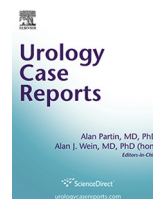


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General Urology

Castleman's Disease: An Interesting Cause of Hematuria



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ABSTRACT

Castleman's disease is a rare benign lymphoproliferative disorder, characterized by benign growths of the lymph node tissue. It is associated with a number of malignancies, including Kaposi sarcoma, non-Hodgkin's and Hodgkin's lymphoma, and POEMS syndrome. This report describes the case of a 38 year old gentleman, presenting with painless hematuria. Initial investigations, including flexible cystoscopy were unremarkable. However, subsequent imaging including CT Urogram and MR pelvis revealed multiple prevesical lesions. Histology obtained from excision biopsy revealed histological features consistent with Castleman's disease. In this report we discuss the nature, presentation and treatment modalities of this rare condition.

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A 38 year old gentleman was referred to the Urology clinic in early October 2012 with painless hematuria. He had no significant medical or surgical history, other than being investigated for obstructive sleep apnea. Initial investigations were normal, including full blood count, renal profile, urine microscopy and cytology. Upon flexible cystoscopy in the clinic, there were no obvious abnormalities, the urethral mucosa appeared normal, both ureteric orifices were clearly visible, the trigonal region appeared normal, and there was no focal mucosal bladder pathology. It was noted that there was some extrinsic compression on the posterior bladder wall at cystoscopy. Ultrasound scan of the pelvis revealed an echogenic area over the anterior bladder wall. These abnormalities were further investigated with a CT Urogram which was performed within the following weeks.

The CT scan revealed evidence of multiple prevesical soft tissue nodules, the largest of which measuring 2.6×1.3 cm (Figs. 1 and 2). The remainder of the abdominal organs were reported as completely normal, of particular importance in this case, there was no evidence of any hydronephrosis, calculi, extrinsic compression or bladder mucosal abnormality. The exact nature of these nodules remained unclear, and the possibility of atypical lymph nodes or urachal remnants were discussed at a Multi-Disciplinary Team (MDT) meeting.

The MDT deemed that a repeat scan would be indicated in 3 months from that time, as the lesions were most likely to be

benign. As a result of this decision an MRI scan of the pelvis was performed in December 2012, this again was reported as showing multiple soft tissue nodules that were essentially unchanged from the previous CT findings (Fig. 3).

The case was again discussed at MDT, whom deemed that histological sampling via excisional biopsy of the prevesical lesions would be the most appropriate modality for diagnosis. This was performed in May/2013 under a general anesthetic.

The histology report revealed fibro-fatty connective tissue with lymphoid infiltrate which were in keeping with features of Castleman's disease (hyaline vascular variant). Further immunohistochemistry revealed positive BCL2 expression excluding lymphoma and confirming Castleman's disease.

Castleman's disease (giant or angiofollicular lymph node hyperplasia) is a rare benign lymphoproliferative disorder that may be localized to a single lymph node (unicentric) or multifocal/systemic (multicentric).¹ It is characterized by benign growths of the lymph node tissue, and can also involve lymphoproliferation of B cells, with stimulation and production of certain pro-inflammatory cytokines, such as interleukin-6 (IL-6).² It is also associated with a number of malignancies, including Kaposi sarcoma, non-Hodgkin lymphoma, Hodgkin lymphoma, and POEMS syndrome.

As mentioned above, Castleman's disease can be categorized into two distinct types of disease. Unicentric Castleman's disease (UCD) involves lymphoproliferation of tissue at a single lymph node site.³ It is often asymptomatic or has very few symptoms other than those directly associated with a local mass affect from direct compression of surrounding tissues by the lymph node, as was found in the case above. The majority of cases can be cured via

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Figure 1. Transverse CT slice demonstrating prevesical lymphoid lesion.



Figure 2. Sagittal CT slice demonstrating prevesical lymphoid lesions.

surgical resection of the affected node without any further complications or local recurrence.

