

Surgical resection for pelvic retroperitoneal Castleman's disease: A case report and review literature

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Abstract. Castleman's disease (CD) is a rare atypical lymphoproliferation disorder first reported in 1954. Clinically, CD is classified as unicentric or multicentric CD based on anatomical distribution. Unicentric CD primarily affects the mediastinum, and rarely affects the retroperitoneal location. The standard treatment for unicentric CD is complete surgical resection; however, this can be complicated by a high degree of attachment with other organs or hypervascularity. Preoperative angiography and embolization of the arteries that feed the problematic mass can reduce intraoperative bleeding in cases of CD with hypervascularity. In the present case report, a 44-year-old man who was found to have a pelvic retroperitoneal mass with calcification based on abdominal imaging results is discussed. Due to the hypervascularity of the mass, preoperative embolization was performed. The mass was completely resected without any complications. Additionally, a review of the literature on pelvic CD and preoperative embolization of CD was performed to provide an up-to-date reference on the management and outcomes of patients with CD.

Introduction

Castleman disease (CD) is a rare atypical lymphoproliferation disorder, also known as angiofollicular hyperplasia (1). CD was first reported by Benjamin Castleman in 1954 and defined in 1956 (2). Clinically, CD is classified as unicentric or multicentric CD based on the anatomical distribution (3). Unicentric CD primarily affects the mediastinum, and rarely affects the retroperitoneal or pelvic locations (4). The standard treatment for unicentric CD is complete surgical resection (5). However, in some cases, it may not be possible to resect the problematic mass due to a high degree of attachment with other

organs or hypervascularity (6). Preoperative angiography and embolization of the arteries that feed the problematic mass can reduce intraoperative bleeding in cases of CD with hypervascularity (7).

In the present case report, a rare case of unicentric CD presented as a pelvic retroperitoneal mass. Due to the hypervascularity of the mass, preoperative embolization was performed. The mass was completely resected without any complications. Additionally, a review of the literature on pelvic CD and preoperative embolization of CD was performed to provide an up-to-date reference on the management and outcomes of patients with CD.

Case report

A 44-year-old man presented with a history of diarrhea at another hospital. He was diagnosed with acute enteritis with computed tomography (CT), and the diarrhea was relieved after a few days. The CT scan incidentally revealed a pelvic retroperitoneal mass with calcification, and he was referred to Osaka University Hospital. The patient underwent appendectomy for appendicitis 30 years ago, and had no viral infection or history of any other diseases. The pelvic calcification was previously identified in previous abdominal X-rays, but further examination was not performed. Physical examination revealed no abnormal symptoms. Laboratory blood tests, including for tumor makers (CA19-9 and carcinoembryonic antigen) were normal. Any abnormal finding was not detected by colonoscopy. The abdominal contrast-enhanced CT scan revealed a well-defined 50x30 mm mass behind the sigmoid mesenteric, under the bifurcation of the aorta in the pelvic retroperitoneal. Non-enhanced phase imaging revealed coarse calcification inside the mass, and evident contrast enhancement was observed in the mass during the arterial phase (Fig. 1). Magnetic resonance imaging (MRI) also revealed a well-defined 50x30 mm solid mass situated in the pelvic retroperitoneal. The mass demonstrated heterogeneous and moderately hyperintense signal intensity, and the low signal intensity corresponded to calcification in the T2-weighted images and diffusion-weighted images (Fig. 2). A positive emission tomography/CT scan was performed to exclude the possibility of paraneoplastic manifestations of a primary tumor, and it revealed a 50x30 mm space-occupying lesion with hypermetabolic activity (SUVmax at 4.1) (Fig. 3).

