Case Report

Castleman disease: A single-center case series in Nepal Mediciti Hospital

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ABSTRACT

BACKGROUND

In 1954, Castleman Disease (CD), was first described and is also known as angiofollicular lymph node hyperplasia or giant lymph node hyperplasia . Among many sites where lesion occurs, commonest is in the thorax (60%), abdomen (11%), neck (14%), and axilla (4%)

MATERIALS AND METHOD

We analyzed five cases of Castleman disease we received in Nepal Mediciti during five-year period from 2020 to 2024. Demographics, clinical variables, anatomical site, centricity, histopathology, immunochemistry, and surgical approach were reviewed.

RESULTS

Among five cases, anatomical location of two cases from retroperitoneum, two from inguinal region and one is from cervical lymph node. Three cases were male and two were female. Age group of these five cases shows three were adult and two were children. All of them underwent surgical resection and under continuous follow up. One of the cases from retroperitoneum had got recurrence.

CONCLUSION

Castleman disease is a diagnosis of exclusion. Case should be evaluated on the basis of proper clinical findings, blood parameters, HIV and HHV-8 test, imaging along with biopsy and IHC. Lymphoma and Kaposi sarcoma may mimic on radiology and histologically with Castleman disease.

KEYWORDS

Unicentric Castleman disease, Hyaline vascular, Lymphoma

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INTRODUCTION

In 1954 , Castleman Disease (CD), was first described and is also known as Angio follicular lymph node hyperplasia or giant lymph node hyperplasia1. Among many sites where lesion occurs, commonest is in the thorax (60%), abdomen (11%), neck (14%), and axilla (4%).2 Pathologically it can be classified as hyaline vascular type (HV-CD), plasma cell type, mixed type, and human herpes virus (HHV)-8 associated Castleman disease.3 Surgery is the primary treatment and has good long-term prognosis. Multicentric Castleman Disease (MCCD) is a more serious systemic condition, often associated with constitutional symptoms. Exaggerated systemic inflammatory response secondary to "Cytokine storm" involving Interleukin-6 (IL-6) may cause multi-organ dysfunction4. Most important the histopathological features encountered in the various forms of Castleman disease are diverse, and for the most part, lack specificity, because they are seen to varying degrees in different clinical variants of Castleman disease, and in reactive (autoimmune/infectious) and malignant (lymphoma) contexts.5 POEMS syndrome is a paraneoplastic syndrome. The important features, other than those in its previously listed acronym, include papilledema, extravascular volume overload, sclerotic bone lesions, thrombocytosis, elevated vascular endothelial growth factor (VEGF), and abnormal pulmonary function. TAFRO syndrome is an acute or subacute systemic inflammatory disorder characterized by the conditions previously listed in the acronym. Of note, the anasarca includes pleural effusion and ascites and the organomegaly includes hepatosplenomegaly and lymphadenopathy.6

After literature review, we analyzed all reported cases of association CD-NHL and CD-HD. NHL is more often associated with multicentric CD, its diagnosis being concurrent with CD diagnosis or occurring within 2 years. B-NHL is predominant (71%), and mantle cell lymphoma represents 40% of these B-NHL cases.7 Incidence of CD based of anatomical location sites based on literature review. Table (1.1)(8). Surgical removal of a unicentric mass of hyaline-vascular or hyaline-vascular/plasma cell type is curative. Partial resection, radiotherapy, or observation alone may avoid the need for excessively aggressive therapy. Patients with multicentric disease, either hyaline-vascular or plasma cell type, do not benefit from surgical management and should be candidates for multimodality therapy. 8

Table 1.1 Incidence of Castleman disease by location

Location	Percentage of cases
Thorax	60
Neck	14
Abdomen	11
Axilla	04
Other	11

In one study, the incidence of Kaposi's-sarcoma- associated, HHV 8-related non-Hodgkin's lymphoma in a cohort of HIV-positive patients with multicentric Castleman's disease was 15-fold higher than the incidence in the general HIV-positive population. 9

Collectively, we were involved in the diagnosis of 5 patients with Castleman's disease. Among five patients three were treated in Nepal Mediciti Hospital and two were treated in another center. All 5 patients had the localized form and the hyaline-vascular type of Castleman's disease as determined by surgical lymph node biopsy. Follow-ups were conducted by telephone calls. In this article, we describe these 5 cases, and we review the entire course of Castleman's disease, including its clinical features at presentation, its histopathological characteristics, and the diagnostic and treatment challenges it poses.

