

# Perivesical unicentric Castleman disease initially suspected to be metastatic prostate cancer

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## Abstract

Unicentric Castleman disease (UCD) is a relatively rare lymphoproliferative disease, which commonly presents as a mediastinal mass and less frequently involves abdomen, pelvis, and retroperitoneum. We report a case of a 64-year-old man with newly diagnosed low-volume, Gleason 3 + 3 = 6 prostate adenocarcinoma, who in considering active surveillance versus treatment was found to have a left perivesical and iliac chain lymphadenopathy concerning for potential metastatic involvement. He underwent magnetic resonance imaging with ferumoxytol to assist in the diagnostic evaluation to better characterize his lymphadenopathy. Subsequently, he underwent robotic-assisted laparoscopic bilateral pelvic lymph node dissection and resection of left perivesical mass exhibiting hyaline vascular variant of UCD.

**Key Words:** Castleman disease, ferumoxytol, fusion biopsy, multiparametric magnetic resonance imaging, prostate adenocarcinoma

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## INTRODUCTION

Castleman disease (CD) is a benign disorder characterized by lymphoproliferation originally described by Castleman in 1954.<sup>[1,2]</sup> Castleman initially described the entity by two microscopic features, lymphoid follicular hyperplasia and proliferation of capillaries with endothelial hyperplasia. The disease has also been characterized as angiofollicular lymph node hyperplasia, giant lymph node hyperplasia, and angiomatous lymphoid hyperplasia. Clinically, CD can be unicentric CD (UCD) or multicentric with more systemic B-like symptoms. There has been an association of formation of tumors and chronic antigenic stimulation and dysregulation

of interleukin-6 (IL-6), particularly in the multicentric variant.<sup>[3]</sup> At present, approximately, 1000 cases of CD have been reported in the medical literature.<sup>[2]</sup> The most common locations of occurrence are the mediastinum (63%), abdomen (11%), retroperitoneum (7%), axilla (4%), and pararenal space (2%).<sup>[4,5]</sup> Though thoracic presentations are most common, the involvement of the genitourinary system is one of the most infrequently involved organ symptoms.<sup>[4]</sup> These lesions have been described in the pararenal, retroperitoneum, pelvis, and involving urachal remnants.<sup>[3]</sup> Intraabdominal presentations of CD are the second most common location, with few documented pelvic presentations and no cases of

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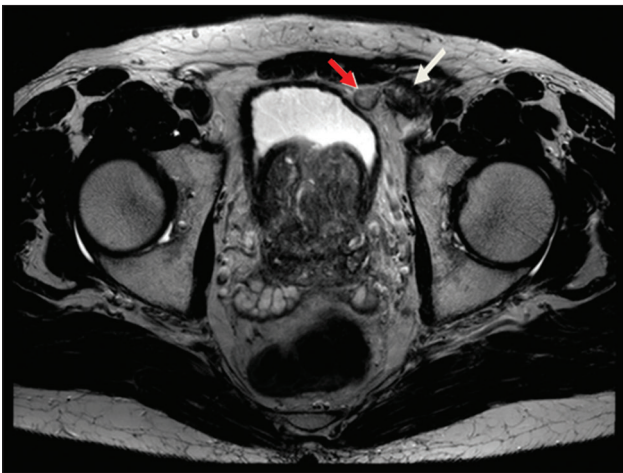
CD in the perivesical space of Retzius readily found reported in the literature.

## CASE REPORT

A 64-year-old Caucasian male with past medical history of benign prostatic hyperplasia (BPH), recurrent prostatitis, and multiple negative transrectal ultrasound (US) biopsies to evaluate for an elevated prostate-specific antigen (PSA) presented for further evaluation of his persistently rising serum PSA level. He has a history of elevated PSA levels in the 8–10 ng/mL range for nearly 5 years. He has had two prior 12-core biopsies and a saturation biopsy with 42 cores obtained, each session with pathology negative for malignancy. He also endorsed 1–2 years history of intermittent night sweats unassociated with fevers or chills.