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Key words: Castleman's disease, unicentric, hyaline-vascular type, pelvic, surgery, embolization

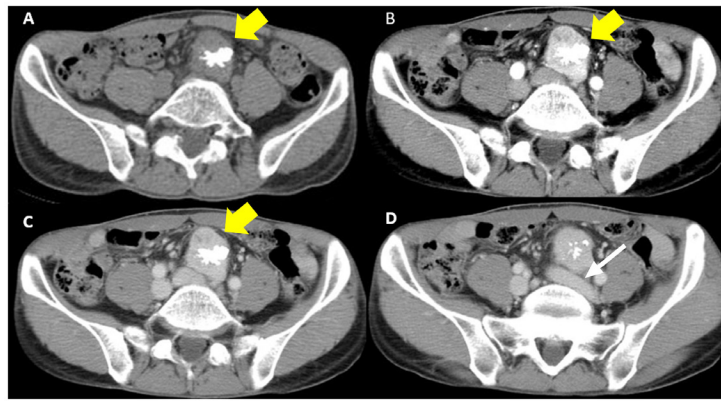


Figure 1. Abdominal and pelvic contrast-enhanced CT findings. (A) CT scan in the non-enhanced phase. The yellow arrow shows the 50x30 mm, well-defined mass with calcification under the bifurcation of the aorta in pelvic retroperitoneal. (B) CT scan in the arterial phase. The imaging revealed an evident contrast enhancement mass. (C and D) CT scan in the venous phase. The white arrow shows the mass is close to left common iliac vein. CT, computed tomography.

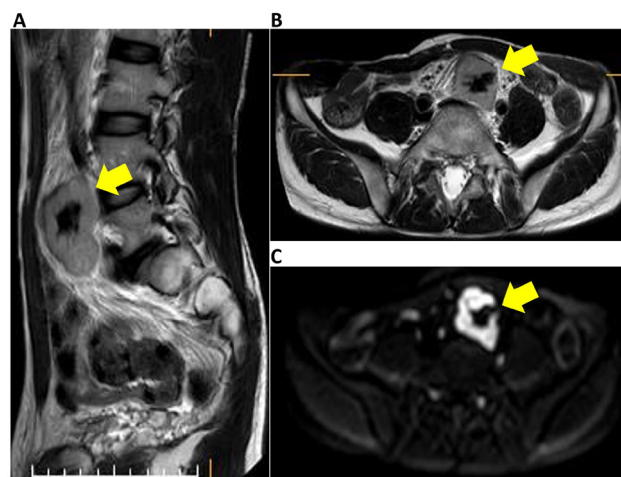


Figure 2. Pelvic MRI findings. (A) MRI sagittal T2; the arrow shows the 50 mm solid mass with high intensity. (B) MRI axial T2; the arrow points to the high intensity mass with a low intensity lesion. (C) MRI axial diffusion weighted image. The arrow points the mass with high intensity. MRI, magnetic resonance imaging.

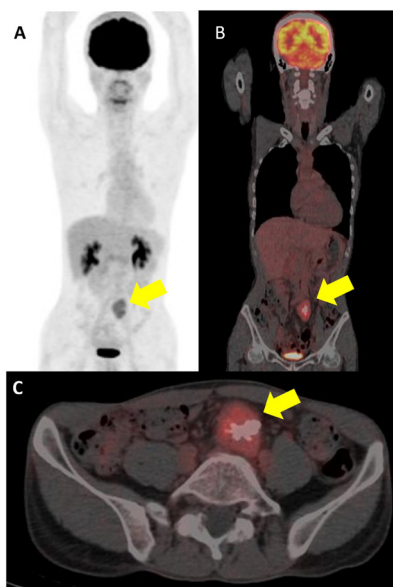


Figure 3. PET CT scan findings. (A and B) PET CT scan sagittal. (C) PET CT scan axial; the arrow shows the 50x30 mm space-occupying lesion with hypermetabolic activity (SUVmax at 4.1) in the pelvic retroperitoneal. PET CT, positron emission tomography computed tomography.

Possible differential diagnosis based on the images were CD, primary mesenteric gastrointestinal stromal tumor or leiomyoma. At first, a diagnosis of CD was doubted as the tumor had calcification, exhibited a strong contrast in imaging, had a uniform edge and a relatively uniform inside on the abdominal CT scan; the tumor was generally isointense on T1 weighted images and hyperintense on T2 images (8). Surgical resection following embolization was suggested. Angiographically, the tumor was hypervascular with a dense capillary blush, and it was supplied by the middle sacral artery (Fig. 4). The vasculature of the mass was embolized by DMSO and the patient was operated on the following day.

