Case Report

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Castleman Disease: An Uncommon and Intriguing Condition Revisited: A Report of Two Cases.

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ABSTRACT

Castleman disease (CD) also called as angiofollicular hyperplasia or giant lymph node hyperplasia of unknown cause is a benign lymphoproliferative disorder. It is a localised (unicentric) or disseminated (multicentric) disease. This disease is uncommon with an incidence of 25 cases per million person per year. Castleman disease is a heterogeneous group of disorders with four characteristic histological variants. The etiology of this disease is poorly understood.

We report two cases of CD, one presenting with a neck mass and the other presenting with para-aortic and mesenteric lymphadenopathy which were classified as hyaline vascular type and mixed type of CD respectively.

Keywords: *Lymph Node, Castleman Disease, Hyaline Vascular, Mixed Variant.*

Introduction

Castleman disease (CD), also called as angiofollicular hyperplasia or benign giant lymph node hyperplasia, is of unknown cause and is a rare, benign lymphoproliferative disorder.[1-10] It was first reported as a localized mediastinal lymph node hyperplasia by Castleman and Towne in 1954.[2,3] Castleman disease commonly involves lymphoid tissues in the thorax (70%), abdomen and pelvis (15%), and the neck (15%).[4] Extranodal sites of involvement are mediastinum, lacrimal glands, pancreas, parotid, lung, larynx, meninges and even muscles of the extremities.[4,5]

Clinically, it can be divided into unicentric (localised) and multicentric (generalised) types.[11] The unicentric form is seen anywhere along the lymphatic chain, most commonly mediastinum followed by other sites such as the neck, axilla, thorax, mesentery, spleen, pancreas, retroperitoneum, and adrenal. The multicentric form characterized by involvement of multiple lymph nodes and multiple organs was first described by Gaba et al in 1972.[10,11] Histologically, CD is classified into four variants, hyaline vascular, plasma cell, mixed type and plasmablastic variant.[6]

We report two cases of CD, one presenting with a neck mass and the other presenting with para-aortic and mesenteric lymphadenopathy which were classified as hyaline vascular type and mixed type of CD respectively.

Case Report

Case 1 - A 16 years old male presented with history of right side neck swelling since 5 years. Patient was asymptomatic 5 years back when he noticed a swelling on the right side of neck which gradually increased in size and was not associated with pain or any discharge. There was no history of trauma, dyspnoea, chest pain, hoarseness of voice, hematemesis or tuberculosis. On local examination there was a firm, immobile swelling on the right side of neck. There was no generalised lymphadenopathy or organomegaly. The blood investigations were normal including liver function and renal function tests. CT scan was suggestive of neurogenic tumor. A surgical excision of the right side neck mass was carried out. Pathological Findings: Gross examination revealed a large, encapsulated mass measuring 9x6x5cm. Cut surface was greyish white, firm without necrosis (Figure 1a). Histomorphology showed effaced lymph node architecture due to numerous hyperplastic lymphoid follicles of varying sizes distributed throughout the cortex and medulla (Figure 1b). Lymphoid follicles showed hyaline deposits in germinal centres along with sclerotic blood vessels. Follicles with atrophic germinal centres were surrounded by broad mantle zone comprising of concentric rings of small lymphocytes giving 'Onion Skin' appearance (Figure 1c). Also seen was "lollipop appearance" focally (Figure 1d) and prominent vascular proliferation. Based on these findings the diagnosis of hyaline vascular variant of Castleman disease was rendered.

The patient was asymptomatic 3 months post operatively with no further lymph node enlargement.

Case 2 - A 15 years old female complained of pain in abdomen since 1 year, which has increased since 2 months.

She gave a history of excision of right breast fibroadenoma. No history of tuberculosis, diabetes and hypertension. On CT scan multiple sub centimeter sized non necrotic lymph nodes were present in pre and para aortic, precaval, aortocaval & mesenteric region. A surgical excision of the node from iliac region was carried out under general anaesthesia.

Pathological Findings: Gross examination revealed multiple lymph nodes, smallest measuring 1.5 cm in diameter and largest measuring 2.0 cm in diameter. Cut surface was greyish white firm (Figure 2a). The histopathology showed lymphoid follicle hyperplasia, vascular proliferation, and clusters of plasma cells (Figure 2b, 2c & 2d). These features were in favour of Castleman disease (mixed type).

