

CASE REPORT

Castleman's Disease - Unicentric Plasma Cell Variant - A Case Report with Review of Literature

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ABSTRACT

Castleman's disease (CD) is a rare disease with two identified forms. The localized form, often pauci symptomatic is characterized by enlargement of an isolated single lymphnode or lymphnode chain. Multicentric form frequently presents with general signs. We report a patient who presented with cough and hemoptysis with imaging revealing right hilar lymphadenopathy. After thoracotomy, lymph node excision biopsy was done, histopathological examination revealed plasma cell - variant (PCV) of CD, a rare location for unicentric PCV of CD. JMS 2012;15(1):57-60.

Key Words: Castleman's disease, Angiofollicular lymphoid hyperplasia, angiofollicular lymph node hyperplasia

Castleman's disease is a rare lymphoproliferative disorder, characterized by lymphadenopathy. It may involve a single lymph node or a lymph node chain or present with disseminated disease. The localized variant is often pauci symptomatic and treatment is surgical, in certain situations radiotherapy. Disseminated form presents with constitutional symptoms, organomegaly, cytopenias or transaminitis and treatment options vary from biological agents to combination chemotherapy.

Case report

A twenty year old man presented with history of cough, hemoptysis, intermittent fever and night sweats for six

months duration. He was evaluated and found to have mild anemia with hemoglobin (Hb) 10.0 gm/dl (N=13.3-16.2 gm/dl) and normal total leucocyte and differential count. Patient also had normal liver and kidney function tests, Sr. LDH, 160 U/L (Normal=115-221U/L), Sr. Calcium 10.0 mg/dl(N=8.7-10.2mg/dl). Sputum was negative for AFB and Mantoux test was also negative. Chest radiography revealed right hilar opacity (Figure 1). CECT revealed right hilar lymph node mass (Figure 2). Fiber optic bronchoscopy revealed a widened spur to intervening right upper lobe and intermediate bronchus with slight hyperemia. Broncho-alveolar lavage (BAL) was negative for PCR tuberculosis and biopsy showed chronic inflammatory changes. Patient again reported back after 6 months with constitutional symptoms. Physical examination was unremarkable. Investigations revealed Hb 9.6 gm/dl, TLC/DLC, platelet count within normal limits, ESR 35 mm/1st hr (N=0-20mm/hr), LFT, KFT, LDH within normal limits.

Chest radiography revealed increased size of right hilar lesion with CECT confirming the same. CECT abdomen and pelvis were normal. Bone marrow aspiration and biopsy

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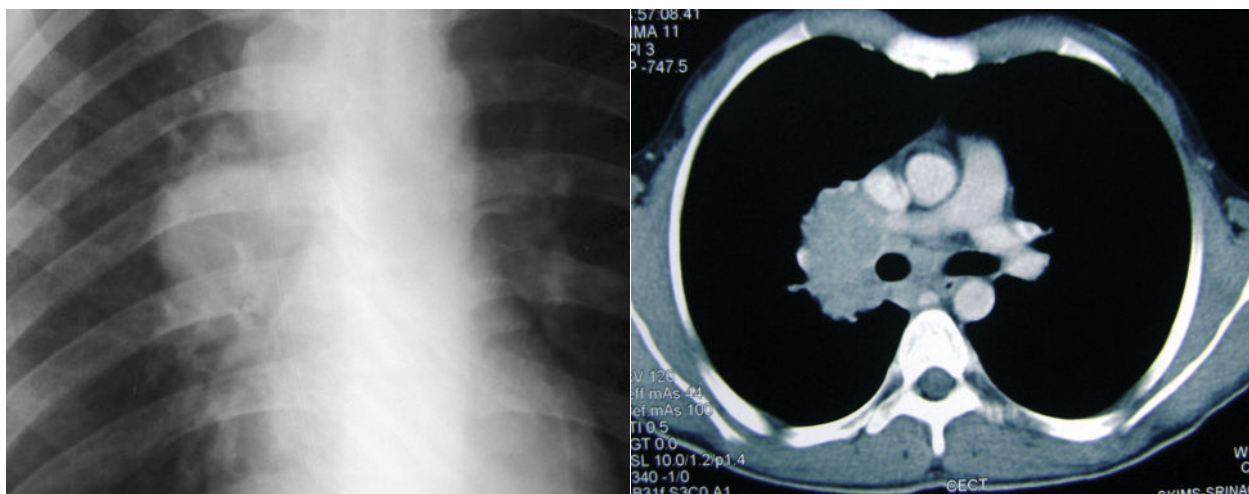