During the laparotomy, the mass was located at the bifurcation of the aorta behind the sigmoid mesentery. Mobilization of the sigmoid mesentery revealed that the mass was 50x30 mm in size, rubbery, rich in vasculature and exhibited a high-degree of attachment to the left common iliac vein. Following surgical ligation and dissection of the vasculature to the mass, the mass was completely resected from the adjacent organs without any complications. The patient lost 160 ml of blood, but no blood transfusion was required. The excised mass was round, well circumscribed and encapsulated. The cut surface was dark red with a central

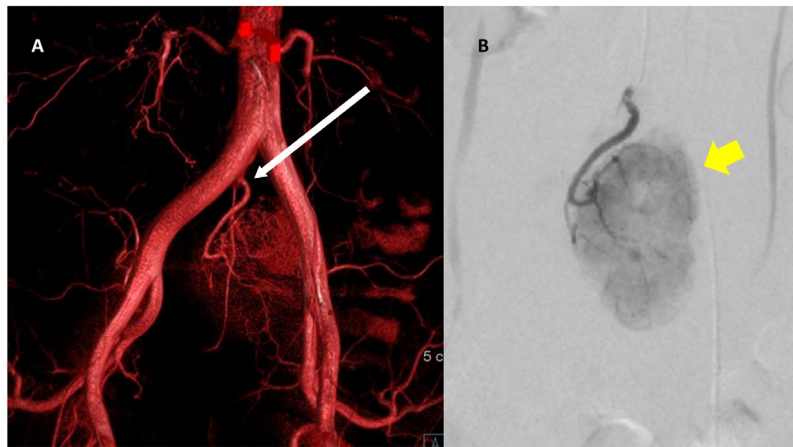


Figure 4. Angiography findings. (A and B) The yellow arrow shows the mass with a dense capillary blush. The mass was supplied by the middle sacral artery (white arrow).

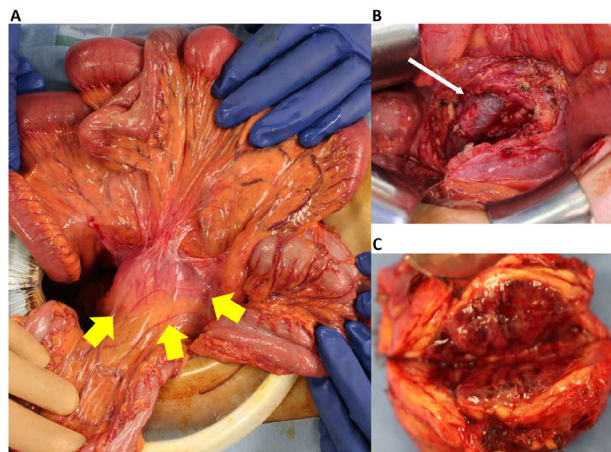


Figure 5. Intraoperative findings. (A) The yellow arrow shows the mass behind the sigmoid mesenteric. (B) After resection of the mass. The mass exhibited a high degree of attachment to the left common iliac vein (white arrow). (C) Resected specimen; the mass was 50x30 mm in size, round, rubbery, well circumscribed and encapsulated. The cut surface was dark red with a central white zone of fibrosis and calcification, and had a granular appearance.

