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CASE REPORT

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Isolated retroperitoneal Castleman's disease: A case report and literature review

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Key Clinical Message

Unicentric Castleman's disease (CD) may rarely present as an isolated retroperitoneal tumor. Even experienced surgeons may misdiagnose CD because of its rarity. Surgeons should consider this disease when faced with an isolated retroperitoneal tumor. Unicentric CD is usually cured with surgical resection. In contrast, multicentric CD need numerous systemic therapies.

KEYWORDS

Castleman's disease, laparoscopic surgery, retroperitoneal tumor

1 | INTRODUCTION

Castleman's disease is a rare lymphoproliferative disease with a poorly understood etiology. We present a 49-year-old woman who had an accidentally noted retroperitoneal tumor. A laparoscopic surgical exploration revealed a oval-shaped mass densely adherent to left psoas muscle. The histopathological examination confirmed the diagnosis of hyaline vascular type CD.

Castleman's disease (CD) is a rare lymphoproliferative disorder that was first described by Dr. Benjamin Castleman in the 1950s.[1] The etiology of CD is still poorly understood, and is sometimes associated with human immunodeficiency virus (HIV) and human herpes virus 8 (HHV-8). CD is characterized by lymphadenopathy with specific histological features and it is usually noncancerous. Clinically, there are two forms of CD: unicentric (localized) and multicentric (systemic).[2] Unicentric CD (UCD) typically manifests as localized enlargement of a single lymph node and is the more common type of CD. On the contrary, multicentric CD (MCD) presents as systemic extranodal symptoms and affects more than one group of lymph nodes. MCD is often associated with HIV and HHV-8, and is believed to be related to elevated cytokine levels in its pathogenesis. By affecting organs that contain lymphoid tissue, MCD causes nonspecific symptoms such as fever, night sweats, weight loss, and fatigue. CD can also be classified, based on its unique histological features, into several subtypes. The hyaline vascular variant subtype is most common and usually presents as a localized lesion. Here, we report a rare case of UCD with presentation of a retroperitoneal mass located on the left psoas muscle that was completely excised by a laparoscopic technique.

2 | CASE PRESENTATION

A 49-year-old woman with an unremarkable medical history consulted our Emergency Department due to intermittent abdominal pain, and her biochemical profile indicated

impaired liver function (SGOT/SGPT: 480/509 IU/L) and hyperbilirubinemia (total/direct bilirubin: 1.22/0.49 mg/dL). The patient underwent abdominal nonenhanced computed tomography (CT) scans and was indicated to have cholelithiasis and extra-hepatic bile duct dilatation. Additionally, a roughly measured 5-cm homogenous tumor in the left side of the retroperitoneal space was accidentally found (Figure 1). The patient underwent laparoscopic cholecystectomy and the pathology report indicated chronic cholecystitis and cholesterolosis.

Subsequent magnetic resonance imaging (MRI)of the abdomen revealed one well-defined, oval-shaped mass lesion in the anterior part of the left side psoas muscle with intermediate to high signal intensity on T2 weighted image (T2WI), high signal intensity on diffusion weighted imaging (DWI), and low signal intensity on the apparent diffusion coefficient (ADC) map (Figure 2). A clear fat plane between the mass and the psoas muscle is noted. No lymphadenopathy, surrounding invasions, or other abnormal signal intensities corresponding to focal lesions in the retroperitoneal space can be identified. Based on the above imaging test results, the patient was referred to our urology department and then underwent a laparoscopic left retroperitoneal mass excision. After general anesthesia, the patient was placed in a right lateral decubitus position, with left side up. A Veress needle was inserted around the umbilicus and pneumoperitoneum was made by carbon dioxide insufflation with a pressure of 15 mm Hg. The first 12-mm port was introduced around the umbilicus for the camera. Then we inserted one 11-mm port at left upper quadrant and one 11-mm port at lower quadrant, and both ports were located at the midclavicular line. We started the operation by mobilizing the descending colon from the peritoneum to identify the retroperitoneal space and left kidney. This operation exposed a well-defined, oval-shaped mass densely adherent to the left psoas muscle (Figure 3). The retroperitoneal mass was widely dissected and excised from the adjacent psoas muscle carefully and without complications. The operation time was 120 minutes and the blood loss estimated 30 mL. The patient had an uneventful postoperative course and was discharged on postoperative day 3.

