*MAR Gynecology & Urology (2024) 7:5*

*Case Report*

# Castleman Disease

Dhaherah AlJahani*

***Correspondence to:** Dhaherah AlJahani, Saudi Arabia.



Received: 13 December 2024

Published: 20 December 2024

***Abstract***

*Castleman Disease (CD), a spectrum of lymphoproliferative disorders, presents diagnostic challenges due to its diverse clinical manifestations and rarity. Here, we report an uncommon case of Unicentric Castleman Disease (UCD) localized in the*

*pelvic retroperitoneum, detailing the clinical presentation, diagnosis, and laparoscopic surgical management.*

*Our patient, a 20-year-old nulliparous female, sought medical attention for chronic lower abdominal pain. Imaging revealed a vascular, heterogeneous pelvic mass, initially misdiagnosed as right external iliac lymphadenopathy. Subsequent laparoscopic*

*surgery successfully excised the mass. Histopathological analysis confirmed UCD, specifically the plasma cell type.*

*This case highlights the diagnostic complexity of CD and the importance of considering rare conditions. It also underscores the feasibility and efficacy of laparoscopic surgery in treating UCD in challenging anatomical locations. A unique twist to the story, our patient achieved an uneventful recovery and later became pregnant.*

*In conclusion, this case serves as a valuable addition to the literature on rare presentations of CD. Improved reporting and understanding of this disease are essential, and this case exemplifies the potential for laparoscopic surgery in managing such cases.*

***Keywords:*** *Castleman Disease, Unicentric Castleman Disease, Pelvic Retroperitoneum, Laparoscopic Surgery, Rare Disease, Case Report, Diagnosis, Surgical Management.*

## Introduction

Castleman disease(CD) is a scarce spectrum of lymphoproliferative disorders with common cellular manifestation(2) .The Disease occurrence is estimated to be around five thousand per year in the USA (2).It has a varying clinical presentation according to its classification and involved anatomy . Possible associated symptoms include regional symptoms associated with mass compression or generalized ones like fever, ascites or splenomegaly.

Castleman disease types mainly include unicentric and multicentric.Unicentric castleman disease(UCD) which is also known as localized castleman disease is associated with solitary lymph nodes with castleman tumor cellular manifestations (2). The other types are associated with multicentric castleman disease which can be further subdivided into human herpesvirus 8 positive or related multicentric castleman disease(HHV-8-associated MCD), idiopathic multicentric castleman disease (iMCD) which can be a TARFO syndrome, Not otherwise specified (iMCD- NOS)and POEMS-associated multicentric castleman disease(POEMS-MCD)(2). Castleman disease can present in multiple areas such as mediastinum, chest or abdomen but castleman disease in pelvic region occurrence is estimated to be around 2% which is considered to be rare among others(1).

This condition lacks its own specific clinical presentation; therefore, it is often misdiagnosed due to the huge range of differential diagnosis which can mimic CD. Consequently, most of the cases were misdiagnosed pre-operatively or discovered late after pathology. Herin, a case of Castleman's disease localized in the pelvic retroperitoneum which was completely resected by laparoscopic surgery. This case is the first diagnosed pelvic CD case in Saudi Arabia.

## Presentation of Case

20 years old nulliparous married female, who is medically and surgically free.

Following in gynecology outpatient clinic as case of chronic lower abdominal pain for 1 year. No history of vaginal bleeding, irregular cycle, dyspurnia, GI or urinary symptoms.

Upon examination, the patient was vitally stable, Per abdominal examination was soft, non tender.

Transvaginal ultrasound examination revealed a high vascular heterogeneous mass anterior to the bladder measured (38X 31X32 mm).

Serum levels of cancer antigen (CA) 19-9, CA125, carcinoembryonic antigen (CEA), Alpha FetoProtein (AFP), Lactate dehydrogenase(LDH) and Beta-Hcg (Bhcg) were within the normal range. Except for the above-mentioned findings, serum biochemical and clotting studies were within the normal limits.

MRI pelvis revealed 2.8 X 4.4 X 3.8 cm homogenous mass seen just superior to the right pubic ramus in the right external iliac group with normal pelvic organs. It shows intermediately high signal intensity in T2 weighted images. It is iso-tense to the muscle in T1 with homogenous mechanism in post contrast images and restricted diffusion. Enlarged external iliac lymph node measuring 1.3X 2 cm with similar signal intensity and pattern of enhancement.