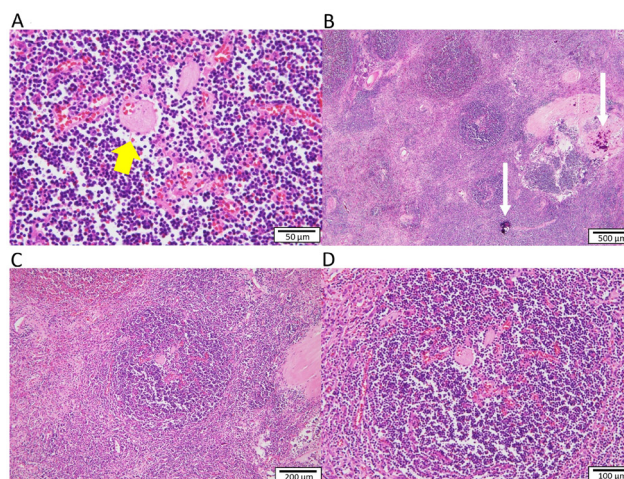


Figure 6. Histopathological findings of the resected specimen. (A and B) Histopathological examination revealed the lymphoid tissue had a hyalinized vasculature (yellow arrow), calcification (white arrow) and noticeable hemorrhaging. (C and D) A germinal center was not observed.

white zone of fibrosis and calcification, and it had a granular appearance (Fig. 5). Histopathological examination revealed the lymphoid tissue had a hyalinized vasculature, calcification and

noticeable hemorrhaging. Furthermore, a germinal center was not observed, and thus germinal center atrophy was suspected (Fig. 6). Immunohistochemical analysis showed protein expression of

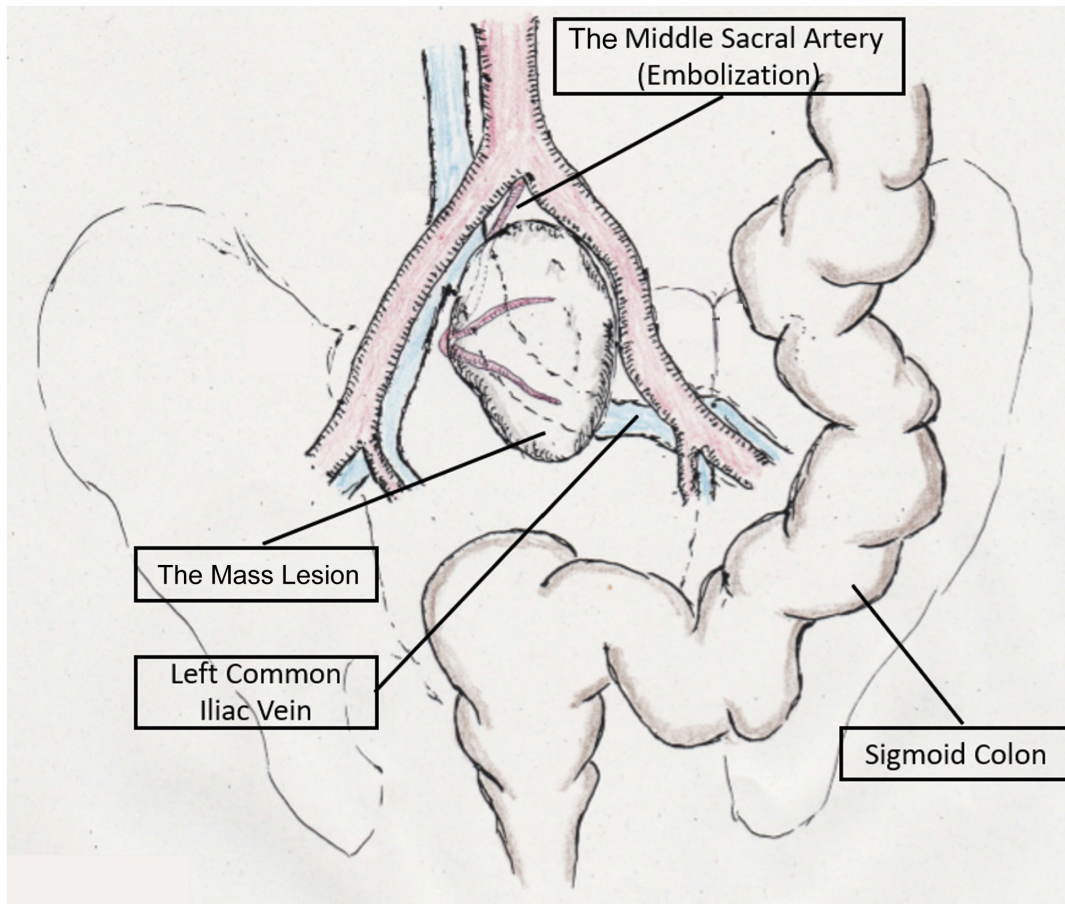


Figure 7. Schema of the present case. The arrow shows the mass was present under the bifurcation of the aorta in the pelvic retroperitoneal and was supplied by the middle sacral artery (dotted arrow) embolized preoperatively.