The resected mass measured 5.7 × 3.5 × 1.5 cm in size. Grossly, it was well-defined, brown-tan in color, and elastic (Figure 4). A microscopic examination revealed an enlarged lymph node composed of multiple follicles of various sizes with involuted germinal centers and sclerotic vessels. Higher magnification revealed that these follicles were surrounded by concentric rings of lymphocytes (Figure 5). The immunohistochemical study (Figure 6) revealed CD20 (+, follicles), CD3 (+, parafollicles), Bc12 (−, follicles), CD21 (+, follicular dendritic cells), and CD34 (+, proliferated venules). The hyaline vascular variant of CD is confirmed. The patient is currently free of disease following resection after 18-months of follow-up.

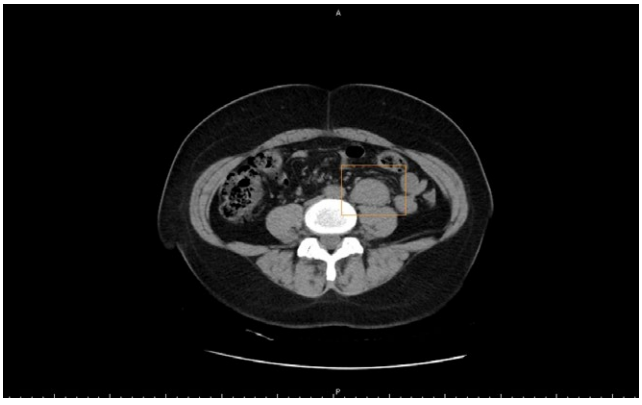

FIGURE 1 Computed tomography (CT). A CT image reveals a 5-cm homogenous tumor in the left side of the retroperitoneal space

3 | DISCUSSION

Castleman's disease, also known as angiofollicular lymph node hyperplasia, is a rare heterogenous group of lymphoproliferative disorders. Data collected from two commercial

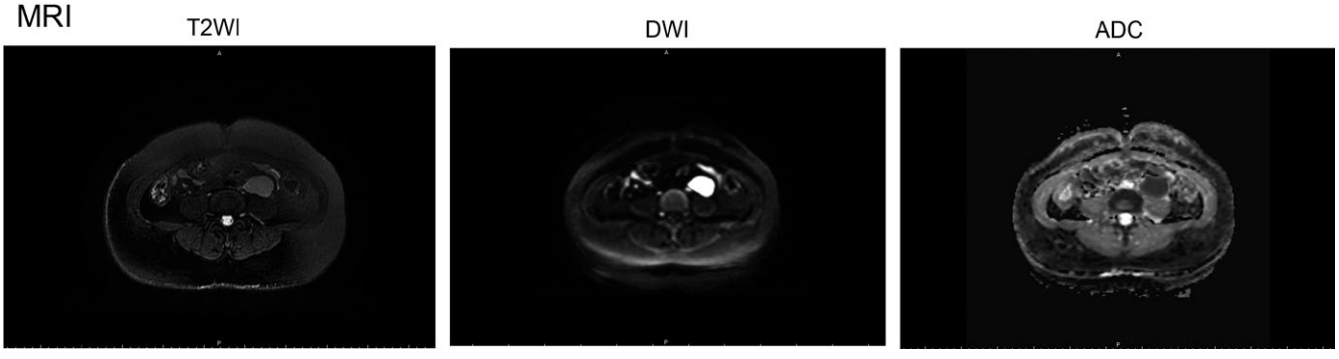

FIGURE 2 Magnetic resonance imaging (MRI). MRI images indicated a well-defined, oval-shaped mass lesion in the anterior part of the left side psoas muscle with intermediate to high signal intensity on T2 weighted image (T2WI), high signal intensity on diffusion weighted imaging (DWI), and low signal intensity on the apparent diffusion coefficient (ADC) map

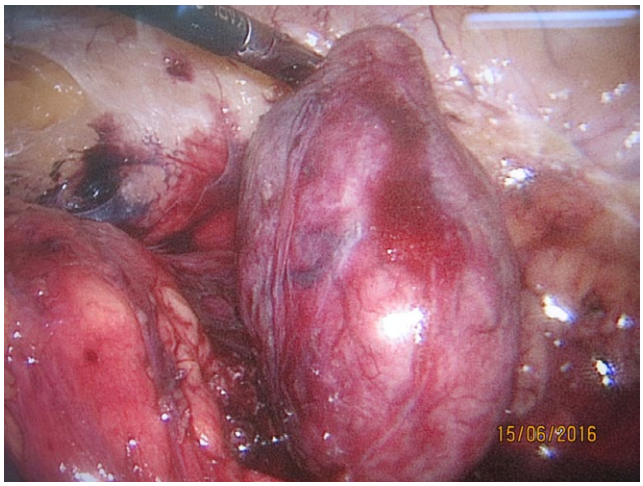

FIGURE 3 Laparoscopic surgical exploration. A laparoscopic surgical exploration revealed a well-defined, oval-shaped mass densely adherent to the left psoas muscle