CASE REPORTS

Patient 1

A 46-year-old woman presented with a 2-year history of a persistent, enlarging left lateral neck mass. The patient also complained of right-sided neck numbness and tingling. The remainder of her medical history was unremarkable. On magnetic resonance imaging (MRI) the mass measured 4.2 x 2.2 cm. Fine-needle aspiration cytology was not done. Core biopsy was performed which shows lymphoid follicles with interspersed sclerotic vessels. IHC findings were negative for diagnosis of lymphoma. The patient was referred to the surgery department and excision biopsy was performed.

Patient 2

A 53-year-old male presented with enlarged lymph node in cervical region for one month associated with pain. CT-Scan shows homogeneously enhancing and necrotic lymph node with septal thickening and ground glass opacities. Excision biopsy was received which shows greyish brown lobulated surface. On Microscopic examination shows follicular architecture of lymphoid architecture is replaced by diffuse proliferation of lymphoid cells, with concentric arrangement of dilated vessels with interspersed plasma cells. Differential diagnosis of lymphoproliferative neoplasm and Castleman disease was made. IHC findings ruled out lymphoproliferative neoplasm.

Patient 3

A 13-year-old male with asymptomatic heterogeneous mass in mesentery in right iliac fossa with minimal internal vascularity. USG features suggestive of conglomerate lymph node with differential diagnosis of lymphoma and tuberculosis. Core biopsy performed from mass microscopically shows diffuse sheets of plasma cells along

with thick-walled blood vessels with areas of hemorrhage and fibrosis. Diagnosis was conformed as plasma cell variant of Castleman disease by IHC.

Patient 4

A 74-year female with previously biopsy proven case of Castleman disease presented with enlarged lymph node in hypogastrium and multiple skin lesions. USG-features suggestive of recurrence of Castleman disease with differential of conversion to lymphoma. On microscopic examination there is diffuse component of polymorphous population of lymphoid cells coursed by conspicuous vascular proliferation with hyalinized wall and prominent endothelial vessels. Plasma cells are noted but not in sheets. Final diagnosis of hyalinized vascular type Castleman disease was made on H and E examination

Patient 5

A 24-year old female with left retroperitoneal mass. CECT-features suggestive of extra- adrenal pheochromocytoma. Excision biopsy microscopically shows lymphoid follicles with thickened mantle zone. Sclerotic arterioles penetrate most of the thyroid follicles. Nodular infiltrate of lymphocytes surrounded by broad band of collagen is seen at places. Scattered large cells with vesicular nuclei were also identified. Microscopic differentials were Castleman lymphadenopathy, diffuse large cell lymphoma and Hodgkin lymphoma

S.N.	Age	Sex	Diagnosis
1	46	Female	Unicentric Castleman disease
2	53	Male	Unicentric Castleman disease
3	13	Male	Unicentric Castleman disease
4	74	Female	Unicentric Castleman disease
5	24	Female	Unicentric Castleman disease

