

Primary mediastinal Castleman's disease

Mohamed A.H. Regal,
Yasser M. Aljehani, Hanan Bousbait
Cardiothoracic Surgery Unit, Surgery
Department, King Fahd University
Hospital, King Faisal University, Al
Khobar, Eastern Province, Saudi Arabia

Abstract

Castleman's disease is a rare entity with an unknown etiology which was first described by Castleman in 1954. It is a lymphoproliferative disorder histologically classified into three types; hyaline-vascular, plasma cell type and mixed type. It might be localized or multicentric and usually involves the mediastinum. We report a case of Castleman's disease discovered accidentally in a case of blunt chest trauma which caused a challenging diagnostic process and management.

Case Report

A 39-year old man presented to the ER with progressive dyspnea and cough for the last six months. He had history of blunt chest trauma eight months ago with right sided fractured ribs and right sided hemothorax that was treated with tube thoracostomy. He was seen by the ER physicians and was found to have a marked decrease in air entry and dullness on percussion on the left hemithorax. Laboratory investigations showed normal blood count and full biochemical screen; no anemia, hypoalbuminemia, or hypergammaglobulinemia. CRP and ESR were normal.

A chest radiograph revealed old fractured ribs on the right side, obliteration of the right costophrenic angle, and near total opacity of the left hemithorax, with evidence of an underlying mass (Figure 1).

Trial aspiration of the left side of the chest was positive and drained hemorrhagic effusion. A left-sided chest tube was inserted and drained more than 2000cc of hemorrhagic effusion with normal analysis, cytology and negative culture. A follow-up CXR showed a persistent opacity of the left hemithorax and CT chest with contrast was performed. The CT revealed collapsed left lower lung lobe, multiple variable size mediastinal lymph node enlargement, and a well defined heterogeneously enhancing mass in left para-aortic area extending to the aorto-pulmonary window, measuring about 8x6.5 cm with a line of

cleavage separating it from the vascular structures. Patchy areas of necrosis were also seen with no calcification or cavitations (Figure 2).

The differential diagnosis of the mass was either lymphoma or thymoma. A rigid bronchoscopy was performed and showed no endobronchial lesions. Left poster-lateral exploratory thoracostomy was performed through the 4th intercostal space. The lesion was a highly vascular mass seen in the anterior and visceral mediastinum and embedded below the arch of aorta with adhesion to the descending thoracic aorta, and completely encircling the hilum of the left lung (Figure 3).

The left pulmonary artery and veins could not be evaluated or seen at all. The left phrenic nerve was involved completely inside the lesion and also the upper part of the pericardium. Enlarged lymph nodes were seen at the apex of the parietal pleura, medial to the subclavian artery. Frozen sections from two lymph nodes and from the lesion were examined but no diagnostic conclusion was made. The pericardium was opened to evaluate the pulmonary artery and veins and to gain access and control. The lesion was dissected from the hilum of the left lung and then from the arch and descending aorta. All the pericardial tissue involved in the tumor along with the left phrenic nerve was excised. The left thymus gland pedicle was ligated and transected. Diaphragmatic plication was performed to correct the left diaphragmatic paralysis.

Macroscopically, the lesion was a single large highly vascular soft tissue mass, grayish-brown in color, measuring 10x12x5 cm, and weighing 175 grams. Upon sectioning, it showed a white gelatinous cut surface with a smooth cystic space. Microscopically (Figure 4), the lesion showed proliferation of lymphoid follicles with hyalinized vessels in the center of the follicles along with concentric layering of lymphocytes in the periphery (onion-like appearance). Marked vascular proliferation was seen in the interfollicular regions. No atypical lymphoid cells were identified. Immunohistochemically, the lesion was highly positive for CD20, CD3 and CD5. These characteristics were consistent with a diagnosis of hyaline-vascular type Castleman's disease. Because of the infiltrative nature of the mass and the involvement of the pericardium, the patient completed 6 cycles of chemotherapy (CHOP-R) and the follow up CT showed complete resolution of the disease.

Discussion

Castleman's disease (CD) is a rare and usually benign lymphoproliferative disorder of unknown etiology and is also known as: angio-follicular hyperplasia, giant lymph node hyper-

Correspondence: Mohamed Regal, Department of Surgery, Cardiothoracic Surgery Unit, P. O. Box: 40233 King Fahd University Hospital, Al-Khobar, Saudi Arabia 31952.
E-mail: mohamedregal@yahoo.com

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plasia, localized nodal hyperplasia, benign giant lymphoma, and lymphoid hamartoma.¹ It was first reported in 1956 by Castleman *et al.*² As reported, the affected age group ranges from adolescence into the seventh decade, and it can be solitary or multicentric.³ About 70% of CD occurred in the thorax, 10-15% in the neck, and 10-15% in the abdomen, retroperitoneum, and pelvis.⁴ Histologically, three forms of the disease have been described; the hyaline-vascular type usually found in the mediastinum (about 90% of cases), the plasma cell type which involves extra-thoracic sites⁵ and a rare mixed type.⁵ Clinically, CD can present as benign localized resectable disease as in our case, or an aggressive multicentric variant associated with systemic symptoms and recurrence despite treatment. Castleman's lesions are typically isointense on T1- and T2-weighted images on MRI and homogeneously enhanced after contrast.⁶ Of the localized forms of CD, the HV type (85% of cases) is often asymptomatic, whereas the PC type (15% of cases) has more aggressive clinical course with constitutional symptoms and laboratory abnormalities including anemia, a raised ESR, polyclonal gammaglobulinemia, hypoalbuminemia, bone marrow plasmacytosis, and thrombocytosis.⁷ Uncommonly, a mixed type also exists. The most common location for this lesion is in the chest, although it can be seen in the pelvis, retroperitoneum, axilla, or in the neck.⁷ Most of the patients are asymptomatic and the lesions are accidentally found on chest X-ray as a rounded mediastinal or hilar mass, often mistaken for thymoma or bronchial carcinoma.⁷ It is challenging in the context of blunt chest trauma management as in our case. On CT scan, there are three different patterns of the mediastinal lesions of the HV type: a solitary, non-invasive mass, a dominant infiltrative mass with associated lymphadenopathy as in our case, or lymphadenopathy without a

