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Castleman Disease with Retroperitoneal Invasion of Iliac Vascular Zone: A Case Report of Unicentric Type & Review of the Literature

Sufei Wang*, Ning Hu*, Yong Chen, Cunjian Yi#

Department of Obstetrics and Gynecology, The First Affiliated Hospital of Yangtze University, Jingzhou, China
Email: #cunjiany@163.com

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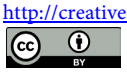

Abstract

Castleman Disease is a rare nonneoplastic lymphoproliferative disorder that can be found in any lymph node station with unknown etiology. The current cumulative number of reported cases is minimal. We report a case of a 44-year-old woman with a hard mass in the pelvic retroperitoneal that has been gradually increasing in size for many years. Abdominopelvic MRI scan showed a left retroperitoneal mass and visible calcifications. The patient underwent resection of the left retroperitoneal mass and the pathological diagnosis was Castleman disease of hyaline vascular type.

Keywords

Castleman's Disease, Unicentric, Surgery

1. Introduction

Castleman disease (CD) is a heterogeneous non-malignant lymphoproliferative disorder. It is also known as giant or vascular lobar lymphoid hyperplasia and lymphatic malformation, included in the *Compendium of China's First List of Rare Diseases* published in 2018. At present, its etiology and pathogenesis remain unclear. However, its incidence rate is reported as about 210 - 250 thousand cases per million people per year [1]. Clinically, CD is classified as unicentric or multicentric CD based on anatomical distribution [2]. Among patients with CD, UCD is more commonly encountered than MCD, Surgery generally offers complete cure of disease. Unicentric Castleman's disease (UCD) is localized lymphoproliferative disease and has favourable prognosis [3] [4]. The

*Co-first authors.
#Corresponding author.

standard treatment for unicentric CD is complete surgical removal of the mass, but treatment becomes relatively difficult if there is a high degree of attachment with other organs or hypervascularity [2].

2. Case Descriptions

A 44-year-old married female who had chronic viral hepatitis B for more than 20 years was admitted to the gynecology ward for a left adnexal mixed tumor. The tumor was detected in the color ultrasound examination at another hospital 20 days before. The patient has a history of laparoscopic left oophorocystectomy in 2018, where a huge retroperitoneal mass could not be completely removed, and intraoperative biopsy for lymphoid hyperplasia. In 1998, she underwent appendicitis resection in another hospital and a cesarean section in 2020. There was no significant history of dysmenorrhea, previous menstruation irregularities, or contributory family history. Other clinical examinations and laboratory findings were normal, including for tumors (CA19-9 and carinoembryonic antigen). Gynecological examination showed a married non-parturition type, a hard and solid mass in the left adnexa uteri with poor activity. Abdominopelvic MRI revealed a space-occupying, probably a neoplastic lesion in the iliac vessels of the left pelvic cavity and local invasion of the left psoas major (**Figure 1**). CTU showed that the left ureter was affected by a right posterior tumor (55 × 49 mm), shifting towards the midline and anteriorly without dilation or stenosis (**Figure 2**). The patient underwent exploratory laparotomy, and the lesion was removed on January 8, 2021.