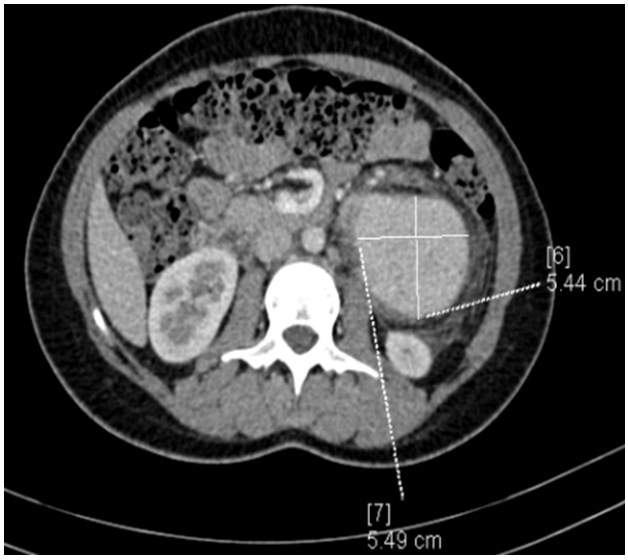

Fig 1. CECT shows enhancing soft tissue density mass

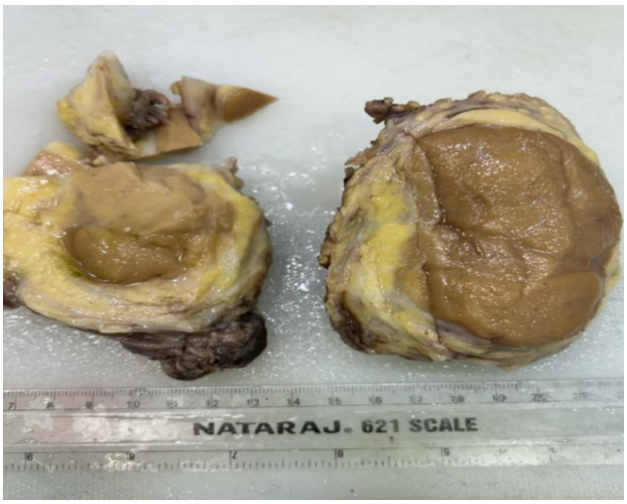

Fig 2. Gross picture showing well circumscribed light grey soft to firm mass

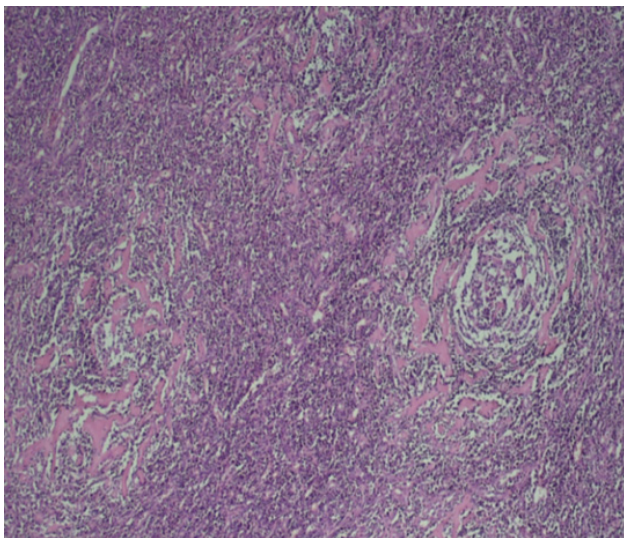

Fig 3. Microscopic image showing onion skin pattern, sclerotic vessels entering into germinal center of lymphoid follicle

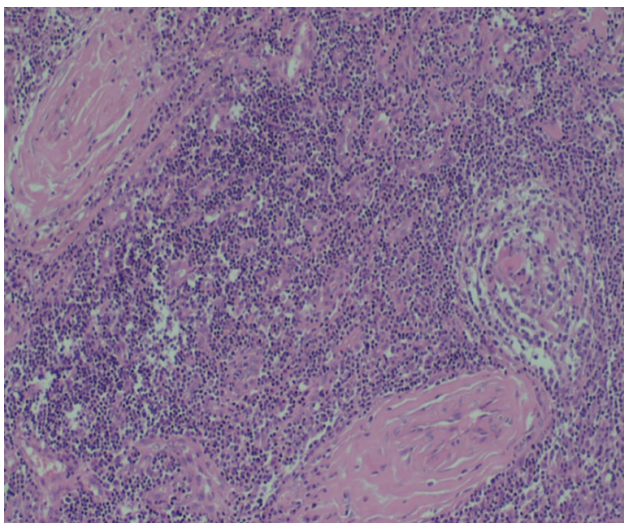

Fig 4. Microscopic image showing sclerotic vessels with increased vascularity in lymphoid follicles