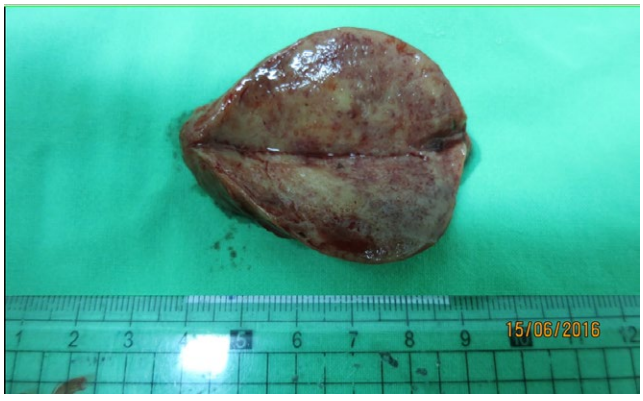

FIGURE 4 Surgical specimen. The resected mass was well-defined, brown-tan in color, and elastic

claims databases showed that the incidence of CD is estimated at 21-25 cases per million person-years.[3] A previous study suggested that increased production of interleukin-6(IL-6) by the lymph nodes may play a role in the development of CD.[4] However, the exact etiology of CD is unclear and the understanding of its epidemiology remains limited because of its low incidence worldwide.

Clinically, CD may be subdivided into unicentric and multicentric types according to the number of lymph nodes involved. UCD is typically free of HIV or HHV-8 infection, but MCD cases are typically associated with HHV-8 infection, especially in HIV-positive individuals.[5] Some researchers suggested that these viruses are associated with oversecretion of inflammatory mediators such as IL-6,[6] but the role of viral infection in the development of CD in HIV-negative cases remains poorly defined. CD affects people of all ages and has no apparent sexual predilection. CD is typically very rare in children and adolescents, but patients with HIV infection can be younger. Talat et al[7] reported that, in HIV-negative patients, the overall median age at which CD is diagnosed is 37 years, and UCD and MCD at 30 and 52 years, respectively. Female and male patients are 33- and 38-years-old, respectively.

The clinical manifestations have great differences between UCD and MCD. UCD is generally asymptomatic and may occasionally cause localized lymph node enlargement with resultant compression symptoms. The mediastinum is the most common site (up to 70%) of UCD, and the cervical region is the second-most common site (15%-20%). A recent case review indicated that in UCD, the mean size of involved lymph nodes at baseline was 5.5 cm, and the main sites of UCD were the chest (29%), followed by neck (23%), abdomen (21%), and retroperitoneum (17%).[8] MCD, on the other hand, typically manifests as multiple lymphadenopathy and systemic symptoms such as fever, night sweats, change of weight, loss of appetite, general weakness and fatigue, shortness of breath, nausea and vomiting, leg edema, and neuropathy. These "B" symptoms are recognized and associated with the overproduction of IL-6. Although CD is usually noncancerous, it can be seen in association with Kaposi's sarcoma, lymphoma, and a syndrome that includes polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, and skin changes (POEMS).[9]

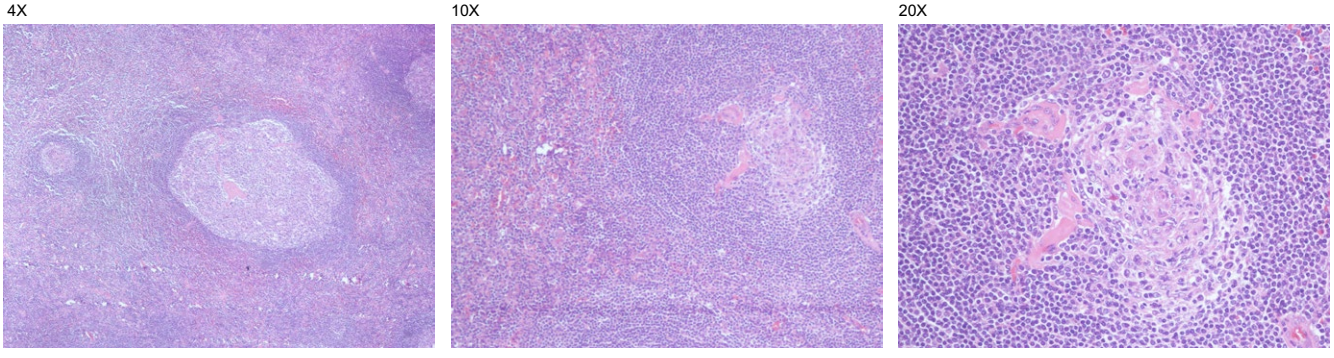

FIGURE 5 Histological examination. The findings of histological examination indicated an enlarged lymph node composed of multiple follicles of various sizes with involuted germinal centers and sclerotic vessels. Higher magnification revealed that these follicles were surrounded by concentric rings of lymphocytes

