Case Report

Retroperitoneal Castleman's Disease: Case Report and Review of the Literature

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Abstract

Castleman's disease (CD) is a benign, rare, lymphoproliferative disorder. The symptoms, treatment and prognosis differ between its two clinical forms, unicentric CD (UCD) and multicentric (MCD). Pre-operative diagnosis is rarely arrived at. We present a case of a surgically treated retroperitoneal UCD originally thought to be a paraganglioma. Complete surgical resection is the gold-standard of treatment for UCD.

ABBREVIATIONS

CD: Castleman's Disease; UCD: Unicentric Castleman's Disease; MCD: Multicentric Castleman's Disease; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; ^{18}F-FDG-PET: Fluorodeoxyglucose- Positron Emission Tomography; CgA: Chromogranin A; HHV-8: Human Herpes Virus-8; HIV: Human Immunodeficiency Virus; HV-CD: Hyaline-Vascular Castleman's Disease; PC-CD: Plasma Cell Castleman's Disease

INTRODUCTION

Castleman's disease (CD) is a benign, rare, non-clonal, lympho-proliferative disorder, first described in 1954 [1]. The disease is divided into two clinical forms that differ in symptoms, treatment and prognosis: Unicentric Castleman's Disease (UCD) which affects a single lymph-node or group of lymph-nodes, and Multicentric Castleman's Disease (MCD) which affects various lymph-node basins in a generalized form [2]. UCD is usually asymptomatic or causes symptoms related to the mass. A pre-operative diagnosis is rarely suspected, and it is often confused with a lymphoma, paraganglioma, sarcomas, or other tumors. In UCD a complete surgical resection with free margins is the initial means for diagnosis and is the gold-standard of treatment [2,3]. In MCD the role of surgery is limited to an excisional biopsy of an affected lymph-node in order to establish the definitive diagnosis [2,3].

We present a case of a retroperitoneal UCD which was initially diagnosed as a non-secreting paraganglioma and underwent a complete surgical resection.

CASE PRESENTATION

A 49-year-old male patient presented with an abdominal mass incidentally found on an abdominal CT scan. He reported a 10-year history of lumbar pain that was controlled with tramadol. A 41 x 44 x 40 mm well-defined, left para-aortic abdominal mass with coarse calcifications had been seen on an abdominal ultrasound performed 10 years prior to presentation. An abdominal ultrasound performed 5 years before presentation showed growth of this mass to 51 x 44 x 65 mm, and it was further characterized with a contrast-enhanced CT scan with homogenous IV contrast uptake and an attenuation of 110 Hounsfield Units (HU) (spontaneous attenuation of 40 HU).

The patient was referred to our institution after the CT scan revealed an abdominal mass, and other complementary studies to further define it were performed. An MRI showed a well-defined, heterogenous, 65 x 60 x 50 mm retroperitoneal mass, located anterior and inferior to the left kidney, with coarse calcifications, hyperintense to the muscle in T1-weighted images (Figure 1a), isointense to the muscle in T2-weighted images (Figure 1b), and with intense IV-gadolinium contrast uptake (Figure 1c). The final radiologic diagnosis was suspicion of a paraganglioma or a schwannoma. An ^{18}F-FDG-PET scan was performed and showed a positive up-take of the mass with a SUVmax of 4.47, with no other zones of up-take (Figure 2a, 2b).

A laboratory work-up for a paraganglioma was performed, with all laboratory and biological markers within the normal range (cortisol/ACTH, free cortisol and catecholamines in 24hr urine, plasma catecholamines, CgA, testosterone, SDHEA, DHEA, 11-deoxycortisol). The case was discussed in a multidisciplinary case-conference meeting, and a clinical diagnosis of a non-secreting paraganglioma was made. Thus, the patient was scheduled for surgical resection.

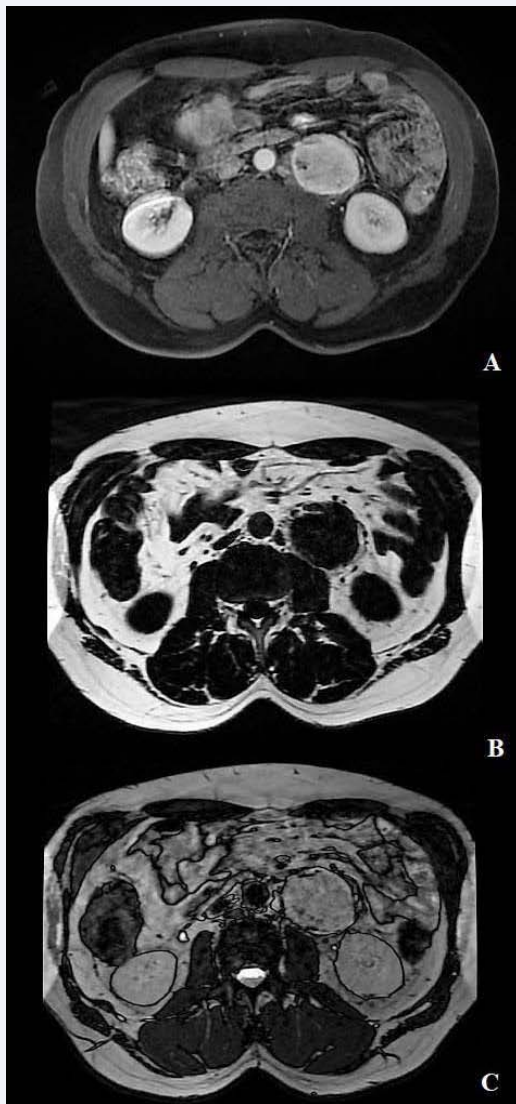The patient underwent an initial laparoscopic exploration.

