Case Report

An unusal case of neck swelling-unicentric castleman's disease

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Abstract

We are reporting a case of a 25 year old female patient with a swelling on left side of the neck for last 15years which was painless and gradually increasing in size. There was no history of fever, night sweating, weight loss, fatigue, loss of apetite. Patient had tested negative for viral markers including HIV I and II. Ultrasonography of neck was suggestive of a well defined lobulated hypoechoic space occupying lesion, probably lymphadenopathy. FNAC done from the left cervical lymph node and the neck swelling was suggestive of reactive hyperplasia. Patient underwent excisional biopsy of the neck swelling along with the left posterior cervical lymph node mass which showed histopathological features of Castleman's disease, hyaline vascular type.

Keywords: Castleman's disease, Angiofollicular hyperplasia, Hyaline vascular type.

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INTRODUCTION

Castleman's disease, also known as angiofollicular hyperplasia, is a disease of unsettled complexity and morbidity which usually involves mediastinum and less commonly neck and abdomen and usually associated with AIDS[7], Kaposi sarcoma and follicular dendritic cell tumour. Dr. Benjamin Castleman in 1954 originally encountered this lesion while reviewing thymic tumours. It was first described as a clinical entity in 1956[6].Two variants have been described more commonly hyaline vascular type and less common plasma cell type and third hybrid type sharing features of both based on histology. Castleman's disease can be Unicentric or Multicentric based on clinical and radiological findings. The exact cause of Castleman's disease is not known though it is speculated that increased production of Interleukin 6 (IL-6) may be involved in the pathogenesis.

CASE HISTORY

A female patient of 25 years age presented to us in with a swelling on left side of the neck for last 15years which was painless and gradually increasing in size. There was no history of difficulty in deglutition or breathing. There was no history of fever, excessive sweating or weight loss. On examination, there was an oval shaped swelling of 7cm x 5cm size on the left side of the neck deep to the left Sternocleidomastoid muscle, firm in consistency, mobile, non-tender, smooth surface with prominent margins. One single left posterior cervical lymph node was palpable, 1.5cm in size, firm, mobile, non-tender with smooth surface [Fig.1]. There was no associated axillary or inguinal lymph node enlargement or hepatosplenomegaly. Patient had tested negative for viral markers including HIV I and II. Chest radiogram and abdominal ultrasound was within normal limits. Ultrasonography of neck was suggestive of a well defined lobulated hypoechoic space occupying lesion, probably lymphadenopathy. FNAC done from the left cervical lymph node and the neck swelling was suggestive of reactive hyperplasia. Patient underwent excisional biopsy

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of the neck swelling along with the left posterior cervical lymph node mass under general anaesthesia. Gross specimen measured 9cm x 4cm x 3cm [Fig.3]. Histopathological examination showed features of Castleman's disease, hyaline vascular type [Fig.2]. Immediate post operative period was uneventful. on follow up patient is asymptomatic with properly healed scar.

Figure 1: Showing mass in the left side of neck

DISCUSSION

Castleman's disease is a rare disease of lymph node and related tissue.It is not a cancer but a lymphoproliferative disorder.

TYPES

A) Localised or unicentric: Unicentric or Localized Castleman's disease presents with a slow growing solitary lymph node mass usually in the mediastinum or mesenteries and rarely in the neck, groin and axilla[1,3]. There are no constitutional symptoms or elevation of acute phase reactants (IL-6, ESR, CRP). Symptoms due to mass effect of the bulky lymphadenopathy may be present. Surgical resection is curative in 90-95% cases and usually do not progress to lymphoma. Prognosis is excellent with a 5 year survival rate close to 100%[1].

B) Multicentric: Multicentric Castleman's disease presents with generalized lymphadenopathy (thoracic, mesenteric and retroperitoneal) and often with hepatosplenomegaly. "B" symptoms like severe fatigue, fever, night sweats, weight loss and anorexia are typically present. Overproduction of IL-6 may be the cause of these symptoms and is associated with elevated ESR, CRP, fibrinogen, thrombocytosis and hypergammaglobulinemia. Peripheral edema, anaemia and hypoalbuminemia are typically present. Other conditions like Autoimmune hemolytic anemia, Multiple myeloma, Amyloidosis, Pemphigus and overlap syndromes with POEMS may be associated. Multicentric disease runs a more aggressive course and may progress to non-Hodgkin's lymphoma and requires systemic therapy[1].

C) Microscopic subtypes: Four subtypes has been described

1. **Hyaline vascular (HV)** type, histopathology shows germinal centers poorly formed with dysplastic or atrophic CD21+ follicular dendritic cell networks surrounded by expanded mantle zone consisting of rims of small CD20+ lymphocytes arranged in an **"onion skin" or "targetoid" or "stadium seating" manner**[1,2]. There is increased interfollicular vascularity with capillary proliferation and endothelial hyperplasia giving a **"lollipop" appearance**[2,4]. HV type is further classified into **"lymphoid subtype"** with marked mantle zone hyperplasia and **"stroma rich subtype"** with prominent vascular and associated myoid component[2]
2. **Plasmacytic** type is characterized by more numerous and larger hyperplastic follicles, which have more expanded mantle zones compared to HV type. Sheets of plasma cells are present in the interfollicular areas.
3. **Mixed cellularity** form has features of both hyaline vascular and plasmacytic types Castleman's Disease[1].
4. **Plasmablastic** type is more recently described.