CD3, CD20 and CD79a. Immunohistochemistry did not show an increase in IgG4 antibody expression compared with total immunoglobulin expression. Clonality analysis using genomic DNA extraction from the surgical specimen showed no clonality and DNA fragmentation. These histological findings suggested CD of a hyaline vascular (HV) type. Currently, at 20 months post-operation, the patient has not experienced a recurrence. A schematic of this case is shown (Fig. 7).

Discussion and literature review

The classification of CD into unicentric or multicentric CD is based on the presence of this lymphoproliferative disorder in one or more regions, respectively (9). There are three histopathological types of the disease, HV, plasmacytic (PC) and mixed type (10). HV type occurs in 80-90% of cases and usually appears more frequently as a unicentric localization, whereas PC is primarily multicentric and accounts for 10-20% of cases (11). Furthermore, 90% of patients with unicentric CD are usually asymptomatic (1). The large lymph node due to unicentric CD is located only at a single site, exhibits slow progression and is rarely observed in radiographs (1). CD is often overlooked as a possible diagnosis due to its low incidence rate. The possibility of CD should be considered following the identification of a homogeneous vascular mass (8). CD most commonly affects the mediastinum (63%), followed by the abdomen (11%), retroperitoneum (7%) and axilla (4%) (12).

Unicentric CD in the retroperitoneum is commonly found in the retroperitoneal space (53%), followed by the pararenal (15%), peripancreatic (9.7%) and pelvic regions (6.7%) (4). The most common presentation is abdominal pain (42%) (13). Due to its rarity and lack of disease-specific makers and indications, preoperative diagnosis is difficult. The differential diagnosis includes lymphoma, sarcoma, lymph node metastasis, gastrointestinal stromal tumor, lipomas, leiomyomas, neurofibromas, paraganglioma and infectious/inflammatory diseases (14). The imaging findings of unicentric CD are commonly seen on contrast-enhanced CT as a well-defined, solitary soft tissue tumor with evident contrast enhancement during the arterial phase (12). Most unicentric CD lesions are isointense or slightly hyperintense relative to skeletal muscle on T1-weighted images, and hyperintense on T2-weighted images, reflecting the vascularity of the mass (15). The first choice of treatment for unicentric CD is surgical resection if it is curatively resectable; the 10-year overall survival rate is 95% and the 5-year disease-free survival rate is over 90%, suggesting a good prognosis following complete resection (16).

All previously reported cases of abdominal, retroperitoneal and pelvic unicentric CD were searched in PubMed, focusing on studies published in English with images to support the location of the masses identified. A total of 152 cases of abdominal, retroperitoneal and pelvic unicentric CD were found (as of July 2020). A summary of the areas of the abdomen where