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Figure 1 MRI showing a well-defined, heterogeneous, 65 mm retroperitoneal mass, with coarse calcifications. Hyper intense to the muscle in T1-weighted images (A), isointense to the muscle in T2-weighted images (B), and intense IV- gadolinium uptake (C).

A large, well-vascularized, firmly adherent para-aortic mass, beneath the inferior mesenteric vein and superior to the left renal vein was observed. The operation was converted to an open surgery and the mass was resected in its entirety without any complications. The patient had an uneventful postoperative course and was discharged without any complications.

Macroscopically the encapsulated mass measured 4.7 x 4.0 x 6.0 cm. The histopathological report revealed an enlarged lymph node with lymphoid follicular proliferation in "onion skin" appearance, and thickened mantle cells arranged in a single layer (Figure 3a). The germinal centers with hyaline deposits (CD 3+, CD 5+, CD 20+) and fibro-hyaline septa, with capillary hyperplasia (CD 31+, CD 34+), (Figure 3b). It was negative for HHV-8. The final diagnosis was of Unicentric Castleman's Disease, hyaline-vascular subtype (UCD-HV). The patient is HHV-8 and HIV negative.

DISCUSSION

Castleman first described the disease subsequently named after him in 1954 [1]. Since then, two distinct entities have been described, with different patient characteristics, symptoms, management and prognosis: UCD (73.7%) and MCD (26.3%) [2]. The disease has been further classified according to its histopathological pattern [4], which is also linked to the centricity and prognosis of the disease [2,4]: 1) hyaline-vascular (HV) CD (35-91%) [5-7], more commonly presenting as UCD in HIV-negative patients, 2) plasma cell (PC) CD (up to 20%), more commonly presenting as MCD in HIV-negative patients, 3) HHV-8-associated plasmablastic MCD (up to 27%), 4) MCD not otherwise specified (usually associated with HIV+ patients and constitutes a completely different entity with regards to presentation, treatment, and prognosis, up to 18%). The hyaline-vascular subtype generally occurs as a UCD (78%) [6,7], while the other three subtypes typically occur as MCD. Although a clear pathogenic factor is unknown, there is an association with increased interleukin (IL)-6 serum levels [8,9]. It is also fundamental to establish the HIV status in all CD patients, as HIV+ patients have a different presentation and prognosis [2].

The median age of presentation is in the 4th decade of life [4], with HV-CD occurring most commonly in patients younger than 37 years, and PC-CD in patients older than 37 years [2]. Although there is no gender predominance, a systematic review found that HV-CD is more common in women and PC-CD is more common in men, with women tending to be younger at the time of diagnosis (<37 years) [2]. CD is most commonly found in the mediastinum (30-70%) and the neck (23-40%); with the abdomen (12-20%), retroperitoneum (12-17%) and pelvis (2-12%), and axilla (4-5.5%) being less common [3,7]. UCD is usually asymptomatic or it presents with symptoms associated with mass effect. Some of the presenting symptoms related to the tumor location may include [7,10]: cough, pain, dyspnea, hemoptysis, and palpable mass. B symptoms are exclusive to patients that have MCD [2,7]. Although outside the scope of this review, it is important to note that CD may be associated to POEMS syndrome, a paraneoplastic syndrome related to plasma cell neoplasms and characterized by polyradiculoneuropathy, clonal plasma cell disorder (PCD), sclerotic bone lesions, elevated vascular endothelial growth factor, and CD [11].