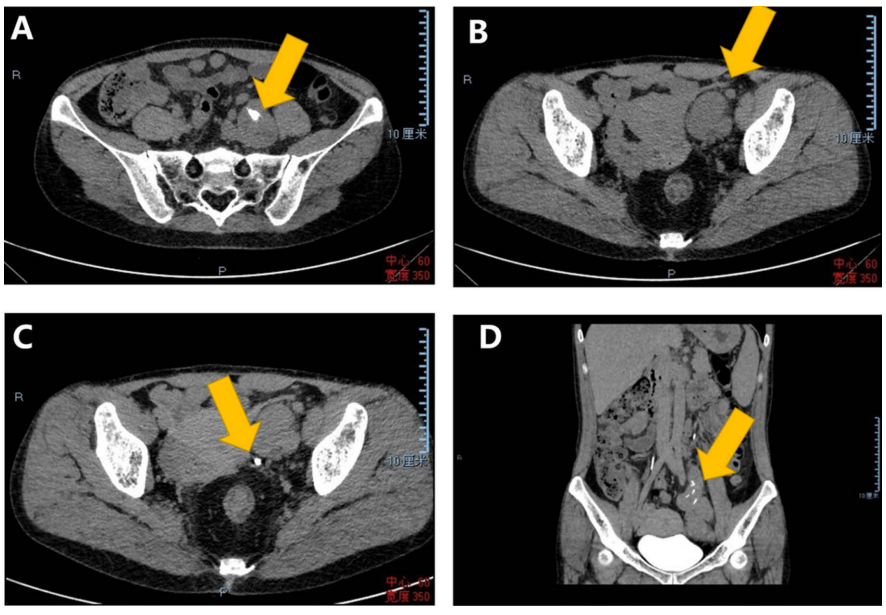

Figure 1. Figure (A)/(B) shows CT flat sweeping the left pelvic retroperitoneal capsule, with calcifications with a maximum diameter of 55*49 mm calcification. Figure (C) shows the left ureter passed by the right posterior mass and displaced to the midline and front, with no signs of expansion and stricture. The (D) plot shows the close adhesion of the left internal iliac vessel to the mass.

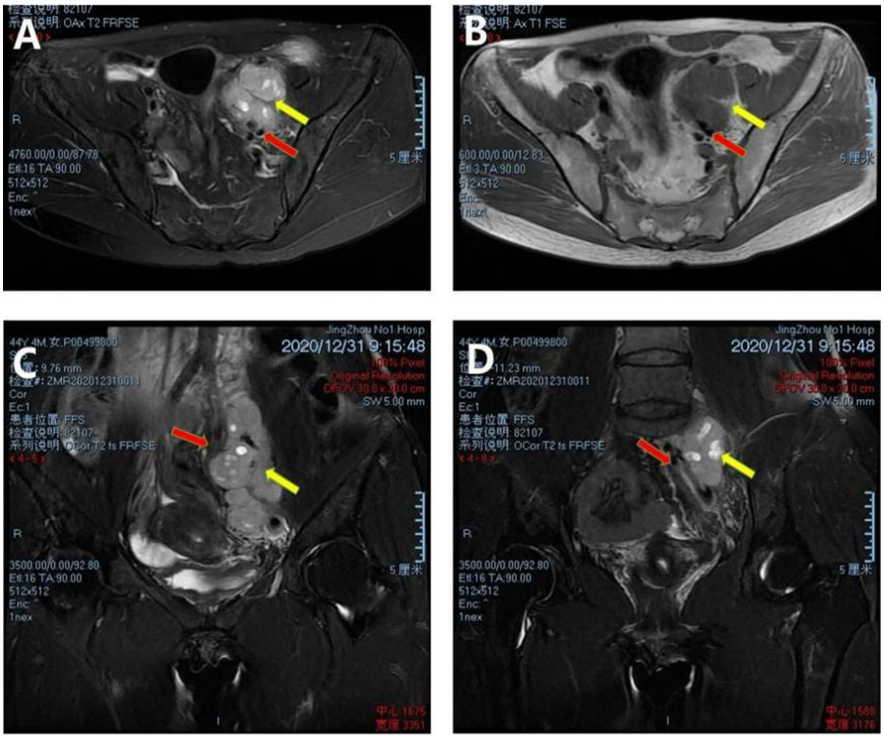

Figure 2. Pelvic MRI images are shown, (A)/(B) shows T1 and T2 images, and coronal images in (C)/(D). Red arrows mark the left internal iliac arteriovenous vein. Yellow arrows are the left retroperitoneal mass and visible calcifications. The left internal iliac AVv was seen surrounded by a mass and pushed medially.

