

## ***Case Report***

---

# **Multicentric Castleman Disease - An Unusual Presentation**

**Arunabha Chakravarti<sup>1</sup>, Meenakshi Mishra<sup>2</sup>, Anita Nangia<sup>3</sup>, Jatinder Kumar Sahni<sup>4</sup>**

### **Abstract**

Castleman disease is a rare clinicopathological disorder associated with lymphoproliferation. We report the case of a 54 year old gentleman initially presenting with dysphagia followed by bilateral cervical lymphadenopathy, and later diagnosed as multicentric Castleman disease. To the best of our knowledge no case of Castleman disease presenting as dysphagia along with neck swelling has been previously described in the literature. This case report highlights a very unusual presentation of this rare disease. It also provides insight into the fact that because of the lack of any specific presenting symptoms and distinguishing radiographic features, an accurate histopathologic diagnosis and careful staging become crucial to planning treatment for this disease.

**Keywords:** *Castleman disease; Lymphoproliferation; Multicentric*

### **Introduction**

Castleman disease (CD) is an uncommon lymphoproliferative disorder that is most frequently seen as an asymptomatic mass in the mediastinum. Extrathoracic sites have

1. Professor, Department of Otorhinolaryngology Head and Neck Surgery, Lady Hardinge Medical College, New Delhi, 110001.
2. Junior Resident, Department of Otorhinolaryngology Head and Neck Surgery, Lady Hardinge Medical College, New Delhi, 110001.
3. Professor, Department of Pathology, Lady Hardinge Medical College, New Delhi, 110001.
4. Director Professor and HOD, Department of Otorhinolaryngology Head and Neck Surgery, Lady Hardinge Medical College, New Delhi, 110001.

**Address of Correspondence:** Dr. Arunabha Chakravarti, MS, DNB, Professor, Department of Otorhinolaryngology Head and Neck Surgery, Lady Hardinge Medical College, New Delhi, 110001, Phone: 09868093035, email- drachakravarti@yahoo.co.in

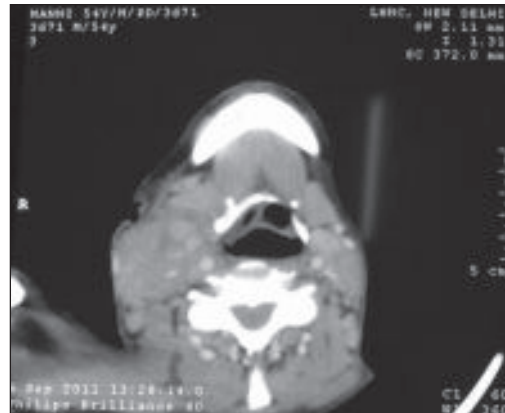
been reported in the neck, shoulder area, mesentery, pelvis, pancreas and retroperitoneum<sup>1-4</sup>. CD is categorized as being either localized or multicentric, and further subdivided into hyaline vascular, plasma cell, or mixed histopathological patterns. Multicentric CD, regardless of the histological subtype, is a more aggressive clinical entity, commonly with a chronic or rapidly fatal course. Little is known about the cause of this disorder, but the bulk of evidence points towards faulty immunoregulation, which results in excessive proliferation of B lymphocytes and plasma cells in lymphoid organs<sup>5</sup>. Interleukin-6 hypersecretion has been found in these patients. The hypothesis of a viral trigger (role of HHV-8) has been raised.<sup>6</sup> We discuss the unusual case of a 54 year old man presenting with dysphagia and bilateral cervical lymphadenopathy and the diagnostic dilemma it posed.

### Case report

A 54 year old man presented with a 7 month history of foreign body sensation in throat and difficulty in swallowing, and a one month history of bilateral neck swelling. The symptoms were waxing and waning in course. There were no symptoms of airway compromise. Generalized weakness, anorexia and low grade fever were present. Remainder of his medical history was non-contributory.

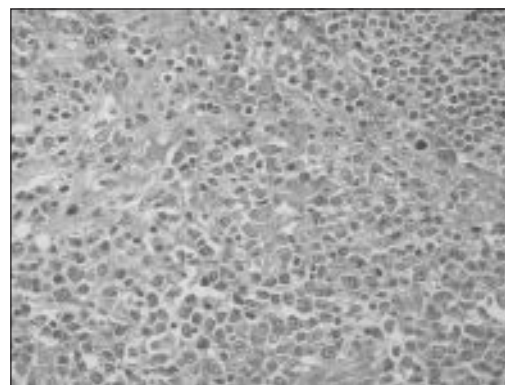
On examination, an irregular firm growth was noticed in the right tonsillar area and an irregular pinkish firm bulge was found on the base of tongue towards right of midline. Besides, there were firm, mobile, lobulated, non-tender lymph nodes on both sides of neck; located in the posterior triangle and extending in to anterior triangle, with dimensions of 8cm x 10cm on left and 12cm x 14cm on right side. Trachea was midline. Rest of the examination findings were insignificant.