Ultrasound guided pelvic mass biopsy was done, pathology report: Polyclonal plasmacytic lymphadenopathy. Patient preoperative diagnosis was right external iliac lymphadenopathy. Counseled for a diagnostic

laparoscopic surgery with right external iliac lymphadenectomy.

Intraoperatively, pelvic retroperitoneal tumor was most likely to represent a lymph node enlargement at the right external iliac area.The mass was adjacent to the external iliac vessels, no direct vascular invasion was noted in the tumor and its surface was well circumscribe. The mass was successfully dissected from the right external iliac artery with minimal oozing. No other enlarged lymph nodes were found at the retroperitoneal region.

Further histopathological studies, showed three cores of lymphoid tissue with partially effaced architecture with few preserved germinal centers. Diffuse infiltrate in plasma cells are noted in the interfollicular areas. These cells are highlighted by CD 38,CD 138 & CD 19, which also showed positive staining for IgG.

Furthermore, the flow cytometry confirms the result of polyclonal nature of the lesion. EBV& HHV8 stains were negative.

The morphological and immunohistochemical features are in keeping with non - malignant plasma cell disorder as unicentric Castelman disease, Plasma cell type, or idiopathic plasmacytic lymphadenopathy with polyclonal hypergammaglobulinemia described in the literatures as IgG4- Related lymphadenopathy.

The postoperative care was uneventful, discharged on the 2nd day of surgery.

Patient was seen 3 weeks post surgery in clinic, informed about the findings of histopathology of castleman disease.

Care plan was made by a multidisciplinary team of Gynecology, and hematology.

Seen by hematology in clinic, CT scan was done post op which revealed that there is no gross lesion or residual disease and confirms that the patient is in remission status.

Patient got pregnant 6 months post surgery, with no complications.

## Discussion

The discussed case in this paper is a case of UCD plasma cell type in the pelvis with presenting symptoms of chronic lower abdominal. Castleman disease or Angio-follicular lymphoid hyperplasia is a disease first identified around the past half century by the American pathologist Dr.Benjamin Castleman in the 1950s and the first case discovered was the unicentric type(3). Castleman disease is a cluster of immunological and lymphoproliferative disorders that have shared lymphoid histo-pathological characteristics but with variant presentation, etiologies and clinical manifestations(2).Overall, the epidemiology of Castleman disease is still not well established due to the disease's rarity . Nevertheless, it is estimated that around 5000 cases are

diagnosed each year in the USA(2).Castleman diseases can be mainly categorized into unicentric and multicentric types. Disease patterns and distributions were studied and found that unicentric Castleman disease can occur in all age groups with average age of presentation estimated to be in the 40s with occurrence frequency equal in both genders(2). In contrast(whereas), multicentric Castleman disease has more prevalence in males with average age of presentation approximately around 60s years of age with multiple possible risk factors like advanced age,impaired immunity status especially in HIV infection cases and presence of human herpesvirus 8(HHV-8) and its associated factors (2).

Unicentric Castleman disease involves one region with histopathological features showing Castleman disease microscopically(2).Pathogenesis of UCD is still not fully clear and there are not many reported cases(4). Furthermore, both UCD and MCD are observed to be associated with high levels of interleukin cytokines(particularly interleukin-6(2)) and lymph nodes with accumulation of plasma cells, immunoblast , hypervascularity , rise in VEGF levels in interfollicular zones(5). Clinical features associated with UCD include constitutional symptoms like fever, night sweats and fatigue or compressive symptoms related to the enlarged tumor. Additionally, UCD can be asymptomatic . Possible abnormal laboratory findings are increased lactate dehydrogenase enzyme (LDH),C reactive proteins(CRP) ,Erythrocyte sedimentation rate(ESR), polyclonal hypergammaglobulinemia and Abnormal complete blood count findings such as thrombocytopenia (2)(6). Unicentric Castleman disease differential diagnosis are HIV lymphadenitis, follicular hyperplasia, toxoplasma lymphadenitis and lymphoma (7) .Radiologically, both unicentric and multicentric Castleman disease presentations are mostly associated with increased vascularity. In a computed tomography(CT) scan,well-defined mass is either present as wide masses with heterogeneous enhancement or a lesser size mass with homogeneous enhancement. MRI mostly show firm mass, central linear hypointense septage and flow within the lesion demonstrating the increased vascularity. In a Positron emission tomography (PET) the masses are mostly FDG-PET avid(8). In Unicentric Castleman disease surgical resection can be considered a gold standard for the treatment(9). Possible surgical approaches might be laparoscopic(10), laparotomy(10) or robotic-assisted surgery(11). In some rare advanced cases, radiotherapy approach might be used(12).