FIGURE 1: X-Ray chest PA view; Right hilar lymphadenopathy

FIGURE 2: CECT Scan showing right hilar lymph node mass

were normal. Right thoracotomy revealed multiple lymph nodes around right hilum. Excision biopsy of the lymph node was done. Histopathology revealed plasma cell variant of Castleman's disease (Figures 3, 4 & 5) and immunohistochemistry highlighting CD20, CD23, MIB-1 reactive T-cells CD3, plasma cells highlighted by CD-138, Kappa and Lambda -2 and negative for BCL-2 and cyclin - D. Patient is planned for radiotherapy as complete excision was not done.

Discussion

Fifty years ago, Dr. Benjamin Castleman described this rare lymphoproliferative disorder and was named as Castleman's disease after him. He initially described a patient who presented with many years of fever and weakness,

eventually found to have large mediastinal lymphadenopathy (LAP).¹ It was followed by a dozen additional patients who were largely asymptomatic, but had mediastinal masses.² This disorder is also known as angiofollicular lymph node hyperplasia, giant lymph node hyperplasia, lymphoid hamartoma and benign lymphoma or follicular lymphoreticuloma.³ HPE revealed increased number of lymphoid follicles. Germinal centers varied in their cellularity, ranging from acellular fibrinous hyalinization of capillaries to proliferation of pale eosinophilic cells with copious cytoplasm. In subsequent years, additional cases of patients with diffuse LAP and the histologically characteristic CD lymph node architecture were identified.⁴ These series also revealed a new verdict of CD, the germinal centres in the involved nodes showed no evidence of hyalinization, but

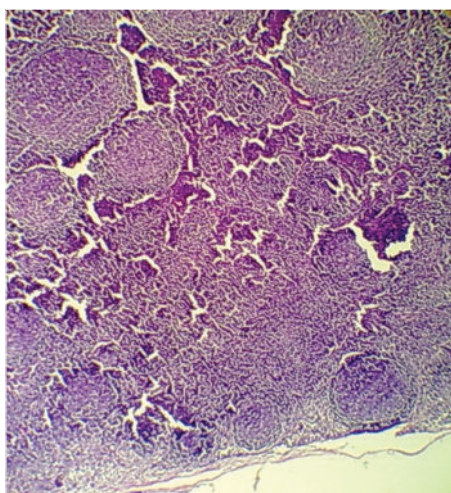


FIGURE 3: Castleman's disease of plasma cell type - Lymph node showing follicular hyperplasia with marked differences in the size of germinal centres having well circumscribed character and surrounded by well defined mantle zone. (H & E × 100).

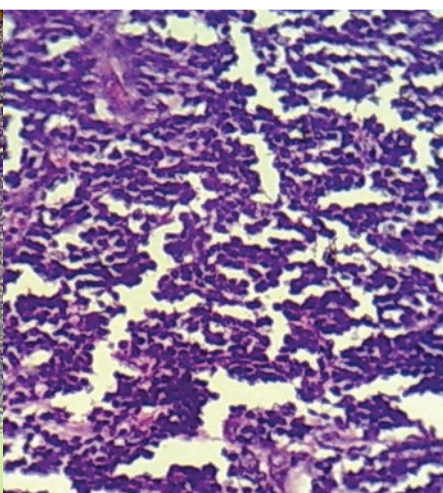


FIGURE 4: Castleman's disease of plasma cell type - Follicular hyperplastic follicle without vascular hyaline changes. (H & E × 400).