For a persistently rising PSA despite prior negative biopsies, he underwent multiparametric magnetic resonance imaging (MP-MRI) of the pelvis [Figure 1] to evaluate the prostate.<sup>[6]</sup> This yielded identifiable intraprostatic lesions on MRI, which were suspicious for biopsy targeting as well as left iliac chain and perivesical lymphadenopathy. He subsequently underwent an MRI-US fusion-guided (Invivo, Gainesville, FL, USA) prostate biopsy with standard 12-core and 6 intraprostatic target biopsies obtained. He was found to have 2 cores positive of Gleason grade 3 + 3 = 6 compromising 5% of each core, all other cores negative for cancer, and discussion was held regarding active surveillance with follow-up MRI and MRI/US fusion-guided biopsies.<sup>[7]</sup>

In the discussion of active surveillance versus treatment, the patient was referred to the molecular imaging program at the National Cancer Institute for USPIO-enhanced MRI with ferumoxytol (Feraheme® AMAG Pharmaceuticals, Waltham,



**Figure 1:** Baseline axial T2-weighted magnetic resonance imaging demonstrating perivesical enlarged lymph node (red arrow) and area of adjacent lymph node enlargement at site of prior left inguinal hernia repair (white arrow)

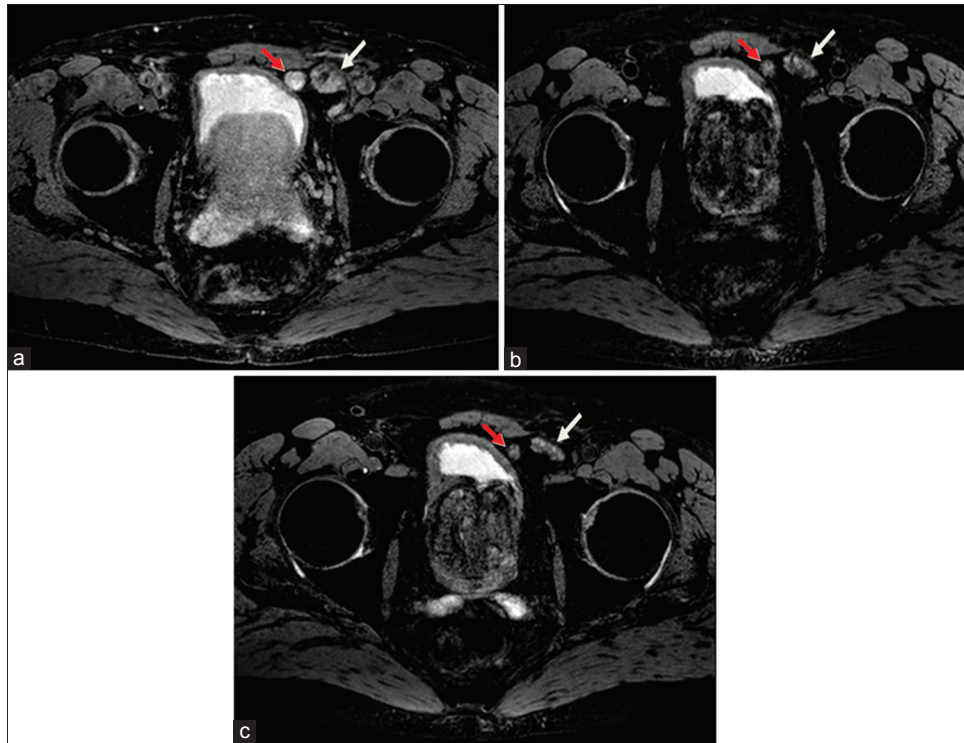
MA, USA) to further characterize his lymphadenopathy.<sup>[8]</sup> On this imaging, the patient was found to have bilateral pelvic nodal enlargement with iron uptake and an additional left perivesical lymph node with no significant iron uptake raising concern that the macrophages were largely replaced by this lymph node [Figure 2a-c]. Due to the shape and location of the mass, there was uncertainty regarding the etiology of lymphadenopathy. This generated concern for a genitourinary or hematologic malignancy versus a chronic infectious spread of bacterial, fungal, or parasitic organism. Due to the possibility of malignancy, the patient had an <sup>18</sup>F-fluorodeoxyglucose-positron emission tomography (FDG-PET)-computed tomography scan [Figure 3], which showed only mild metabolic activity.