Multicentric category can be further subdivided into three types according to clinical manifestations and etiologies. Types include POEMS(polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, skin changes) associated multicentric disease, idiopathic multicentric disease(iMCD) and HHV-8 associated multicentric disease(HHV-8 MCD) .Idiopathic multicentric Castleman disease can be further

subdivided into two types; one is TAFRO syndrome which constitute of thrombocytopenia, ascites, myelofibrosis, renal dysfunction and organomegaly and the latter is not other specified idiopathic multicentric Castleman disease(NOS iMCD) . On the other hand, HHV-8 associated multicentric Castleman disease(HHV-8 MCD) might be associated with HIV positive cases (HIV+MCD) or otherwise absent HIV condition(HIV- MCD)(2). Additionally, Castleman disease has different histopathological types and patterns. Currently identified patterns include hyaline vascular, plasma cell, plasmablastic and mixed histopathological variants(5). Multicentric castleman disease is a multi-systemic disease affecting multiple lymph nodes and can be associated with constitutional symptoms like night sweats and fever . Contrary to UCD, MCD has several risk factors and association such as HIV and Human Herpesvirus-8 (HHV-8) infections specifically in HHV-8 associated MCD(2). Probable clinical presentations associated with MCD include edema,effusion in variant organs,skin manifestations and rashes,cytopenias,anasarca ,neuropathies and kidney and liver dysfunction(2).

Clinically, possible differential diagnosis of castleman disease includes acute HIV, systemic lupus erythematosus,rosai dorfman and autoimmune lymphoproliferative syndrome(2). Treatment of MCD is diverse and variable according to the type,severity and clinical manifestations but generally it might include antiviral treatment ,immunotherapy,glucocorticoids and Chemotherapy(2).

Castleman disease can occur in different regions. For instance in the chest, abdomen, pancreas and retroperitoneum(5). Furthermore, Castleman disease can also manifest in the pelvis and its surroundings. Previous study reported 15 cases in the female pelvis from the year 1962 until 2019 (4). While in our paper we collected the cases from the year 2019 until now and found another 10 Cases which can be found in table 1. Which concludes that there are only 25 Castleman disease cases in the female pelvis(including our case). Table 1 demonstrates the reported cases from different aspects. For instance when considering the age , the average age of presentation was around 40. Maximum age was 70 and minimum was 20. Most common presentation was pain/discomfort followed by asymptomatic presentation. Tumor sites were highly variable but all were confined to the pelvis. All cases were diagnosed with hyaline vascular type except for our case which was plasma cell type . Tumor size was diverse ranging from small masses to large and bulky masses.

Table 1 showing female retroperitoneum cases from march 2019 until now.

| Author,Yea r | Ag e | Presentation | site | Diagnosis | Tumor size? | Treatment | Ref No. |
|---|---|---|---|---|---|---|---|
| Antonella Smedile et al,2019 | 52 | Pelvic pain | Near right ovary/right obturator LN | hyaline-vas cular type UCD | 5 × 3 cm | laparosco pic surgery resection | 13 |
| Masaki Murata et al,2019 | 70 | Abdominal discomfort | Between aorta and IVC | hyaline-vas cular type UCD | 25mm | laparosco pic surgery resection | 14 |
| Luyanne Azevedo Cabral Ferreira et al,2020 | 20 | Asymptom atic | right adnexal region | hyaline-vas cular type UCD | 33cm3 | Laparotom y resection | 15 |
| Pham hong duc,2020 | 44 | Asymptom atic | Right pelvic space(bet | hyaline-vas cular type UCD | 42 × 39 × 25 mm | Laparotom y(partial hysterecto | 16 |
| | | | ween uterus and iliac vessels) | | | my) resection | |
| Divyesh V. Shukla et al,2020 | 24 | Lower abdominal pain and weakness | Right iliac fossa | hyaline-vas cular type UCD | 75 × 48 mm | Laparosco pic surgery resection | 17 |
| Suzuki R et al, 2021 | 22 | Asymptom atic | Pelvis,righ t to bladder | hyaline-vas cular type UCD | 10×9× 4.5 cm | Preoperati ve Transcath eter Arterial Embolizati on and Tumor Resection with Lower Abdominal and Posterior Approach | 18 |
| D'Antonio et al,2021 | 58 | Abdominal pain | Right ovary | hyaline-vas cular type UCD | unspe cified | hysterecto my and bilateral salpingo-o ophorecto my | 19 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Salinas et al, 2021 | 56 | Asymptomatic | Retropubic space(space of Retzius) | hyaline-vascular type UCD | 5x4x4cm | Exploratio n of the pelvic cavity and mass excision | 20 |
| Karaman et al, 2021 | 36 | Pregnant, left inguinal region pain | left adnexal lodge | hyaline-vascular type UCD | 8 x 6 x 2.5 cm | Laparotom y approach and tumor excision | 21 |
| Ion et al,2022 | 51 | genital bleeding (caused by uterine fibromatosis) | Mesorectal(behind the uterus) | hyaline-vascular type UCD | 49/51 mm diameter | Open total hysterecto my with bilateral anexecto my,mass resection and low colorectal anastomo sis with temporary protective ileostomy | 22 |
| Presented Case | 20 | Lower abdominal pain | Right external iliac group | Plasma cell type UCD | 2.8 X 4.4 X 3.8 cm | laparoscopic surgery with right external iliac lymphaden ectomy | |