The diagnosis of CD is rarely suspected before taking the patient to the operating room, with the typical preoperative differential diagnosis including lymphoma, sarcoma, paraganglioma, neuroendocrine tumor, metastatic adenopathy, and infectious or inflammatory diseases [10,12]. A recent review of the radiologic features in patients with CD characterizes the appearance and imaging findings that may be helpful in distinguishing CD from other pathologic entities [7]. On ultrasound, typical CD lymph nodes were found to be hypoechoic and homogeneous with posterior acoustic enhancement [7]. On CT scan the mean node size has been found to be 4.5 to 6.1 cm at presentation with well-defined margins, a homogeneous character (83.3%) and with a mean attenuation of 40.3 HU (hypo-/isodense to skeletal muscle) in non-contrast CT, and homogeneous enhancement with IV contrast (80.8%) [7]. There are some reports of heterogenous enhancement on CT especially if the tumor is greater than 5 cm,
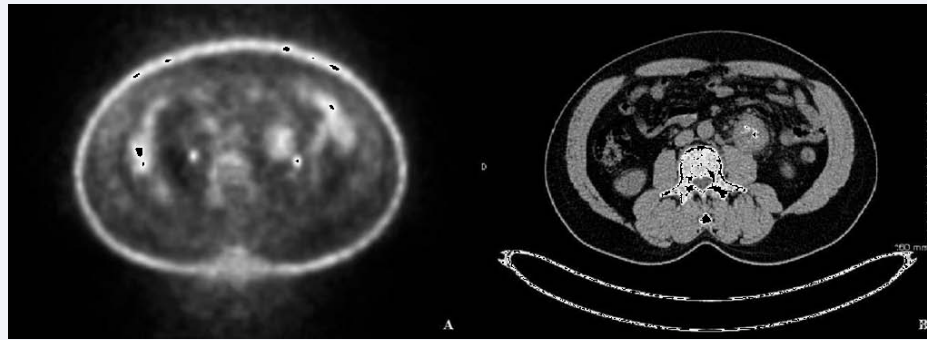
Figure 2 ^{18}F-FDG-PET scan showing a positive up-take of the mass with a SUVmax of 4.47 (A) that corresponds to a well-defined left para-aortic mass with coarse calcifications on CT (B).
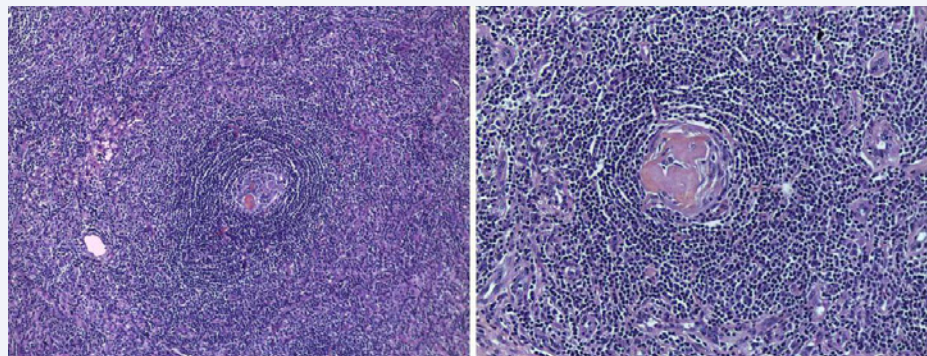

Figure 3 Histopathology with hematoxylin and eosin stain. At 10x (A) we observe a lymphoid follicule with onion skin appearance and thickened mantle cells in a single layer, and vascular hyperplasia. At 20x (B) we observe the germinal center with onion skin appearance and hyaline deposits, with mantle cells arranged in concentric layers.

along with coarse, punctate or arborizing calcifications (26.7%-31%) [7,10,12]. On MRI the lymph nodes are hypo-intense to iso-intense compared to the muscle in T1 weighted images, and hyper-intense to iso-intense to the muscle in T2 weighted images, with homogeneous post- gadolinium enhancement [7,12]. It is important to highlight that CD lymph nodes characteristically have intense contrast enhancement both on CT and MRI because they are highly vascularized lesions. In a PET scan most cases were ^{18}F-FDG avid with a mean SUVmax of 4.7-5.8 [7,13].

In UCD most of the literature is in the form of case reports or small series, therefore it is not easy to define important prognostic factors. However, a recent systematic review of 416 CD patients has helped to clarify the question of prognosis [2]. The factors that were shown to adversely affect 3-year disease free survival (DFS) were MCD, histopathology, male gender and age >37 years [2]. In this review, 3-year DFS was 92.5% for HV-UCD, 78.8% for PC or mixed histology UCD, and 45.7% for PC-MCD [2].

The role of surgery is completely different for UCD versus MCD. In UCD surgery serves as both the diagnostic and primary therapeutic tool. In contrast, MCD is treated systemically with immunotherapy, immune-mediating agents or chemo-immunotherapy, leaving the only role for surgery for diagnostic purposes in the form of an excisional biopsy of an affected lymph-node for histopathologic diagnosis [14].

In a systematic review of surgery in 404 CD published cases, the mean size of the resected lymph-node was 5.5 $\pm$ 3.8 cm [3]. In this study, the long-term outcome of UCD was significantly better if patients underwent a complete resection as opposed to a partial or wedge resection, and completeness of resection was the only factor associated with better outcome on multimodal analysis [3]. The surgical approach (laparoscopic vs open) did not influence outcomes, and the decision for which approach to use should be made based on surgeon's skill, tumor location, and ease of dissection. Death due to UCD was rare (0-2%) if CD was found in the axilla, groin, neck or pelvis, and highest (11%) when located in the retroperitoneum. Moderate mortality rates occurred with locations in the mediastinum (6.1%), and in the abdomen (2.4%) [3]. This study concludes that surgery with complete *en- bloc* resection should be considered the gold-standard of treatment for UCD, with no need for further multimodal approach [3].

CONCLUSION

CD is a rare benign, non-clonal, lympho-proliferative disorder. The diagnosis should be considered when evaluating lymph-node enlargement. It is of the utmost importance to establish centricity and histopathology to dictate optimal treatment and prognosis. Complete surgical resection is curative for UCD and therefore the treatment of choice.

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