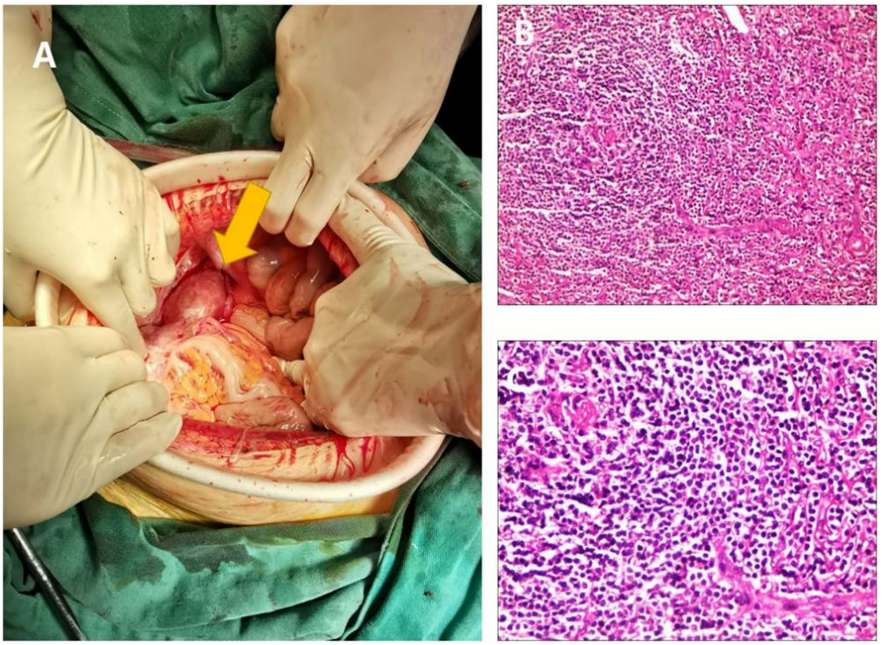

Figure 3. Figure (A) shows a picture of the intraoperative lesion. Figure (B) 200X shows cardiovascular conditions in lymphoid follicles-follicles, with the surrounding coat cells arranged in concentric circles of "onion skin-like" rows, a vessel-like structure extends into the center of the lower right corner. Figure (C)-HE 400X and Figure (B) of the follicle center under a high magnification microscope.

A tissue mass of approximately 5.5 × 4.9 × 4 cm was found at the time of surgery. In the exposed iliac vessels area, the left external iliac arteriovenal was surrounded by a fusion of multiple hyperplastic lymph node-like texture masses. Histopathological examination revealed Castleman's disease (hyaline vascular type) (Figure 3). Immunohistochemistry showed follicular area of CD20 (+), CD19 (+), CD22 (+), CD79b (+), CD79α (+), CD10 (+), BCL6 (+), HGAL (+), BCL2 (+), CyclinD1 (−), SOX11 (−), IgD (+), MNDA (−), LEF1 (scattered+), C-MYC (scattered little+), MCM2 (+), Ki-67 (LI high), interfollicular area CD3 (+), CD5 (+), CD43 (+), P53 (portion, wild-type), HHV8 (−), CD38 (scattered+), CD138 (scattered+), and MUM1 (scattered+). Postoperative PET-CT showed the metabolism of the operation area slightly increased, without lymphoid hyperplasia or enlargement of the rest (Figure 4). After 7 days of surgery, the patient recovered and was discharged. During the follow-up at 6 months, no recurrence was found in the abdominal CT scan.

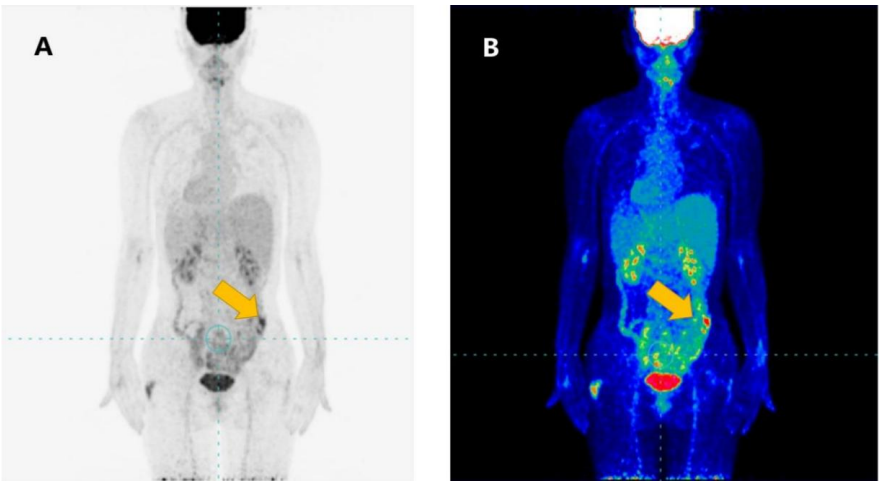

Figure 4. The (A) (B) chart shows the results of PET/CT examination: the change after Castlmen, and the arrows show the mild concentration of imaging agents in the surgical area, SUVmax5.3. Multiple lymph nodes in the retroperitoneal and left lateral iliac vessels had slightly larger lymph nodes, imagagent distribution is slightly concentrated, SUVmax2.5.

