

Unicentric Retroperitoneal Castleman Disease Presenting with Pleural Effusion

Jaafreh AA¹, Ahmad Alaqqad¹, Kholoud Alqasem² and Ali Al-Daghmin¹

¹Department of Surgery, King Hussein Cancer Centre, Jordan

²Department of Medicine, King Hussein Cancer Centre, Jordan

*Corresponding author: Daghmin AA, Department of surgery, King Hussein Cancer centre, Jordan, Tel: + 9626 53 00 460; E-mail: AA.11672@KHCC.JO

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Abstract

Castleman disease (Angiofollicular Lymph Node Hyperplasia AFH) is a rare lymphoproliferative disorder that is especially uncommon in the retroperitoneal area. We report a case of 32 year old male who was complaining of shortness of breath and was found to have right sided pleural effusion. Further investigations revealed right sided retroperitoneal mass which was completely excised laparoscopically. Pathologic diagnosis came out as Castleman disease. The patient recovered well after surgery and his shortness of breath and pleural effusion did not recur for the subsequent 6 months of follow up.

Abbreviations: CD: Castleman's Disease, MCD: Multicentric Castleman's Disease, HHV: Human Herpes Virus, HIV: Human Immunodeficiency Virus

Introduction

Castleman disease (first described by Benjamin Castleman 1950) is a heterogeneous group of lymphoproliferative disorders. Although Castleman disease is not cancerous, it may also be associated with malignancies such as Kaposi sarcoma, non-Hodgkin lymphoma and Hodgkin lymphoma [1].

Unicentric or localized Castleman disease is generally asymptomatic but may cause Localized lymphadenopathy with resultant compressive symptoms, or even systemic symptoms like those seen in MCD. MCD usually presents with multiple lymphadenopathy or systemic symptoms such as Fever, Night sweats, Weight loss, Loss of appetite, Fatigue (driven by elevated IL-6 and the resultant increase in acute phase reactants), Shortness of breath, cough, Nausea and vomiting, Neuropathy, Leg edema, Skin rashes, Haemangiomas, Pemphigus, and Kaposi sarcoma. Here we introduce a case with unusual presentation of shortness of breath and non-productive cough that turned out to be a Castleman disease.

Case Report

We are presenting a 32 year old male patient, previously healthy, with no past medical or surgical history. He started to complain of shortness of breath and non-productive cough that worsened over two months prior to presentation, it was associated with eight Kilograms weight loss over that period. He had no fever, night sweats, fatigue, nor hemoptysis. He sought medical advice and a Chest X Ray was obtained which showed a right sided pleural effusion. Chest tube was inserted and pleural biopsy was taken, afterwards he underwent bronchoscopy and lung biopsy which came back with insignificant results. Contrast CT was obtained and showed a right sided paraspinal mass and pleural effusion (Figure 1). A biopsy was taken and showed vascular proliferative lesion infiltrated by reactive lymphoid cells, but definitive diagnosis needed excisional biopsy.

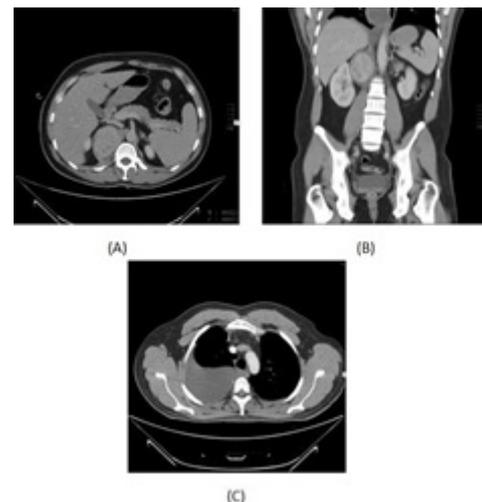


Figure 1: (A) Axial CT scan showing a right sided paraspinal mass. (B) Coronal CT scan showing a right sided paraspinal mass. (C) Axial CT scan showing right sided Pleural effusion.

The chest tube was removed but the pleural effusion recurred so a right sided rocket drain was inserted. New CT scan obtained and showed an inhomogeneously enhancing right retrocrural mass lesion measuring 6.7×5.2 cm. The lesion was displacing the right kidney laterally and causing bowing of the renal vessels. MRI three weeks after that showed a large hypervascular right paravertebral soft tissue mass lesion measures approximately $4.9 \times 6.4 \times 10.2$ cm in transverse, anteroposterior and craniocaudal dimensions, respectively. The mass showed many signal voids mostly representing an internal vessels. The mass was displacing the right renal vein anteriorly, but no definite direct invasion (Figure 2).

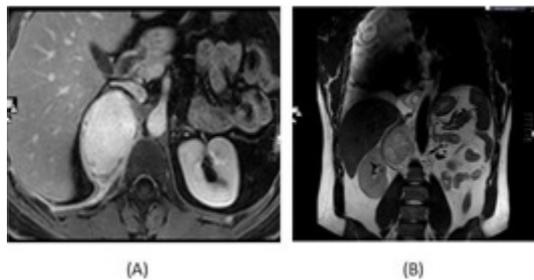


Figure 2: (A) Axial T1 MRI scan showing large hypervascular right paravertebral soft tissue mass lesion. (B) Coronal T2 MRI scan showing a right sided paraspinous mass.