DISCUSSION

1. Etiology

Conditions that result in Castleman disease is associated with chronic low-grade inflammation, lymphoid-hamartomata's hyperplasia, viral infections, abnormal modulation of cytokines, and angiogenesis. HIV and human herpes virus (HHV)-8 has also been associated with multicentric Castleman disease. Advances in diagnosis, classification, pathogenesis, and therapy are substantial since the original description of UCD by Benjamin Castleman in 1954.10

2. Pathogenesis

Overexpression of Interleukin (IL)-6 and some epidermal growth factor receptor is seen on signaling pathways involved in patient with UCD. FDCs (Follicular dendritic cells role in lymphocyte trafficking is largely mediated through secretion of chemokine ligand 13 also known as B lymphocytic chemoattractant .11

3. Diagnosis

Castleman's disease can pose several diagnostic dilemmas. Most often it manifests as an asymptomatic, unifocal, soft-tissue mass without any trademark signs or symptoms.

4. Imaging test

X-ray, CT, MRI, PET scan can allow health care provider to locate the enlarged lymph node. 12 Vascularity within the lymphoid follicles can be studied by the imaging technique. Definite diagnosis of Castleman is always not possible but differentials can be listed out. In our cases also imaging technique have listed differentials of paraganglioma and lymphoma as differentials.

5. Blood parameters

Castleman disease is mostly presented with low red blood cell count. Thrombocytosis or thrombocytopenia. HHV-8, test and HIV test must be performed to rule out multicentric Castleman disease (MCD). We have ruled out MCD in our all cases.13

6. FNAC

FNAC have been very low helpful in case of diagnosis of Castleman disease. Differentials of reactive lymphadenopathy and lymphoma could only be made as in FNAC we see lymphoid population only. In our cases we have made reactive lymphadenopathy as diagnosis in cases where we have performed FNAC.

7. Biopsy

Biopsy is the gold standard for diagnosis of Castleman disease. Hyperplastic lymphoid follicle with sclerotic blood vessels entering into germinal center along with twinning of germinal center is most common histological finding we have encountered in our cases. IHC markers along with HHV-8, and HIV test is co- performed to rule out lymphoma and multicentric Castleman disease, which we have performed in our cases.

8. Treatment

Corticosteroids, low dose chemotherapy oral etoposide, cyclophosphamide has been used in most cases. Recent development of monoclonal antibodies is also been widely used now. Surgical excision remains the gold standard followed by chemotherapy.14 MCD and recurrent cases of UCD should be in close follow up as there is always risk of conversion into lymphoma.

CONCLUSION

Among five cases we received, three were female and two were male. Two among five were of younger age children. All of them were diagnosed as UC Castleman disease. So, we can conclude that Castleman disease can occur in any age, irrespective of gender and is most common type is UC type.

Castleman disease is a diagnosis of exclusion. Case should be evaluated on the basis of proper clinical findings, blood parameters, HIV and HHV-8 test, imaging along with biopsy and IHC. Lymphoma and Kaposi sarcoma may mimic on radiology and histologically with Castleman disease. Diagnosis of Castleman disease is insufficient we should separate into HV and PC (HHV8- or HHV-8 +) as they have different prognosis. We should perform HHV8 IHC on all cases with plasma cell CD, HHV-8 – (differentiate with autoimmune disease, IG4 related disease). HHV8+ should be carefully evaluated for KS and Lymphoma.

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