3. Discussion

Castleman disease mainly presents as painless lymph node enlargement of unknown origin. It can be clinically divided into unicentric and multicentric types, differentiated by the number of lymph node sites involved in the body. CD mainly involves the mediastinum (63%), followed by the abdomen (11%), retroperitoneum (7%), and axilla (4%) (12%) [5], the histological CD has four types: plasma cell type, hyaline vascular, HHV-8 (human herpes virus) associated, and mixed type. While the unicentric CD is usually of hyaline vascular type, accounting for 80% - 90% of cases. The multicentric type does not have any specific type microscopically. In addition, 90% of UCD patients are asymptomatic because the giant lymph nodes are usually located at only one site and progress

slowly.

CD is often overlooked and misdiagnosed due to its unclear etiology and pathogenesis, low incidence, and preoperative diagnosis. In addition, it is difficult to differentiate from other diseases. Some viruses/cytokines/growth factors, like cytomegalovirus (CMV), giant cell colony-stimulating factor, tumor necrosis factor, epidermal growth factor receptor, IL-1, IL-5, and IL-10, may be involved in the pathogenesis of MCD [6]. IL-6 in serum and lymph node tissue of patients with CD was up-regulated but significantly down-regulated in serum after complete resection of lymphoid tissue hyperplasia. For HIV-negative and HHV-8 negative patients, antibodies for IL-6 receptors such as siltuximab and tocilizumab can be used for treatment [7]. According to the previous studies, most MCD patients have autoimmune diseases, such as SLE, POEMS syndrome, idiopathic thrombocytopenic purpura, and rheumatoid arthritis, suggesting that MCD might be related to immunological abnormalities [6].

UCD mainly has many lymphoid follicular hyperplasia under the microscope, such as onion skin-like concentric circles around the germinal center, penetrating blood vessels in the germinal center, calcification foci, and vascular hyperplasia in the center and between follicles accompanied by fiber hyalinization. The possibility of UCD can be ascertained when a color ultrasound reveals a clear mass boundary, strong signals of hemorrhage, homogeneous low-echo image, circumferential blood flow signals of annular or semi-annular, and vascular penetration into the mass. If strong echo calcification is seen in color ultrasound imaging, especially radiating from the center to the periphery, its pathology may be of hyaline-vascular type [8]. In CT, there will be soft round or oval tissue in UCD and fissure or strip low-density shadow in larger CD. Whereas "Mosaic" enhancement can be observed in Contrast-enhanced CT, and the low-density shadow decrease after delay. As arteries nourish the giant CD, the arterial phase is significantly enhanced in Contrast-enhanced CT. The degree of enhancement is similar to that of adjacent arteries, presenting a "fast-in and slow-out" mode [9].

4. Diagnosis and Treatment of CD

Incidences of pelvic UCD were lower than intraperitoneal or extraperitoneal retroperitoneal UCD, accounting for 15.1% of total abdominal UCD. Due to the clinical rarity of this disease, no special clinical manifestations, specific markers, or preoperative diagnosis of CD makes clinical examination difficult and requires differential diagnosis with various diseases [6]. The best treatment for UCD is surgical excision, which is usually curative if the lesion can be completely removed. Laparoscopy or laparotomy can be a feasible approach. However, local low-dose radiotherapy, rituximab, prednisone, cyclophosphamide, or local embolization can be used for patients with surgical contraindications. Most of these alternative treatments can attain long-term survival after surgery [4].

In this case, dense adhesion was formed between the lesion and the iliac arteries and veins. Thus, the lesion was prone to massive hemorrhage and vascular

injury during the separation of adhesion. For patients with a higher risk of bleeding, KITAKAZE *et al.* [2] suggested angiography and embolization reduce the risk. The embolization might be feasible if the lesion was invading adjacent vessels. KITAKAZE *et al.* [2] conducted a retrospective analysis of the clinical data and surgical results of 10 patients undergoing preoperative CD embolization. Their study demonstrated a significant reduction in the bleeding; still, preoperative embolization may lead to necrosis, thus affecting the pathological specimens.

5. Characteristics and Treatment Experience of This Case

This patient had undergone laparoscopic surgery in another hospital, which found the serious adhesion between the pelvic tumor and iliac vessels. As complete resection of the lesion was difficult, only the biopsy was performed. After 2 years of biopsy, she was admitted to our hospital for further surgical treatment for her pelvic tumor, which was enlarged further.