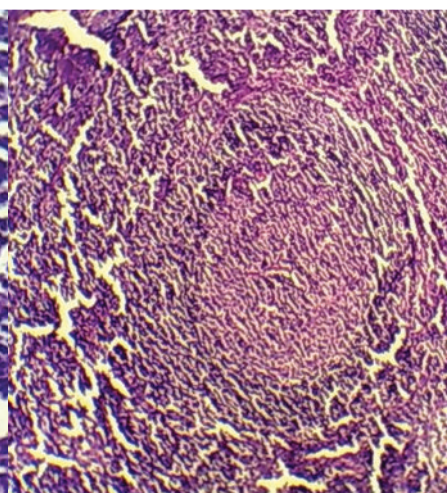


FIGURE 5: Castleman's disease of plasma cell type - Interfollicular region showing a massive infiltration by plasma cells some of which were multinucleated. (H & E × 400).

were surrounded by concentric sheets of plasma cells in the inter follicular space.⁵ This novel histologic variant was termed 'plasma cell variant (PCV-CD). The recognition of both patients with localized LAP and disseminated disease led to an additional clinical categorization of CD: 'Unicentric(UCD) versus "multicentric" (MCD). More, recently a third 'sub variant' known as 'plasmablastic MCD' has been described in association with particularly aggressive cases of MCD. In such first series CD patients with POEMS syndrome (Polyneuropathy, organomegaly, endocrinopathy, monoclonal proteins, skin changes) were found to have lymph nodes which resembled PCV, but also had large plasma cells in mantle zone with copious cytoplasm and prominent single or multiple nucleoli, second series found it associated with HHV-8 infection and progression to plasma blastic lymphoma.^{6,7,8}

The initial step in the development CD appears to be production of IL-6 by B-cells in the lymph node mantle zone, stimulated in the majority of cases by HHV-8 infection and in a minority of cases by a heretofore unidentified exogenous or endogenous factor. Local elaboration of IL-6, and in turn VEGF, produces the characteristic B-cell proliferation and vascularization of CD. In patients with multicentric disease, systemic symptoms may result from circulating IL-6, IL-6 producing B-cells, the generation of excess antibodies or disseminated HHV-8 infection.^{1,9,10}

Clinical categorization (subtypes) and characteristics			
Characteristics	Unicentric hyaline vascular type	Unicentric plasma cell type	Multicentric plasma cell type
Demography	Median age(years) Sex (M:F) Prevalence(%age)	32 1:1 80	32 60 1:12:1 1010
Lymph node region	Mediastinum Peripheral nodes Abdomen	Abdomen-most common Mediastinum-rare	Abdomen- most common
Disease association	Paraneoplastic - Pemphigus - TTP	Amyloidosis Renal - insufficiency	HIV POEMS Kaposi' sarcoma Amyloidosis Renal insufficiency

Unicentric-Hyaline Vascular Variant (U-HVV), most common with no predilection for either gender, median age tends to be fourth decade. By definition a single lymph node or chain of lymph nodes is involved. All lymph node groups are involved equally.^{3,4,11} These patients are often asymptomatic, but can present with compressive symptoms.

Unicentric- Plasma cell Variant (U-PCV), accounts for less than 20% of cases. It is characterized by hypertrophy of single lymph node chain⁴, most frequently involving abdomen, reported in third decade.¹² Majority present with

constitutional symptoms. Anemia and raised ESR is found in 80% of cases.

Multicentric-Plasma cell Variant (M-PCV), least common, affects the people in 5th and 6th decade. Patients present with fever, weight loss and night sweats, organomegaly, anemia, thrombocytopenia or transaminitis.¹³ One of the most devastating disease associated with M-PCV is POEMS syndrome, seen in upto 15% of cases, more likely infected with HHV-8.¹⁴ Case reports have been documented of association of Hodgkin's lymphoma, development of follicular dendritic cell sarcoma, paraneoplastic pemphigus.¹⁵ The best treatment of localized form is complete surgical resection^{2,3,4,11} and radiotherapy may be a viable option for patients who are poor surgical candidates. A myriad of treatment options exist for patients with MCD. Gancyclovir, interferon-alpha and rituximab may be the best treatment for patients with HHV-8 infection and CD-20 positivity, while CHOP and VAD may be more appropriate for patients with severe systemic manifestations of MCD.¹

In conclusion, five decades of steady research into the etiology and management of the unusual and fascinating lymphoproliferative disorder has resulted in many answers, but generate a myriad of questions. Innovative treatment strategies have been developed.

In the coming years, however, fundamental questions remain to be answered. Why is CD seen only in small proportion of patients infected with HHV-8? Why do some patients present with localized disease only? What is the role of IL-6 and angiogenesis? What are the best treatment options?

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