Patient presented to us as a diagnostic dilemma. He had undergone repeated biopsies from tonsillar mass and oropharyngeal mass in the last 6 months from various other institutions, the reports of which were inconclusive. FNAC was done twice in the last one month from the cervical lymph nodes which pointed towards inflammatory etiology. Chest X-ray of the patient was normal. We admitted the patient for further diagnostic work-up. The patient was investigated with the differential diagnosis of oropharyngeal malignancy with metastatic neck node, lymphoma, chronic granulomatous infection, hematologic malignancy and HIV. Routine blood investigations, liver function tests and kidney function tests of the patient were normal. CECT of the neck showed growth in right tonsillar region, right lateral oropharyngeal wall, and base of tongue on right side. Multiple discrete as well as conglomerate lymph nodes were present on both sides of the neck (Figure 1).



**Figure 1:** Contrast-enhanced CT of neck revealing bilaterally enlarged lymph nodes

Bone marrow aspiration revealed a normal study. The patient was non-reactive for HIV-1, 2. We took a wedge biopsy specimen from right cervical lymph node which showed partial effacement of lymph node architecture with attenuated germinal centres, dense inflammatory infiltrate comprising of plasma cells, lymphocytes, immunoblasts, eosinophils. There were occasional binucleate plasma cells and occasional typical mitosis. Immunophenotyping revealed a polyclonal population. The findings were consistent with Plasma cell type CD (Figure 2).

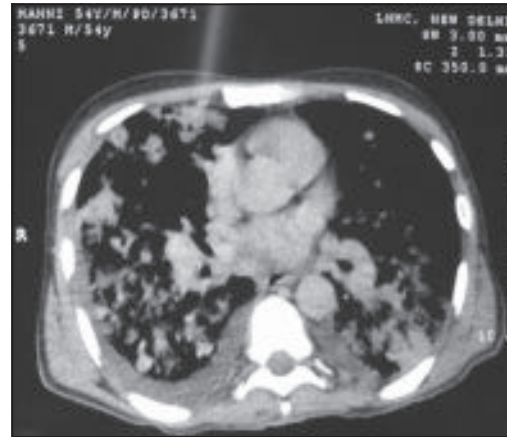


**Figure 2:** Biopsy specimen from right cervical lymph node showing Plasma cell type Castleman disease [1280 X 960 resolution, 40 X magnification, H & E stain]

The biopsy reports from tonsillar fossa mass and tongue base were also consistent with plasma cell type CD. The previous reports had been issued from other institutions and hence could not be reviewed.

Serum protein electrophoresis of the patient revealed hypoalbuminemia and hypergammaglobulinemia. The patient was administered intravenous Inj. Cyclophosphamide (750mg/m<sup>2</sup>) on day 1, Inj. Vincristine (1.4mg/m<sup>2</sup>) on day 1 and Inj. Dexamethasone (6mg/m<sup>2</sup>) from day 1 to day 4. The neck swelling and oropharyngeal mass started reducing in size. Six days after the first cycle of chemotherapy, the patient developed intractable cough with high grade fever. The total leucocyte count of the patient was 12000 cells/cumm. Patient was put on intravenous broad spectrum antibiotics. Over the next three days, patient progressively developed symptoms of respiratory distress. Chest examination revealed crepitations in bilateral lower lung fields. Chest X-ray of the patient was repeated which showed fluffy non-homogenous air space opacities in bilateral lower lung fields, with right paratracheal lymphadenopathy and bilateral pleural effusion. The 2-D echo findings showed normal heart functioning. CECT of the chest confirmed chest X-ray findings, and also showed multiple lymph nodes in pre/paratracheal, subcarinal, bilateral hilar and prevascular locations (largest approx 1.9cm x 1.4cm in size) (Figure 3).

Pleural tap revealed exudative pleural effusion. A provisional diagnosis of Acute Respiratory Distress Syndrome (ARDS) secondary to sepsis was made. The patient was intubated and had to be put on mechanical ventilator. Despite rigorous efforts, the general condition of the patient continued to deteriorate and over the next 48 hours he expired.



**Figure 3:** CECT of chest showing bilateral fluffy opacities and mediastinal lymphadenopathy

### Discussion

Castleman disease was first described by Dr. Benjamin Castleman from Boston in the year 1956<sup>7</sup>. This disease is known by various synonyms which are- angiofollicular lymph node hyperplasia, angiofollicular lymphoid hyperplasia, giant lymph node hyperplasia, lymphoid hamartoma, benign lymphoma or follicular lymphoreticuloma. It is a very rare disease and the precise incidence is not known. People of any age group can be affected, although the peak incidence is seen during adulthood. The disease appears to have a predilection for men<sup>8,9</sup>. The most common location of CD is thorax, followed by neck. It can affect the lymphoid tissues of body namely lymph nodes, thymus gland, spleen, tonsils/adenoids and bone marrow. HIV infection is the only known risk factor for the causation of this disease. The time to establish diagnosis is often long, attributable to the clinical polymorphism and the poor awareness of the disease. The possible pitfalls of this disease on cytology are missing the hyalinized capillaries with eosinophilic material in reactive hyperplasias and misdiagnosing single large cells and Reed Sternberg-like cells as Hodgkin's lymphoma. The differential diagnosis mostly includes all

reactive hyperplasias of lymph nodes and, occasionally, Hodgkin's lymphoma. Since this disease is so rare, the combined effort of a good clinician and an experienced hematopathologist is required to reach a definitive diagnosis.