Multicentric Castleman's disease (MCD) is distinguished from UCD by the multi focal nature of its presentation.⁴ There will often be multiple lymph nodes involved at different tissue sites. It is not classified as malignant and therefore differs from lymphoma, however it does share similarities with lymphoma, and in fact, may even progress into lymphoma. This type of Castleman's disease is more common amongst immunosuppressed patients, as it has been identified in approximately 50% of cases with human herpes virus 8 (HHV-8), a gammaherpesvirus that is also the cause of Kaposi's sarcoma and primary effusion lymphoma.^{4,5} The remaining 50% of cases are of unknown causes. The histological form of MCD most closely associated with HHV-8 is the plasmacytic form of Castleman's disease while another histological form, the hyaline-vascular type is often found to be negative for herpes virus. Symptoms of MCD are more common than those of UCD, as a result of the over expression of cytokines. These symptoms may include "B symptoms" similar to those with lymphoma, which involve; pyrexia, weight loss, anemia and loss of appetite, all of which may be due to the overproduction of IL-6.²

Castleman's disease can also be categorized into histological subtypes. The hyaline vascular type is most common. It tends to be localized, but in rare cases can be multicentric. In addition, the plasma cell type is slightly more likely to be multicentric. There is also mixed histological subtype that illustrates characteristics of both cell types. This is the least common subtype.

Unicentric disease can often be treated easily with surgical resection.⁴

Treatment of MCD is often a little more complex, secondary to the systemic nature of the disease. Treatment modalities include antiviral drugs for human herpes virus type 8 (HHV-8), various immunomodulators, corticosteroids, chemotherapy, and more recently; monoclonal antibodies against IL-6 or B-cells themselves.²

Recent work with HIV-positive patients with HHV-8-related MCD suggests that treatment with the antiherpesvirus drug ganciclovir or the anti-CD20 B cell monoclonal antibody, rituximab, may markedly improve outcome.⁴ Due to the rarity of MCD, there is a paucity of evidence that has addressed standardized approaches to therapy.

The above case outlines a rare example of unicentric Castleman's disease. The patient described was essentially asymptomatic other than painless hematuria. The findings were incidental on CT/MR scanning. The treatment modality here was surgical resection via excisional biopsy. Whether or not this patient will go on to develop any post-operative complications or local recurrence will become apparent during the follow up period, which is planned on an annual basis.

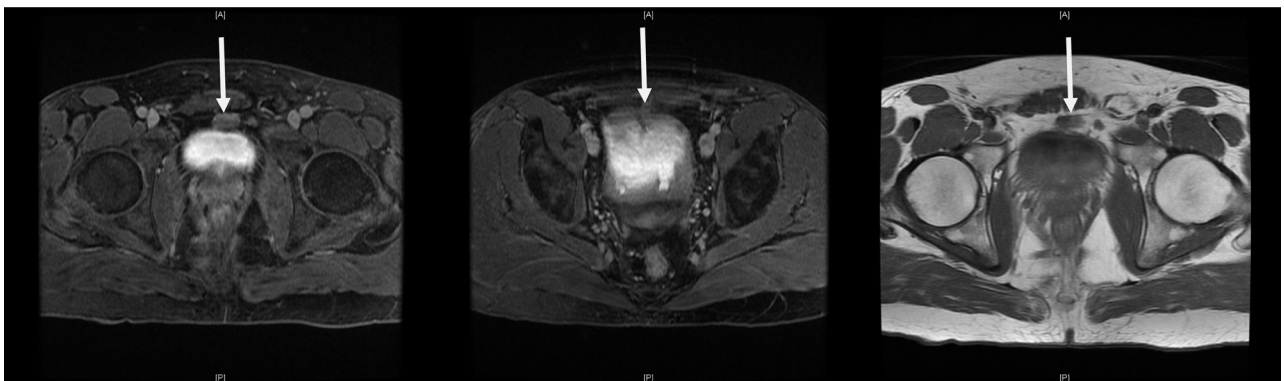


Figure 3. Transverse MR slice demonstrating prevesical lymphoid lesion.

Conflict of interest

None declared.

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