Ultimately, Castleman disease in general and pelvic CD specifically are rare presentations which can be confused with many conditions and can lead to misdiagnosis or delayed diagnosis. To avoid such incidents clinicians should consider the occurrence of rare conditions. There should be proper reporting and sharing of cases which might help with understanding disease patterns and characteristics to set up an appropriate and evidence based treatment.

## Conclusion

This paper discussed castleman disease and a case of unicentric castleman disease in a medically free 20 year old nulliparous female who was treated with laparoscopic excision. Patient was followed up and got pregnant after six months. Castleman disease is a rare disease and needs further studying,research and reporting to gain a full understanding of the disease.

## References

1- Nepal, S. P., Shichijo, T., Ogawa, Y., Naoe, M., Oshinomi, K., & Morita, J. (2021). Surgical challenges of Castleman's disease of the pelvis. Urology Case Reports, 34(101518), 101518. https://doi.org/10.1016/j.eucr.2020.101518

2- Dispenzieri, A., & Fajgenbaum, D. C. (2020). Overview of Castleman disease. Blood, 135(16), 1353–1364. https://doi.org/10.1182/blood.2019000931

3- Nishimura, M. F., Nishimura, Y., Nishikori, A., Yoshino, T., & Sato, Y. (2022). Historical and pathological overview of Castleman disease. Journal of Clinical and Experimental Hematopathology: JCEH, 62(2), 60–72. https://doi.org/10.3960/jslrt.21036

4- Nakata, K., Iwahashi, N., Matsukawa, H., Noguchi, T., Yahata, T., Ota, N., Mabuchi, Y., & Ino, K. (2020). Laparoscopically resected Castleman's disease in the pelvic retroperitoneum: A case report. Molecular and Clinical Oncology, 12(2), 169–173. https://doi.org/10.3892/mco.2019.1963

5- Saeed-Abdul-Rahman, I., & Al-Amri, A. M. (2012). Castleman disease. The Korean Journal of Hematology, 47(3), 163–177. https://doi.org/10.5045/kjh.2012.47.3.163

6- Kim, T. J., Han, J. K., Kim, Y. H., Kim, T. K., & Choi, B. I. (2001). Castleman disease of the abdomen: imaging spectrum and clinicopathologic correlations. Journal of Computer Assisted Tomography, 25(2), 207–214.

https://doi.org/10.1097/00004728-200103000-00008

7- Madan, R., Chen, J.-H., Trotman-Dickenson, B., Jacobson, F., & Hunsaker, A. (2012). The spectrum of Castleman's disease: mimics, radiologic pathologic correlation and role of imaging in patient management. European Journal of Radiology, 81(1), 123–131. https://doi.org/10.1016/j.ejrad.2010.06.018.

8- Germaine, L. M., & Newhouse, J. H. (2003). Castleman's disease. Clinical Imaging, 27(6), 431–434. https://doi.org/10.1016/s0899-7071(03)00022-6

9- Mitsos, S., Stamatopoulos, A., Patrini, D., George, R., Lawrence, D., & Panagiotopoulos, N. (2018). The role of surgical resection in Unicentric Castleman's disease: A systematic review. Advances in Respiratory Medicine, 86(1), 36–43. https://doi.org/10.5603/arm.2018.0008