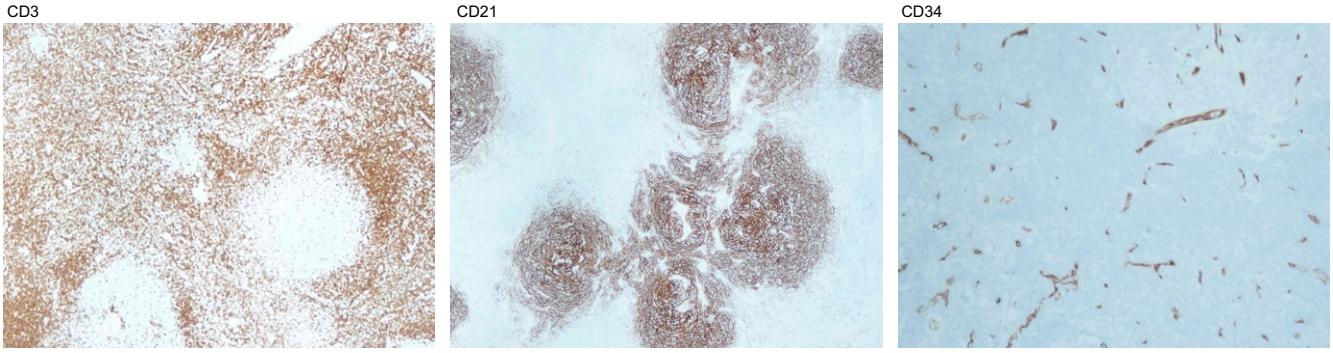

FIGURE 6 The immunohistochemical staining. The immunohistochemical study revealed positive findings of CD3 (parafollicles), CD21 (follicular dendritic cells), and CD34 (proliferated venules)

Histologically, CD may be classified into several subtypes based on its specific features, including hyaline vascular variant, plasma cell variant, plasmablastic variant, and mixed cell subtype.[10] The hyaline vascular subtype is the most common one, accounting for approximately 90% in some studies. This subtype usually involves a single lymph node or a group of nodes, but it may be multicentric in rare cases. The histological pattern of hyaline vascular subtype is unique with multiple tight aggregates of follicular dendritic cells and radially penetrating vessels. The lymphocytes typically form a concentric pattern around the dendritic cells just like "onion layers." Besides, the vascular pattern between these lymphoid nodules is prominent. The plasma cell subtype is more often symptomatic and multicentric. It is less well-defined histologically, and presents as preserved architecture of lymph nodes and sheets of mature plasma cells within interfollicular tissues that surround large germinal centers. A previous study indicated that dysregulation of IL-6 might play a role in the pathogenesis of this subtype of CD.[4]

Treatment of CD varies depending on whether it is unicentric or multicentric. In patients with UCD, complete surgical resection is usually curative without recurrence. In MCD, by contrast, surgical removal of node is rarely curative. A large case review revealed that complete resection of UCD leads to excellent outcomes with 10-year overall survival rates of 95%.[8] The benefits regarding embolization of the feeding artery to prevent massive operative bleeding of hypervascular tumor have been reported.[11] For unresectable cases of UCD, partial resection of the mass may remain stable and asymptomatic. Radiation therapy seems to be an acceptable alternative treatment option. Although available relevant literature is limited, a previous report showed a 38-year-old female patient with retroperitoneum UCD having achieved complete response after receiving 40-Gy radiation treatment during a follow-up of 17 months.[12] Numerous systemic therapies have been applied for MCD, including interleukin-6-directed therapy, anti-CD20 monoclonal antibody therapy, cytotoxic chemotherapy, immunomodulators, and antiviral agents. However, there is no standard therapy, and most of the literatures documenting treatments for MCD are confined to case reports or small case series. A systematic review suggested that the emerging use of biological therapies (including anti-IL-6 and anti-CD20 monoclonal antibody therapy) was useful, particularly in treating HIV- and HHV-8-negative MCD cases, but there is still limited understanding regarding the underlying disease mechanisms in this subgroup.[13] With regard to HIV/HHV-8-positive CD patients, a previous study recommended a combination of antiviral agents plus rituximab (an anti-CD20 monoclonal antibody), with cytotoxic chemotherapy for symptomatic and aggressive disease.[14] The prognosis of CD is also greatly variable. Generally, MCD is difficult to cure and has an unfavorable long-term outcome compared with UCD. From a systematic analysis of 416 CD patients, the 3-year disease-free rate ranged from 93% (UCD with hyaline vascular variant subgroup) to 46% (HIV-negative MCD with plasma cell variant subgroup) to 28% (HIV-positive MCD subgroup), respectively.[7]