Consequently, the patient underwent robotic-assisted laparoscopic bilateral pelvic lymph node dissection and resection of the left perivesical mass for definitive diagnosis. Twenty-one lymph nodes were resected of which one was the 1.7 cm × 1 cm × 0.7 cm left perivesical mass. This specimen was negative for malignancy but showed abundant small follicles with regressed germinal centers and hyalinization [Figure 4a-c]. There were scattered follicles of lymphocyte depletion with follicular dendritic cells and hyaline deposits and penetration of sclerotic blood vessels. These findings were compatible with unicentric, hyaline vascular variant CD. All other lymph nodes removed were benign, without features of CD.

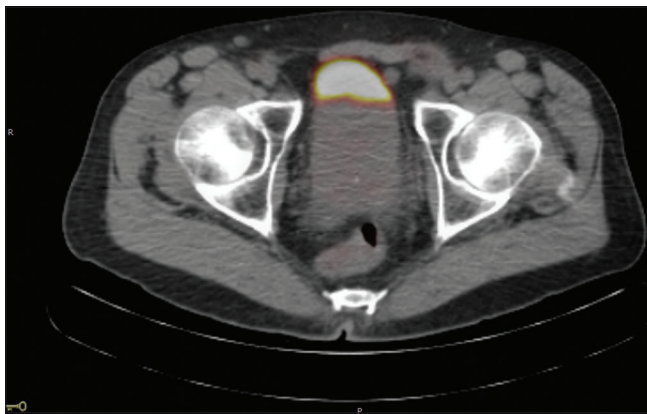
## DISCUSSION

CD or angiofollicular lymphoid hyperplasia is a heterogeneous group of lymphoproliferative disorders. It is frequently classified on histologic presentation as either hyaline vascular, plasma cell variant or mixed. Hyaline vascular variant consists of small hyaline vascular follicles and interfollicular capillary proliferation and accounts for nearly 90% of cases.<sup>[2-4]</sup> These lesions are localized to a single well-circumscribed lymph node, often can be asymptomatic, and progress along a benign course.<sup>[5]</sup> Plasma cell variant consists of large hyperplastic follicles with intervening sheets of plasma cell proliferation in the interfollicular regions. This accounts for only 9% histological subtypes. Nearly, 50% of these patients may present with systemic manifestations of anemia, fevers, weight loss, fatigue, or hyperglobulinemia.<sup>[9]</sup> Cutaneous symptoms such as paraneoplastic pemphigus, erythema multiforme, or lichen planus have been described.<sup>[10]</sup> These patients are more likely to have multifocal disease and have worse outcomes.

The disease has clinically been subclassified as either unicentric or multicentric. The average age of patients with UCD is around 30–40 years old. While the multicentric form is usually found in patients 50–60 years of age.<sup>[2,4,5]</sup> UCD presents as

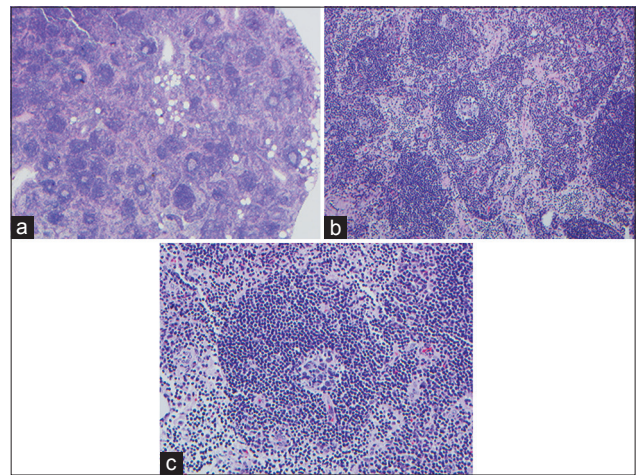


**Figure 2:** Fat saturated T2\*-weighted magnetic resonance Imaging at (a) baseline, preinjection of ferumoxytol, (b) 24 h postinjection of intravenous ferumoxytol, and (c) 48 h postinjection of intravenous ferumoxytol demonstrating perivesical lymph node (red arrow) without significant iron uptake enhancement, but the presence of relative iron uptake in other pelvic lymph nodes visualized near inguinal hernia repair (white arrow)