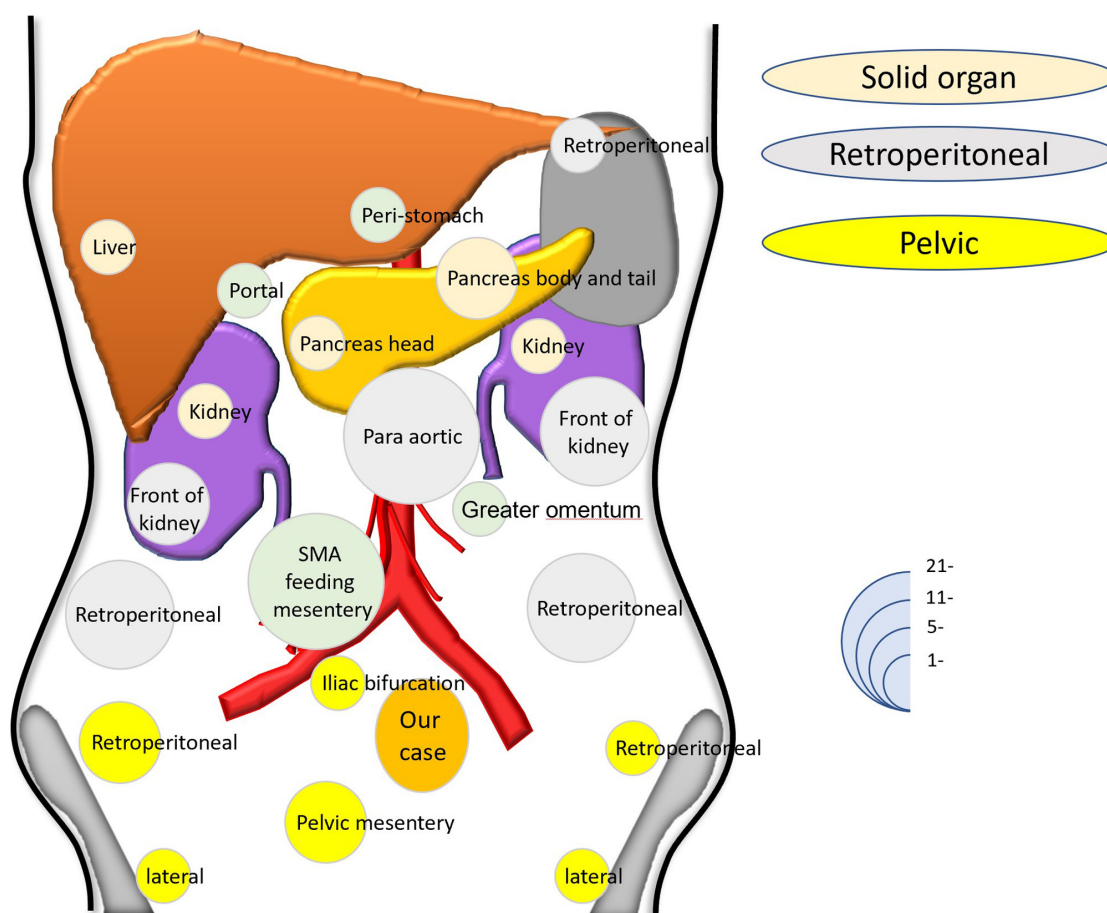


Figure 8. A literature review of abdominal unicentric CD (n=152 cases). The size of the circles indicates the number of cases associated with that region/organ. The present case is shown in an oval shape.

unicentric CD has been reported is shown in Fig. 8. The most frequently reported site was the superior mesenteric artery feeding mesentery (25%; 38/152). In the retroperitoneal, the paraaortic and left peri-renal areas were found to be the most common: 13.8% (21/152) and 11.2% (17/152), respectively. A small number of cases have also been reported in solid organs such as the liver, pancreas and kidneys (17-19). Pelvic unicentric CD occurred less frequently than intra-abdominal or extra pelvic retroperitoneal unicentric CD, accounting for 15.1% (25/152) cases of abdominal unicentric CD.

Intraabdominal presentations of CD were the second most common location, and pelvic presentations were rare. The present case report was compared with other reported cases in which unicentric CD was present as a pelvic mass. There were 10 cases, and the clinical data and surgical outcomes of these patients are reviewed and listed in Table I. The mean age of the patients was 35.4 years, and the mean greatest diameter of the lesion was 5.88 cm. HV type was observed in 10 out of 11 cases. Furthermore, 2 cases were treated using a laparoscopic approach. All cases in Table I were treated with complete resection and there were no cases of recurrence. Unicentric CD with calcification was found in 2 cases in Table I. The case reported in the present study was the only case in which calcifications were present, and was resected after embolization for pelvic CD.