10- Serpa Carmoma, F., Cueva, M., Serpa Carmoma, F., Molina, G. A., Yu Lee, A., & Flores, E. (2021). Castleman's disease: Laparoscopic resection of unicentric disease in the hepatic hilum: A case report. Annals of Medicine and Surgery (2012), 67(102494), 102494. https://doi.org/10.1016/j.amsu.2021.102494

11- Sbrana, F., Zhou, D., Zamfirova, I., & Leonardi, N. (2017). Castleman's disease: a rare presentation in a retroperitoneal accessory spleen, treated with a minimally invasive robotic approach. Journal of Surgical Case

Reports, 2017(10), rjx195. https://doi.org/10.1093/jscr/rjx195

12- de Vries, I. A. C., van Acht, M. M. S., Demeyere, T. B. J., Lybeert, M. L. M., de Zoete, J.-P., & Nieuwenhuijzen, G. A. P. (2010). Neoadjuvant radiotherapy of primary irresectable unicentric Castleman's disease: a case report and review of the literature. Radiation Oncology (London, England), 5(1), 7. https://doi.org/10.1186/1748-717X-5-7

13- Smedile, A., Capuano, F., Fraticelli, S., Lucioni, M., & La Fianza, A. (2019). Unicentric or Multicentric Castleman disease? A case report of a pelvic intraperitoneal mass in a middle aged woman. Journal of Radiology Case Reports, 13(3), 28–36. https://doi.org/10.3941/jrcr.v13i3.3387

14- Murata, M., Nagano, O., Hasegawa, G., Ikeda, Y., Nakagawa, Y., Seki, Y., Nishiyama, T., & Tomita, Y. (2019). Unicentric Castleman's disease located between the aorta and inferior vena cava: A case report. SAGE Open Medical Case Reports, 7, 2050313X19839532. https://doi.org/10.1177/2050313X19839532

15- Ferreira, L.A., Pinel, R., Ferreira, R.N., & Filho, A.C. (2020). Unicentric castleman disease in the differential diagnosis of a paravesical mass: A case report. European Journal of Gynaecological Oncology, 41, 644-647.

16- Duc, P. H., Van Doan, N., & Huy, H. Q. (2020). Unicentric Castleman's disease in the female pelvis. Radiology Case Reports, 15(11), 2221–2224. https://doi.org/10.1016/j.radcr.2020.08.044

17- Shukla, D. V., Shukla, S. D., Shah, A., Patel, S., & Shukla, S. (2020). Unicentric Castleman's disease presenting as retroperitoneal pelvic lymph node in young female—laparoscopic excision: A case report. Open Journal of Obstetrics and Gynecology, 10(11), 1590–1608. https://doi.org/10.4236/ojog.2020.10110143

18- Suzuki R., Goto T., Banno H., Fuchigami Y., Hattahara K., Hida T., Fujiwara M., Yoshino T., Kita Y., Sawada A., Akamatsu S., Saito R., Kobayashi T., Yamazaki T., Inoue T., Shimizu H., Kurata M., Maeda H., Okamoto T., … Ogawa O. (2021). A case of pelvic unicentric Castleman disease treated by preoperative transcatheter arterial embolization and tumor complete resection with combined lower abdominal and posterior approach. Hinyokika kiyo. Acta urologica Japonica, 67(4), 157–162. https://doi.org/10.14989/ActaUrolJap_67_4_157

19- D'Antonio, A., Caleo, A., Addesso, M., Caputo, A., Fraggetta, F., & Ponzoni, M. (2021). A rare case of Castleman disease presenting as an ovarian tumor. International Journal of Gynecological Pathology: Official Journal of the International Society of

Gynecological Pathologists, 40(4), 379–382. https://doi.org/10.1097/PGP.0000000000000721

20- Treviño Salinas, E., Dávila Flores, N., Hernández-Salas, R., Barboza-Quintana, O., & Marroquin-Luna, C. (2021). EPV240/#380 Pelvic castleman´s disease: a case report. E-Posters, 31.

21- Karaman, Ö. E., Kılıççı, Ç., & Önder, P. Ö. (2021). A rare disease with pregnancy: Castleman case report. Malawi Medical Journal: The Journal of Medical Association of Malawi, 33(4), 300–302. https://doi.org/10.4314/mmj.v33i4.12

22- Ion, D., Bolocan, A., Filipescu, A. G., Andronic, O., Oproiu, A.-M., Popa, A., & Păduraru, D. N. (2022). A mesorectal incidentaloma: Rare localization of Castleman disease (Case report). Experimental and Therapeutic Medicine, 23(4), 268. https://doi.org/10.3892/etm.2022.11194.