Clinically, CD can either be localized, in which disease is restricted to one site, or multicentric, in which several sites are involved. The localized form is more common, multicentric variety being very rare. The present case had involvement of the cervical lymph nodes, tonsil as well as lymphoid tissues of base tongue. On search of available literature, we didn't find any similar case report with simultaneous involvement of lymphoid tissues of these sites. The patient was also found to have enlarged mediastinal lymph nodes during the terminal stage of his illness.

Keller et al in 1972, subclassified CD into two histological subtypes- hyaline vascular and plasma cell type<sup>2</sup>. In addition, some patients have mixed variant. Approximately 90% of the localized form are of the hyaline vascular type which typically follow a benign course. Most cases of the multicentric form are plasma cell type. Patients with multicentric CD present with a systemic illness that manifests as disseminated lymph nodes, constitutional symptoms, autoimmune abnormalities, recurrent infections and laboratory abnormalities (e.g.- anemia, hypoalbuminemia, hypergammaglobulinemia and an elevated ESR)<sup>10</sup>.

Localised CD is treated by surgical excision which allows full recovery without relapse in almost all cases. However, no therapeutic consensus exists for multicentric CD and diverse treatments (surgery/corticotherapy/chemotherapy) are used, often in combination. Anti-interleukin-6 antibody has also been successfully tried in the alleviation of systemic manifestations. Localized form

follows a benign course. The multicentric form is aggressive and often culminates in death secondary to infections, complications or malignancy (lymphoma, kaposi's sarcoma)<sup>2,7,10</sup>. Our case succumbed to ARDS secondary to sepsis.

In conclusion, this case report brings to light the importance of obtaining definitive histological diagnosis in patients presenting with lymphadenopathic presentation associated with systemic symptoms. It highlights a rarer variety (multicentric) of this rare disease, at uncommon sites (neck nodes and oropharyngeal lymphoid tissues), with an unusual presentation (dysphagia along with neck swelling). Although CD rarely presents as oropharyngeal growth along with cervical lymphadenopathy, it should be kept as the differential diagnosis whenever a diagnostic or therapeutic dilemma arises. From a clinical standpoint, establishing an accurate diagnosis is difficult because of its rarity and polymorphic character.

#### References:

1. Castleman B, Iverson L, Menendez VP. Localized mediastinal lymph node hyperplasia resembling thymoma. *Cancer*, 1956; 9: 822-830
2. Keller AR, Hochholzer L, Castleman B. Hyaline-vascular and plasma-cell types of giant lymph node hyperplasia of the mediastinum and other locations. *Cancer*, 1972; 29: 670-683
3. Baikovas S, Glenn D, Stanton A, Vonthehoff L, Morris DL. Castleman's disease: An unusual cause of a peripancreatic hilar mass. *Aust N Z J Surg*, 1994; 64: 219-221
4. Bjarnson I, Cotes MP, Knowles S, Reid C, Wilkins R, Peters JT. Giant Lymph node hyperplasia (Castleman's disease) of the mesentery: Observations on the

- associated anemia. *Gastroenterology*, 1984; 87: 216-223
5. Summerfield GP, Taylor W, Bellingham AJ et al. Hyaline vascular variant of angiofollicular lymph node hyperplasia with systemic manifestations and response to corticosteroids. *J Clin Pathol*, 1983; 36: 1005-1011
  6. Soulier J, Grollet L. Kaposi's sarcoma associated herpesvirus- like DNA sequences in multicentric Castleman's disease. *Blood*, 1995; 86: 1276-1280
  7. Castleman B, Iverson L, Menendez VP. Localized mediastinal lymph node hyperplasia resembling thymoma. *Cancer* 1956; 9(4): 822-830
  8. Bowne WB, Lewis JJ, Fillipa DA et al. The management of unicentric and multicentric Castleman's disease: A report of 16 cases and a review of literature. *Cancer*, 1999; 85(3): 706-717
  9. Greiner T, Armitage JO, Gross TG. Atypical lymphoproliferative diseases. *Hematology Am Soc Hematol Educ Program*, 2000(1): 133-146
  10. Herrada J, Cabanillas F, Rice L, et al. The clinical behaviour of localized and multicentric Castleman disease. *Ann Intern Med* 1998; 128(8): 657-662