Several previous cases were diagnosed with abdominal unicentric CD following post-surgical histological examination.

The optimal therapy for unicentric CD is surgical resection, which is usually curative if the disease is amenable to complete resection (5). Surgical resection is a useful approach for the diagnosis and treatment of the disease (8).

The masses found in patients with CD often exhibit a moderate to high degree of attachment contiguous with surrounding anatomical structures (6). A high degree of attachment to the contiguous anatomical structures is often observed in lesions >5 cm in diameter (6). Furthermore, significant bleeding may obstruct surgical procedures (4).

In cases of HV-type CD where there is a notably higher risk of massive bleeding due to the hypervascularity, preoperative angiography and embolization of the arteries that supply the tumor should be considered to reduce intraoperative bleeding (7). Preoperative embolization has also been suggested where there is encasement or invasion of the adjacent structures (20-22).

The present case was compared with the other reported cases in which patients with unicentric CD were treated using complete surgical resection after angiography and embolization of the feeding artery. There were 10 such cases, and the clinical data and surgical outcomes of these patients were reviewed and are listed in Table II. The mean age of the patients was 28.6 years and the mean greatest diameter of the lesion was 8.58 cm. HV type was observed in 10 of 11 cases (aforementioned 10 cases and the present case; Table II) The mean blood loss during operation ranged from minimal to 940 ml, and the clinical course

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

First author, year	Case	Age, years	Sex	Greatest diameter, cm	Histological subtype	Calcification on US, CT or MRI	Preoperative diagnosis	Preoperative embolization	Treatment	Follow up period	(Refs.)
Menenakos <i>et al</i> , 2007	1	63	Male	10.3	HV	Exist on CT	Castleman's disease	-	Laparotomy, complete resection	No recurrence in 2 months	(26)
Sato <i>et al</i> , 2013	2	22	Female	9.5	HV	No on US and MRI	Could not be made	-	Laparotomy, complete resection	No recurrence in 108 months	(27)
Al-Natour <i>et al</i> , 2010	3	41	Male	8	HV	No on CT	Extra-adrenal pheochromocytoma	-	Laparotomy, complete resection	No recurrence in 6 months	(28)
Yu <i>et al</i> , 2019	4	23	Male	6.2	Mixed	No on US and MRI	Castleman's disease	+	Laparotomy, anterior resection	N/A	(29)
Benjamin <i>et al</i> , 2015	5	29	Female	6	HV	No on MRI	Ovarian torsion	-	Laparotomy, low anterior resection	No recurrence in 23 months	(30)
Hwang <i>et al</i> , 2011	6	34	Female	6	HV	No on MRI	Neurogenic tumor	-	Laparoscopy, complete resection	N/A	(31)
Watson <i>et al</i> , 2000	7	46	Female	4	HV	No on MRI	Vascular tumor, AVM	-	Laparotomy, complete resection	N/A	(32)
Zhang and Jia, 2008	8	10	Female	4	HV	No on CT	N/A	-	Laparotomy, complete resection	No recurrence in 6 months	(33)
Schelble and Merritt, 2019	9	13	Female	4	HV	No on US and MRI	Biopsy: HV type Castleman's disease	-	Open retroperitoneal approach, complete resection	N/A	(34)
Guthrie <i>et al</i> , 2016	10	64	Male	1.7	HV	No on MRI	Genitourinary or hematologic malignancy	-	Robotic-assisted laparoscopy, bilateral pelvic lymph node dissection	N/A	(35)
Present case	11	44	Male	5	HV	Exist on CT	Castleman's disease	+	Laparotomy, complete resection	No recurrence in 21 months	Present case report

US, ultrasound; MRI, magnetic resonance imaging; CT, computed tomography; HV, hyaline vascular; N/A, not available.

Table II. Summary of clinical data and outcomes in patients with unicentric Castleman's disease who underwent preoperative embolization.