He underwent laparoscopic resection of the mass en-bloc with the right adrenal gland. Pathology showed a well-defined, encapsulated mass measuring $8 \times 5 \times 4$ cm and weighing 90 gram. Tissue diagnosis was Castleman disease (hyaline vascular variant). CD31 and Factor VIII immunostains highlight the vasculature. CD21 immunostain highlights the atrophic follicles. The tumor cells are negative for HHV8 and ALK immunostains Figure 3.

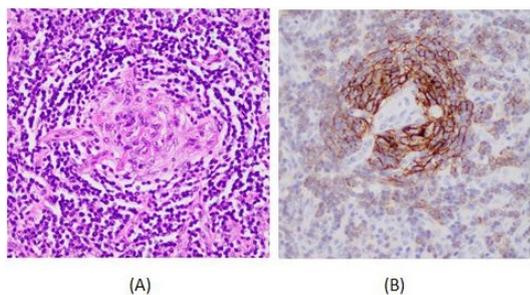


Figure 3: (A) Hematoxylin and eosin stain showing a lymphoid follicle with atrophic germinal center. A blood vessel is seen penetrating the follicle. Lymphocytes within the follicle have concentric arrangement with an onion skin-like appearance. (B) CD21 immunostain illustrating the large number of dendritic cells with brown membranous staining occupying the center of the lymphoid follicle. A blood vessel is also seen penetrating the lymphoid follicle (Original magnification X-40).

The patient recovered well after surgery and was discharged on day two post operatively, and the right sided rocket drain was removed 1 month after surgery.

The patient consent was obtained.

Discussion

CD can be grouped into localized and multicentric. Localized (unicentric) Castleman disease is the more common type affecting only a single supra or infradiaphragmatic group of lymph nodes, while Multicentric Castleman disease (MCD) affects more than one group of lymph nodes. It can also affect organs that contain lymphoid tissue. This form is often associated with HIV and HHV-8 and results in systemic symptoms such as serious infections, fevers, weight loss,

fatigue, night sweats, and nerve damage that can cause weakness and numbness. Anemia and hypergammaglobulinemia are common. In addition, MCD may transform to lymphoma.

Microscopically, CD can be classified into four types, the most common type is the hyaline vascular type (approximately 90% in some studies) [2]. It is localized and causes few symptoms. The prognosis is typically good, but, in rare cases, it may be multicentric. The plasma cell type: often symptomatic and multicentric but may be localized. Histologically, there are sheets of mature plasma cells within interfollicular tissues that surround normal to large germinal centers, and the intense capillary proliferation seen in the hyaline vascular subtype is absent. Dysregulation of interleukin-6 (IL-6) has been implicated in the pathogenesis of plasma cell Castleman disease [3,4]. The mixed subtype where areas of both hyaline vascular and plasma cell types. This is a rare subtype of Castleman disease. Finally, the plasmablastic type which is usually multicentric and symptomatic. It has a less favourable prognosis.

The exact cause of Castleman disease is unknown. An increased production of IL-6 by lymph nodes appears to have a role in the development of Castleman disease [4]. HHV-8 and release of IL-6 or related polypeptides also appears to have a role [5].

In localized CD, Surgery is usually curative and even partially resected masses may remain stable and asymptomatic for many years. Radiation therapy with 30-45 Gy can result in complete and partial remission rates of 40% and 10%, respectively, but can cause radiation-induced fibrosis that makes subsequent surgical intervention more difficult [6].

Treatment options in MCD include immunotherapy with monoclonal antibodies directed at IL-6 (siltuximab) or the IL-6 receptor (tocilizumab) which reported to yield a 2-year overall survival rates and relapse-free rates of 94%-95% and 79%-85%, respectively [7,8].

The anti-CD20 monoclonal antibody rituximab yields good response, especially when used with chemotherapy, but showed to worsen Kaposi sarcoma when used in HIV-positive patients with high viral load [9,10].

Combination chemotherapy with vinblastine and etoposide showed improvement of symptoms and partial response in almost all patients, however, the maintenance dose should be continued as symptoms recur when chemotherapy is stopped [11].

Antiviral therapy (ganciclovir, cidofovir and interferon alpha) should be used as part of treatment in HIV/HHV8 positive patients [12].

Unicentric Castleman disease has an excellent prognosis, while MCD has a variable prognosis, from indolent disease to an episodic relapsing form to a rapidly progressive form leading to death within weeks (the last commonly seen in individuals with HIV infection).

In Conclusion, This case of unicentric castleman disease highlights the importance of obtaining a certain pathological diagnosis before initiating treatment, as well as showing that infradiaphragmatic lymph node involvement can present with pleural effusion.

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