Our case is not the first retroperitoneal UCD treated laparoscopically. Shuai Wang and his colleagues reported a case series involving 14 cases with retroperitoneal UCD and 3 of 14 patients underwent laparoscopic resection.[15] Fabio Sbrana et al[16] reported a case of UCD presented in a retroperitoneal accessory spleen and treated with a robotic-assisted laparoscopic approach. Maciej Otto et al[17] reported a case of UCD presented as a right adrenal tumor and the patient was operated on laparoscopically in the lateral, transperitoneal approach. Keun Soo Ahn et al[18] reported 2 cases of UCD located between ascending colon and duodenum and treated with laparoscopic resection. Mohammad Hadi Radfar also reported a case of UCD presented as an renal hilar mass that was managed effectively using laparoscopy.[19] We compared our case with the other reported cases in which UCD presented as a retroperitoneal mass. The clinical data and surgical outcomes of these patients were reviewed and listed in Table 1. No major complication was reported in these available case reports. No patients received chemotherapy or radiotherapy after their surgical resection.

Even experienced surgeons and radiologists may misdiagnose CD because of its rarity and no specific imaging

TABLE 1 Summaries of clinical data and outcomes in patients with retroperitoneal UCD underwent laparoscopy

Age (y)	Sex	Lesion location	Greatest diameter of lesion (cm)	Approach	Operation time (min)	Blood loss (mL)	Postoperative hospital stay	Reference
49	F	Adherent to left psoas muscle	5.7	Transperitoneal	120	30	3	Our case
31	F	Occupation of right adrenal	6	Retroperitoneal	127	100	6	[15]
15	F	Ectopic pheochromocytoma	3	Retroperitoneal	135	100	7	[15]
24	M	Occupation of pancreas	7.5	Transperitoneal	472	200	24	[15]
33	F	Accessory spleen	7.7	Transperitoneal	140	N/A	2	[16]
33	M	Right adrenal gland	4.5	Transperitoneal	N/A	N/A	4	[17]
25	M	Between ascending colon and duodenum	7	Transperitoneal	150	300	5	[18]
31	M	Posterior of duodenal 2nd portion	3.3	Transperitoneal	40	10	8	[18]
32	F	Left renal hilum	7	Transperitoneal	N/A	N/A	N/A	[19]

F, female; M, male; N/A, Not applicable.

findings. The preoperative diagnosis of CD remains a great challenge, especially in case of CD located in the retroperitoneal space. A recent review of the literature indicated only 8 of 105 cases of retroperitoneal CD that were suspected preoperatively in Japan.[11] The use of fine-needle aspiration biopsy was ever reported for preoperative diagnosis,[20] but most of cases were confirmed with diagnoses using exploratory resection and histology reports. Therefore, surgical resection for the diagnosis and treatment of UCD seems to be the standard strategy. In our present case, the retroperitoneal mass was noted accidentally by imaging studies, and the diagnosis of CD was confirmed ultimately of hyaline vascular type of the resected lesion after a laparoscopic technique. Our experience and the previously reported cases supported that laparoscopic approach is feasible and effective in the diagnosis and management of retroperitoneal UCD.

4 | CONCLUSION

In conclusion, CD, even if rare, should be taken into consideration in the differential diagnosis of retroperitoneal tumors. In cases where UCD is suspected, a complete surgical resection should be performed. Here, we presented a rare case of a patient with a retroperitoneal well-defined mass densely adherent to the psoas muscle that was accidentally encountered on a CT scan. After complete resection, the UCD was confirmed to be of hyaline vascular type. Overall, UCD has a good prognosis following complete surgical removal.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Approval for the study was obtained from the institutional review board of Kaohsiung Municipal Ta-Tung Hospital.

CONSENT FOR PUBLICATION

Informed consent was obtained from the patient for the publication of this case report.

AVAILABILITY OF DATA AND MATERIALS

The authors do not wish to share the patient's data. The privacy of this participant should be protected.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHORS' CONTRIBUTIONS

C-CL and H-YL: performed the surgery. W-JW and H-YL: analyzed and interpreted the patient's image of CT and MRI. J-HJ: reviewed the related articles, and was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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