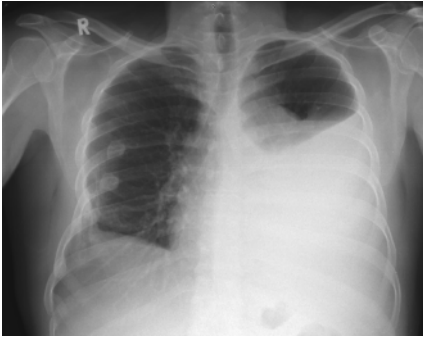


Figure 1. Frontal chest radiograph demonstrating evidence of old trauma on the right side. A near total opacity on the left side with fluid raising to the axilla. There is evidence of an underlying mass

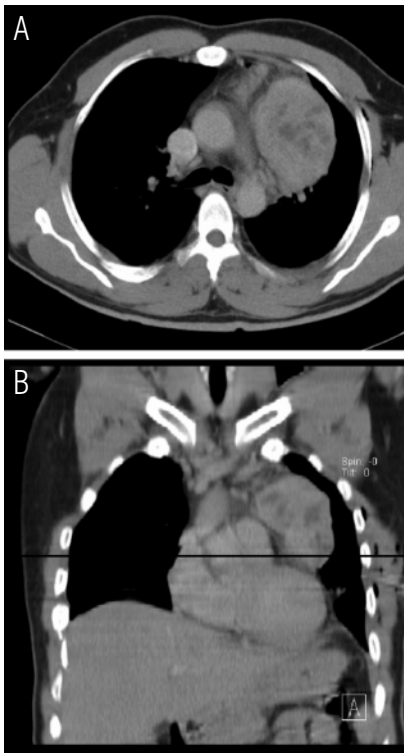


Figure 2. contrast axial computed tomography scan showing A: soft tissue, and B: coronal reformations. There is a large homogeneous left visceral mediastinal mass

dominant mass which is often seen with the PC type.^{8,9} The curative treatment of the localized CD is surgical resection, although recurrence can occur with subtotal resection.⁷ Owing to the vascular nature of the disease, surgery is often complicated by excessive blood loss which could be minimized using pre-operative embolization, a facility that we lack in our hospital. It is recommended to screen for malignancies in patients with CD to exclude malignant lymphoma or Kaposi sarcoma that can occur as long-term complications of the

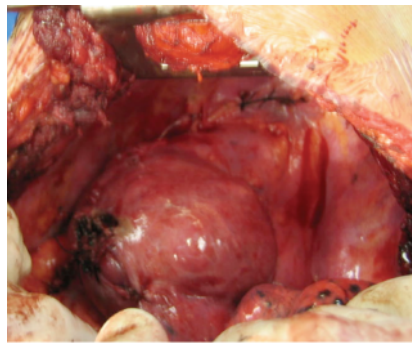


Figure 3. The mass lying in the visceral mediastinum, starting from the aortic arch to the left pulmonary hilum

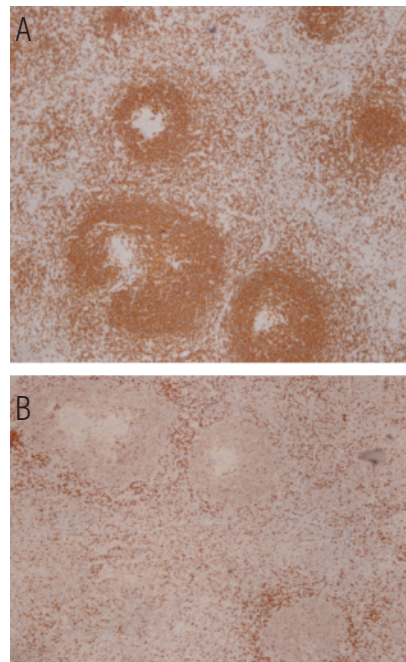


Figure 4. Microscopically, the lesion showed proliferation of lymphoid follicles with hyalinized vessels in the center of the follicles along with concentric layering of lymphocytes in the periphery (Onion-like appearance). Marked vascular proliferation was seen in the interfollicular regions. No atypical lymphoid cells were identified. Immunohistochemically, the lesion was highly positive for CD20 (A) and CD5 (B).

disease.⁹ The multicentric CD (MCD) affects older people (median age of onset is 55.5 years, range 19-85 years) and slightly more often in males than females (1.4:1).⁷ The underlying pathogenic mechanism in all cases of MCD was found to be deregulation of IL-6.⁷ Patients usually present with systemic symptoms and multiple peripheral lymphoma. Other manifestations include, hepatosplenomegaly, skin rash, rheumatological symptoms, renal failure and neurological involvement (seizures, peripheral neuropathy).⁷ The labo-

ratory abnormalities are similar to the localized PC type. In contrast to the unicentric variant, surgical resection is not enough and post-operative immunosuppressive therapy and radiation is a must.⁴

In conclusion, Castleman's disease is a rare entity that requires a high index of suspicion, especially in the context of blunt chest trauma management. The surgical approach is curative in the majority of the cases. Therefore, it should be on the list of the differential diagnosis of any mediastinal mass or lymphadenopathy even in trauma cases.

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