First author, year	Case	Age	Sex	Greatest diameter, cm	Location	Feeding artery	Time to operation, day	Preoperative diagnosis	Procedure	Blood loss, ml	Follow up period	(Refs.)
Robert <i>et al</i> , 2008	1	31	Female	12	Posterior mediastinum	Bronchial and extrabronchial arteries	7	N/A	Right anterior thoracotomy	200	N/A	(23)
Nagano <i>et al</i> , 2013	2	33	Male	11	Next to the right kidney	Right lumbar arteries	1	Schwannoma, inflammatory myofibroblastic tumor, and liposarcoma	Complete resection	940	No recurrence in 12 months	(36)
Gorospe <i>et al</i> , 2017	3	31	Male	10	Mediastinum	Right bronchial artery	N/A	Biopsy: CD	Right posterolateral thoracotomy	Little blood loss	No recurrence in 18 months	(37)
Sanchez-Ros-Sanchez <i>et al</i> , 2012	4	34	Female	9	Cervical region	Left transverse cervical artery and dorsal scapular artery	1	CD	Complete resection	N/A	No recurrence in 30 months	(38)
Aydemir <i>et al</i> , 2010	5	32	Female	9	Under the azygous vein	Right bronchial artery	14	N/A	Complete resection	N/A	No recurrence in 12 months	(39)
Safford <i>et al</i> , 2003	6	11	Male	8	Middle mediastinal masses	Right intercostal artery and right internal mammary artery	1	Open biopsy: CD	Complete resection	50 (Open biopsy: Lots of blood loss)	No recurrence in 1 month	(40)
Swee <i>et al</i> , 2009	7	15	Female	7	Right paratracheal lesion	Bronchial artery	N/A	Biopsy: CD	Complete resection	50	N/A	(22)
Yu <i>et al</i> , 2019	8	23	Male	6.2	Pelvic	Bilateral iliac artery branches	7	CD	Laparoscopic anterior resection	N/A	N/A	(29)
Williams <i>et al</i> , 1998	9	31	Male	N/A	Erector spinae muscle	Right fifth lumbar artery and right internal iliac artery	1	Biopsy: CD	Erector spinae muscle resection	Little blood loss	No recurrence in 24 months	(41)
Amano <i>et al</i> , 2013	10	30	Female	N/A	Subcarinal azygoesophageal recess	Right bronchial artery	1	Paraganglioma and CD	VATS, complete resection	400	No recurrence in 12 months	(42)
Present case	11	44	Male	5	Under the bifurcation of aorta in pelvic retroperitoneal	Middle sacral artery	1	CD	Complete resection	160	No recurrence in 21 months	Present case report

CD, Castleman's disease; N/A, not available; VATS, video-assisted thoracic surgery.

was uneventful in all cases (Table II). Preoperative embolization may affect the histological findings on the resected specimens. In relation to the histological findings after embolization, fibrosis and marked hemorrhage were reported.

In the present case, the patient had previously been shown to possess a pelvic calcification in an abdominal x-ray. It has been reported that calcifications are seen in 31% of patients with abdominal or pelvic CD (23). Pelvic calcifications are usually indicative of neurogenic tumors, teratomas, uterine fibroids and intravesical stones, amongst other potential conditions (24,25). However, it is important to consider the possibility of pelvic CD in the differential diagnosis of a pelvic calcification in an abdominal X-ray.

In conclusion, CD is a rare lymphoproliferation disorder of uncertain etiology. Pelvic CD is extremely rare, so it is important to consider CD as a differential diagnosis when a pelvic lesion is found. Although the clinical course of complete surgical resection for unicentric CD is good, surgical resection may be difficult due to attachment with the surrounding tissues or high hypervascularity. Preoperative angiography and embolization of the arteries feeding the tumor can prevent or limit intraoperative bleeding.

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Availability of data and materials

All data generated and/or analyzed in the present study are included in this published article.

Authors' contributions

MK, NM, SF, TO, HT, MU, TM, YD and HE contributed to the diagnosis at the preoperative conference, NM and SF performed the resection, and contributed to the follow-up. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient for the publication of this case report and the accompanying images.

Competing interests

The author declare that they have no competing interests.

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