Classically it is thought that Unicentric Castleman's disease is usually of the hyaline vascular variety and multicentric disease (MCD) of the plasmacytic type or mixed cellularity variety. However, the histopathology of multicentric disease can be evenly divided between hyaline vascular variety on one hand and plasmacytic type and mixed cellularity variety on the other hand. Mixed cellularity clinically behaves more like plasmacytic type rather than hyaline vascular disease. HIV status is important as HIV+ patients with multicentric Castleman's Disease have much more frequent plasmacytic disease and the clinical course is less favorable than in HIV-ve patients[2] Plasmablastic is usually multicentric which usually causes symptom and has poor outcome.

CAUSES

HHV-8 is proposed to be the causative agent in **HIV+ Castleman's Disease patient**. HIV+ patients have more often Kaposi's sarcoma and more frequently progress to non-Hodgkin's lymphoma. There is presence of HHV8 DNA in Lymph nodes and peripheral blood mononuclear cells in HIV+ patients with multicentric Castleman's disease. **Viral IL6** and other cellular homologue genes are exposed in lymph nodes from HIV+ patients. HHV8

DNA positivity by nested PCR and vIL6 protein has been detected in lymph nodes of HIV negative patients, as well as vIL6, vBCL-2, vCyclin-D, and viral G-protein coupled receptor. However, no conclusive evidence so far has been found that HHV8 has been involved in HIV-ve patients[1,5].

IL-6 has been implicated in the pathophysiology of CD. It causes B-cell proliferation resulting in hyperplastic follicles and hence the enlarged lymph nodes. IL6 also increases secretion of vascular endothelial growth factor (VEGF), causing angiogenesis and capillary polarization of T lymphocytes to a Type 2 cytokine profile leading to autoimmune phenomena including AIHA, ANA positivity and elevation of IgE. with endothelial hyperplasia. IL6 induces an acute phase reaction comprising increases in ESR, CRP, IgGs, serum fibrinogen, and serum Amyloid A Protein (SAA). Increased SAA levels may result in AA Amyloidosis, whilst hyperfibrinogenemia may play a role in venous thrombosis and pulmonary emboli. B-type symptomatology is virtually always associated with increased IL-6 levels[1].

Clinical Feature

Unicentric: Localised form start as swelling. In neck and axilla only felt as lump. In chest it causes difficulty in breathing, wheeze, cough, chest fullness. In abdomen it causes pain and abdominal fulness, nausea and vomiting.

Multicentric: Multiple lump under skin. Organomegaly in abdomen.

Common to both: Fever, night sweat, weight loss, weaknees, fatigue, skin rash.

Diagnosis

Blood: a) Complete blood count
b) IL-6
c) ESR
d) CRP

Imaging: To look for enlarged lymph node causing symptom and in other part of body and also follow up.
a) CT scan and CT guided biopsy.
b) MRI
c) Chest x-ray
d) Ultrasound-local,abdominal
e) PET scan and Gallium scan

Incisional and excisional biopsy fnac

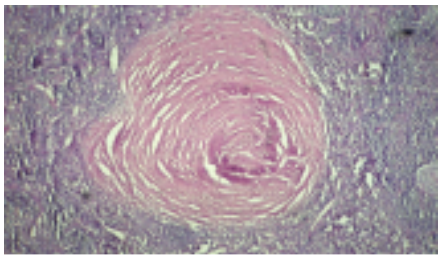

Figure 2: Large follicles scattered in a mass of lymphoid tissue

The follicles show marked vascular proliferation and hyalinization of abnormal germinal centre. There is tight concentric layering of lymphocytes at the periphery of follicles resulting in an "onion-skin" appearance. The interfollicular stroma is also prominent with numerous hyperplastic vessels of post-capillary venule type and an admixture of plasma cells, eosinophils and immunoblasts.

Treatment

Surgical excision is the preffered treatment in unicentric but its role in multicentric is limited. External beam radiation is used in certain cases of unicentric to destroy cells not surgically removed but avoided nowdays. Cotricosteroid (prednisolone) is also used. Chemotherapeutic agents (carmustine, cladribine, chlorambucil, chyclophosphamide, doxorubicin, etoposide, melphalan, vincristine, vinblastine) are used. Immunotherapy with monoclonal antibodies (siltuximab, rituximab) and immunomodulating agents (thalidomide, linalidomide, interferon-alfa). Anti virals (gancilcovir, valganciclovir, foscarnet) can be used but controversial.

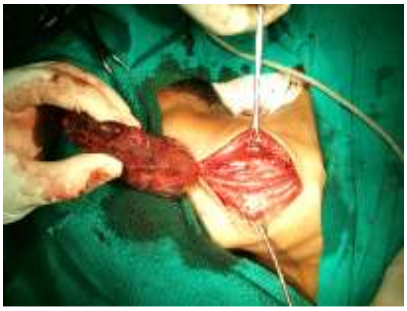

Figure 3: Intraoperative picture

Newer drugs under study

a) sirolimus, cyclosporine, mycofenolate mofetil-suppress immune system
b) suramin-inhibit IL-6 from attaching to lymphocyte.
c) bortezomib-also used in multiple myeloma
d) CX-4945-it blocks CK-2 a protien which helps in proliferation.

Follow up

It is very important several years after treatment completion. complete physical examination, imaging for signs of recurrence. Multicentric disease can recur within first year of treatment. some patients with multicentric disease especially HIV + might develop non hodgkin lymphoma or kaposi sarcoma at some point of time. These cancers may be hard to treat and so follow up will help to recognise these entity early and early treatment will be possible.

CONCLUSION

The subject of our case report had unicentric Castleman's disease of Hyaline vascular type in neck, which is an unusual site for nature of the disease. Surgical excision proved to be an optimal treatment for this patient and adjuvant treatment was not administered.

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