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 demonstrated calcification in 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. 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).
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
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
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 markers and indications, preoperative diagnosis is difficult. The differential diagnosis includes lymphoma, sarcoma, lymph node metastasis, gastrointestinal stromal tumor, lipomas, leiomyomas, neurilemmomas, 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
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 intra-operative 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 I. 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 | (Ref.) |
|--------------------|------|------------|-----|-----------------------|----------------------|-------------------------------|------------------------|--------------------------|-----------|------------------|-------|
| Menenakos et al, 2007 | 1    | 63         | Male | 10.3                  | HV                   | Exist on CT                   | Castleman’s disease     | -                        | Laparotomy, complete resection | No recurrence in 2 months | (26) |
| Sato et al, 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 et al, 2010| 3    | 41         | Male | 8                     | HV                   | No on CT                      | Extra-adrenal pheochromocytoma | -                        | Laparotomy, complete resection | No recurrence in 6 months | (28) |
| Yu et al, 2019       | 4    | 23         | Male | 6.2                   | Mixed                | No on US and MRI             | Castleman’s disease      | +                        | Laparotomy, anterior resection | N/A                 | (29) |
| Benjamin et al, 2015 | 5    | 29         | Female | 6                    | HV                   | No on MRI                     | Ovarian torsion          | -                        | Laparotomy, low anterior resection | No recurrence in 23 months | (30) |
| Hwang et al, 2011    | 6    | 34         | Female | 6                    | HV                   | No on MRI                     | Neurogenic tumor          | -                        | Laparoscopy, complete resection | N/A                 | (31) |
| Watson et al, 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 et al, 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.
| 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 et al, 2008 | 1    | 31  | Female | 12 | Posterior mediastinum | Bronchial and extrabronchial arteries | 7 | N/A | Right anterior thoracotomy | 200 | N/A | (23) |
| Nagano et al, 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 et al, 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 et al, 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 et al, 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 et al, 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 et al, 2009 | 7    | 15  | Female | 7 | Right paratracheal lesion | Bronchial artery | N/A | Biopsy: CD | Complete resection | 50 | N/A | (22) |
| Yu et al, 2019 | 8    | 23  | Male  | 6.2 | Pelvic | Bilateral iliac artery branches | 7 | CD | Laparoscopic anterior resection | N/A | N/A | (29) |
| Williams et al, 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 et al, 2013 | 10   | 30  | Female | N/A | Subcarinal azygousosophageal recess | Right bronchial artery | 1 | Parangangioma 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 lymphoproliferative 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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