can be associated with paraneoplastic pemphigus, and this variant behaves more aggressively.[23]

To MCD, although the outcomes and prognosis can be uncertain, systemic therapy is still necessary. With the use of Rituximab-based therapy, 5-years overall survival (OS) for HHV8-MCD has increased from 33% to 90%.[24] For iMCD, siltuximab, which is an anti-IL-6 antibody, is widely recognized as the first-line option and the only Food and Drug Administration (FDA)-approved treatment for iMCD because 34% of patients demonstrated symptomatic and tumor responses in the registration study.[25] In addition, several therapies, including cytotoxic regimens, corticosteroids, rituximab, thalidomide, lenalidomide, bortezomib, cyclosporine, sirolimus, interferon, and even autologous stem cell transplant (ASCT), have been recommended for varying severities and subtypes of iMCD.[10] While some of these treatments have shown significant improvements, relapse and side effects are not uncommon. As most of these findings are based on small case series and anecdotal evidence, large-scale and multi-center clinical trials are urgently needed.

Conclusion

As a rare lymphoproliferative disorder, there is an urgent need to raise awareness of Castleman disease (CD). Clinicians should remain vigilant when encountering single or multiple suspicious lymph node enlargement and establish a diagnosis based on pathology. Surgery can effectively cure unicentric Castleman disease (UCD), while the treatments and prognoses for multicentric Castleman disease (MCD) are diverse and unpredictable.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical statement

Ethical approval

Permission was taken from the patient.

Informed consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

Contributorship

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Data availablility statement

Patient data may be obtained from the corresponding author for appropriate reasons.

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