The treatment plan was made by vascular surgeons, urologists, and imaging doctors. For the dense adhesion between the lesion and vascular nerves, fine dissection and segmental resection was used to avoid damaging vital organs. The broad ligament was opened during the operation, and the ureter was separated. Next, the lateral bladder space was opened, then the lateral umbilical ligament and obturator nerve were further exposed. After exposure to the obturator nerve, the lesion was gradually separated from caudal to cephalic along the vein wall. For calcification and adhesion between lesions and vascular wall, separation is particularly difficult, so an ultrasonic knife was used for progressive separation and gently pushing the lesions on the vascular wall with scissors. Finally, the lesion was removed without damaging the vessels.

6. Summary

By consulting relevant literature, 11 cases of retroperitoneal UCD were included from 2000 to 2021. The average age of Castleman patients was 35.5 years (12 - 61 years), with an average lesion size of 7.6 cm (4.0 - 15.0 cm) [1] [10]-[19] (**Table 1**). For pelvic UCD, a preoperative preliminary diagnosis is difficult, and most UCD forms dense adhesion with important pelvic vessels, resulting in refractory operation and a high risk of hemorrhage. Therefore, surgery appears to be the most effective treatment. However, with the advent of laparoscopy, better results with fewer complications are possible as precise and bloodless dissection can be performed in areas of major vascular structures. Multidisciplinary assistance should be encouraged to develop specific surgical plans to reduce surgical complications. The feasibility of surgical resection should be weighed against the risks and benefits of surgery, and vascular surgeons, radiologists, vascular interventionalists, pathologists, oncologists, obstetricians and gynaecologists should work together to discuss treatment options. Multidisciplinary assistance in developing specific surgical protocols is encouraged to reduce surgical complications.

Table 1. Summary of the clinical data and outcomes of patients with pelvic unicentric Castleman's disease who underwent surgical resection.

First author, year	Age	Sex	Greatest diameter, cm	Histological type	Preoperative diagnosis	Location	Treatment	Follow up period
Menenakos *et al.* [10] 2007	63	Male	10.3	HV	CD	Next to the right iliac vessel	Laparotomy, complete resection; immunosuppressant	No recurrence in 2 months
Sato *et al.* [11] 2013	22	Female	9.5	HV	retroperitoneal mass	Left posterior pelvic peritoneum	Laparotomy, complete resection	No recurrence in 9 years
Benjamin *et al.* [12] 2015	29	Female	6	HV	ovarian torsion	presacral bone	Laparotomy, low anterior resection; glucocorticosteroid	No recurrence in 23 months
Yu *et al.* [13] 2017	23	Male	6.2	mixed type	N/A	Rectal and sacral interstitium	Iliac artery branch vessel embolism; Laparotomy, anterior resection	N/A
Ashjaei *et al.* [14] 2020	12	Male	3.8	mixed type	lymphomas	Posterior peritoneum at aortic bifurcation	Laparotomy, complete resection	N/A
ma *et al.* [15] 2020	61	Male	undescribed	mixed type	N/A	Posterior pelvic peritoneal invasion of the right iliac vein and inferior vena cava	Laparotomy, complete resection; glucocorticosteroid	N/A
Imen *et al.* [16] 2020	53	Male	88	HV	Retroperitoneal liposarcoma	Retroperitoneal, adjacent to psoas major/cecum	Laparotomy, complete resection	N/A
Nepal *et al.* [16] 2021	41	Male	9	HV	Pelvic retroperitoneal tumour	Near the internal iliac artery	Laparotomy, complete resection	No recurrence in 10 years
NAKATA *et al.* [17] 2020	47	Female	5.6	HV	Pelvic Tumour	retroperitoneum	Laparoscopy, complete resection	No recurrence in 6 months
Schelble *et al.* [18] 2017	13	Female	4.1	HV	ovarian torsion	Left posterior pelvic peritoneum	Laparotomy, complete resection; Placement of ureteral stent	No recurrence in 7 years
Lee *et al.* [19] 2015	27	Female	7	HV	benign ovarian tumor	Next to the right pelvic external iliac vessels	laparoscopy, complete resection	No recurrence in 3 months

Ethics

Informed Consent: Informed consent was obtained from the participant before inclusion in the case report. The authors declared that this study received no financial support.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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