**Figure 3:** <sup>18</sup>F-fluorodeoxyglucose-positron emission tomography-computed tomography imaging showing lack of fluorodeoxyglucose uptake of left-sided perivesical lymph node

isolated lymphoproliferative lesions and typically is benign. They occur most commonly in younger patient populations and have near 100% 5-year survival following *en bloc* surgical resection.<sup>[4]</sup> The disease can also present as multicentric or generalized CD. The disease can also present with generalized lymphadenopathy, organomegaly, and constitutive symptoms as seen in multicentric type. Multicentric CD is often seen in plasma cell or mixed hyaline vascular and plasma cell subtypes and has the risk of progression to Kaposi sarcoma or systemic lymphomas, particularly in immunocompromised patients.<sup>[11]</sup> The symptomology of multicentric has been related to acute



**Figure 4:** Histopathologic examination of the perivesical lymph node shows (a) distinctive follicles with expanded mantle zones, (b) mainly atrophic germinal centers with hyalinization, and (c) regressed germinal center showing hypervascularity with a "lollypop" appearance

phase proteins, such as IL-6 and C-reactive protein, as well as an association between the human herpesvirus 8 and the hyperplastic lymphatic response of CD.<sup>[3]</sup>

Though imaging modalities are commonly used to diagnosis pelvic masses, there are lacks radiologic criteria that diagnosis with certainty CD. MRI can show hypointensity signal on T1-weighted images and hyperintensity signal on T2-weighted images.<sup>[12]</sup> MRI can be helpful in identifying the hypervascular



appearance of hyaline vascular types. CT imaging often will show solid, homogeneous mass with enhancement and a radial or stellate calcifications present. Differences in enhancement patterns have been described between plasma cell and hyaline vascular variants. Hyaline vascular variant has more prominent enhancement on CT imaging, with fewer enhancements for plasma cell variant. However, the difference in contrast enhancement is not a reliable diagnostic criterion to distinguish the histologic subtypes.<sup>[13]</sup>

CD remains a difficult diagnosis to be made preoperatively due to resemblance on imaging studies to primary malignant or metastatic lesions. In this era of increased cross-sectional imaging, including increased use of MP-MRI for detection and management of pelvic malignancies, such cases may be more commonly mistaken for metastatic lymphadenopathy.<sup>[14]</sup> Due to this fact, exclusion of another disease such as systemic lupus erythematosus, rheumatoid arthritis, HIV, lymphoma, and metastatic disease, which may have lymphadenopathy, should be excluded. CD presents often in young, otherwise healthy individuals though case reports have ranged from 8 to 66 years of age, with males and females being equally affected. Unicentric tumors are localized lesions that commonly present in younger patient populations, typically the third decade of life, while multifocal lesions develop in more elderly patients (the sixth decade of life or later).<sup>[15]</sup> Localized tumors respond well to surgical resection, with near 100% disease-free survival after resection.<sup>[4]</sup> Following the removal of lymphoid mass, these symptoms will often resolve as levels of IL-6 decline.<sup>[3]</sup> In contrast, the multifocal type is more difficult to be treated completely and is often resistant to corticosteroid therapy, chemotherapy, and radiotherapy, thus requiring multimodality therapies.

Our patient had a history of intermittent night sweats and a recent diagnosis of focal, low-grade prostate cancer which lead to his imaging presentation of lymphadenopathy. Imaging modalities are not always accurate at the diagnosis of CD which complicated management for our patient with concern for metastatic prostate adenocarcinoma on imaging. The use of enhanced MRI with ferumoxytol helped to evaluate indeterminate adenopathy, as there is no enhancement of the lymph node due to lack of macrophages in the node in which to phagocytosis iron oxide. The potential etiologies were further narrowed by the use of FDG-PET showing no uptake, leading to the need of surgical excision to reach a final diagnosis of CD. In the final pathology, there was no ferumoxytol uptake proofing lack of macrophages and replacement by lymphocytic invasion.

Abdominal presentations of CD are the second most frequent location; however, the clinical course of disease progression is difficult to generalize. Complete surgical resection and histologic evaluation are the only way to accurately characterize the tumor and allows for near complete recovery in a majority of patients.

There have been no prior reports of prevesicular presentation of CD in association with prostate cancer. Preoperative suspicion for CD can be based on imaging with CT or MRI or with testing of abnormally high levels of IL-6 in cases of multicentric CD. CD is exceedingly rare but should be considered in the differential diagnosis of patients with hypervascular and heterogeneous pelvic lymphadenopathy. Furthermore, a tissue sampling is warranted for the accurate diagnosis.

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### Conflicts of interest

There are no conflicts of interest.

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