

## Two cases of Castleman Disease with Nonspecific Clinical Presentations

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### Abstract

Castleman disease (CD) is a rare, lymphoproliferative disorder of uncertain etiology. We are reporting on two cases of Castleman disease. Both patients were female. This disease can be found wherever lymph nodes are present. We have reported two unusual cases of Castleman disease. A 29- year old woman was referred for evaluation because of a cervical lymph node, weight loss and night sweats. There was a history of Hodgkin's disease. A 80- year old woman was referred to the oncology clinic because of progressive generalized pruritus and vertigo, weight loss, night sweats and fever. In two cases, a biopsy of the cervical lymph node revealed a plasma cell variant of Castleman disease.

CD can present symptoms in patients. Therefore, clinical, hematological and histological features of lymph node revealed a plasma cell variant which can be suggestive of Castleman disease.

**Key words:** Castleman Disease, Nonspecific Clinical Presentations, Lymph Nodes

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### Introduction

Castleman disease CD is an uncommon, lymphoproliferative disorder that manifests itself as a local or generalized tumor-like condition affecting both lymph nodes and non-nodal tissues, usually in the chest or abdomen. CD is a variety of lymph node hyperplasias of unknown etiology. This disease is characterized by an angiofollicular lymph node hyperplasia and associated with a dysregulated, overproduction of interleukin-6 (IL-6).(1,2,11,12) There are two main types of the disease. The hyaline vascular type (which is the most frequently observed one) is characterized by hypervascular hyaline germinal centers and an extensive capillary proliferation in the nodes.(3) The plasma-cell variety of CD presents itself as a multicentric process associated with generalized lymphadenopathy and hepatosplenomegaly (1,3,4,5,7,8,9,10,13). The etiology of Castleman disease is unclear; many origins have been proposed, such as immunocompromised states, chronic inflammation or infection and autoimmune processes(6). The diagnosis of multicentric Castleman disease (MCD) was established by lymph node biopsy.(13) Several reports have described the incidence, pathogenesis, and clinical features of Castleman disease.(3) CD represents an

atypical lymphoproliferative disorder, infrequently associated with various immunologic abnormalities or subsequent development of malignancy such as Kaposi sarcoma, malignant lymphoma and plasmacytoma. Its clinicopathologic features depend on various etiologic factors such as Kaposi sarcoma herpes virus, an oversecretion of IL-6, an adhesion molecule and follicular dendritic cell dysplasia, etc.(21) We have reported a rare form of this disease with nonspecific clinical presentations in two cases.

### Case No1:

A 29- year old woman was referred to us for evaluation of cervical lymph node. The patient was well and vigorously active until five months earlier. She complained of night sweats and weight loss. There was a history of Hodgkin's disease and radiotherapy which had been administered 12 years earlier. On physical examination, the patient was ill and cervical lymph nodes were palpated bilaterally. The physical examination was otherwise normal. The clinical, hematological and histological features of the lymph node revealed a plasma cell variant of CD. Immunohistochemical staining was positive for CD20 and negative for CD15, CD30.

**Case No 2:**

A 80-year old woman was referred to Imam Sajjad Hospital in Ramsar, Iran because of progressive, generalized pruritus. The patient had been in excellent health until 10 months earlier. She suffered from vertigo, weight loss, night sweats and fever. Her past medical history was negative for any significant medical disease. On physical examination, the vital signs were normal. The patient appeared pale. Lymph nodes (1-2cm), were palpated in cervical and both axillae. The lung, heart and abdomen were normal.

Her blood count showed moderate hypochromic microcytic anemia (Hb=8.9 gr/dl, HbA2=5.6). The white blood cell count and platelet count was normal and the ESR was 90 mm per hour. A biopsy of the cervical lymph nodes revealed a plasma cell variant of CD.

**Discussion**

Since Castleman et al, first reported a case of "localized mediastinal lymph node hyperplasia resembling thymoma", similar cases have been reported as "Castleman disease". Although most of these lesions occur within the chest, other regions, including the neck, pelvis, retroperitoneum, and axilla, may be involved.(2) There is no remarkable sex predominance or identifiable risk factors for the development of Castleman disease.(14) Its morphological recognition is based on a combination of various histological features, but it is generally classified into two subtypes, the hyaline-vascular type and plasma cell type. However, CD can be further classified into two types: solitary and multicentric.(15,16) Our case was of the multicentric type because there were multiple symptoms. Two major histological types of CD exist, namely HV and plasma-cell(PC) types; uncommonly, a transitional or mixed type may be seen.(17) In adults, CD usually (70%) presents itself in the mediastinum, where it commonly occurs in the abdomen, chest (mediastinum or lung hilum) or neck in children.(18)

Patients are usually either asymptomatic or have nonspecific symptoms, such as coughing, dyspnea, chest pain, respiratory infection, and back pain, mainly caused by tracheobronchial compression.(19) In children, systemic features such as fever, weight loss, hepatosplenomegaly and abnormal laboratory findings such as anemia, thrombocytosis and hypogammaglobulinemia may be present. In adults, these symptoms are rare. But, our cases showed the same symptoms in children. Two pathogenetic mechanisms for this association

have been suggested(1) secretion of IL-6 by Hodgkin's Reed-Sternberg cells and histocytes and(2) manifestation of an abnormal immune state associated with HD. IL-6 is reported to play a key role in these systemic symptoms.(4)

Fine-needle aspiration biopsy in CD is often not diagnostic. Definitive histopathological diagnosis is possible by the investigation of large pieces of tissue obtained during an open biopsy.(20) In our cases, diagnosis was made after excision biopsy and a hematologic examination. The differential diagnosis of multicentric CD in the subpectoral, supraclavicular and axillary regions includes lymphoma. The typical enhancing characteristics of a CD mass may be helpful in establishing the diagnosis since lymphoma generally does not show contrast enhancement. Patients with multicentric CD of either histological subtype have a poor prognosis.(4) In our two cases, prognosis was poor and they died. The treatment of CD is directed toward the specific symptoms that are apparent in each individual. Specific therapies for the treatment of this disorder are symptomatic and supportive. Surgical removal (excision) of the growth is the preferred treatment in most cases of localized CD. New approaches include high dose chemotherapy with autologous bone marrow transplantation, anti-IL-6 receptor or anti-CD antibodies and retinoic acid.(20)

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