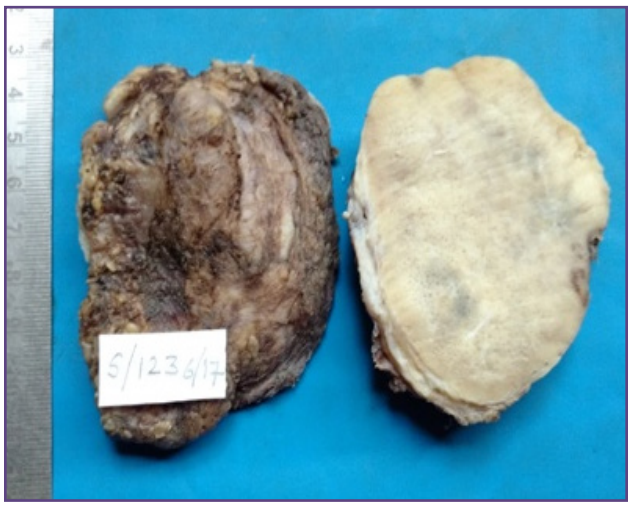

Fig. 1a: Lymph node mass measuring 9x6x5cm, c/s grayish white, firm.

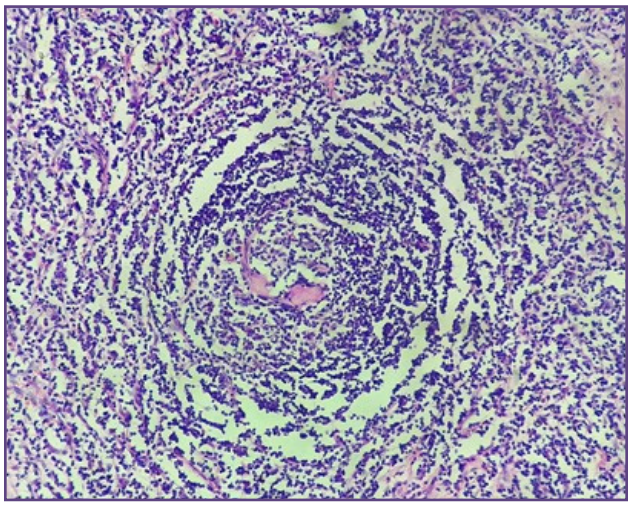

Fig. 1c: "Onion skin" pattern.

Discussion

Castleman disease (CD) is also called as angiomatous lymphoid hamartoma, angiofollicular mediastinal lymph node hyperplasia, follicular lymphoreticuloma and lymph nodal hamartoma.[7,11] The incidence of Castleman disease is estimated to be 25 cases per million person per year.[8]

The aetiology of Castleman disease is not definitively established and is poorly understood. The role of human herpesvirus 8 (HHV-8) has been implicated. Recent studies have demonstrated that HHV-8 is able to produce an IL-6 homologue, the interleukin responsible for hypergammaglobulinaemia and plasmacytosis seen in multicentric Castleman disease (MCD).[12] The controversy remains regarding whether CD variants are separate entities

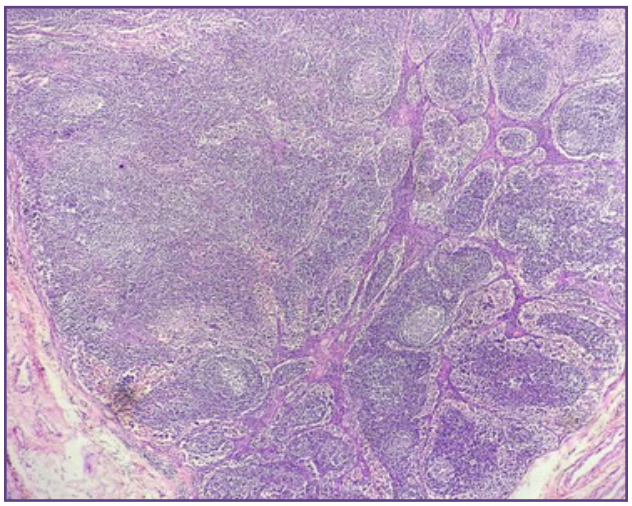

Fig. 1b: Hyperplastic lymphoid follicles in the cortex & medulla.

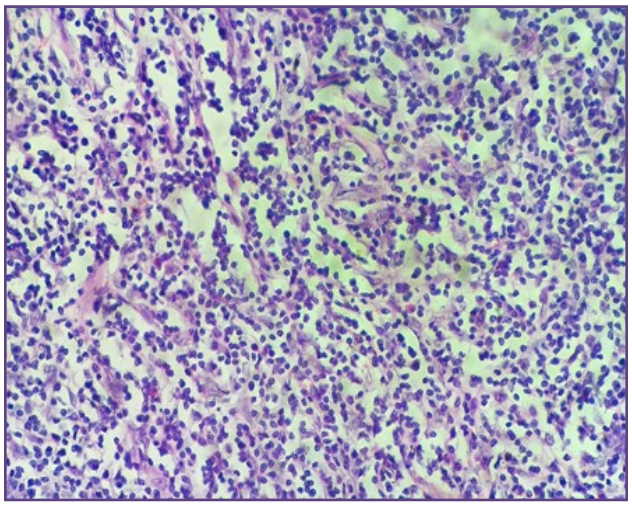

Fig. 1d: Vascular proliferation.

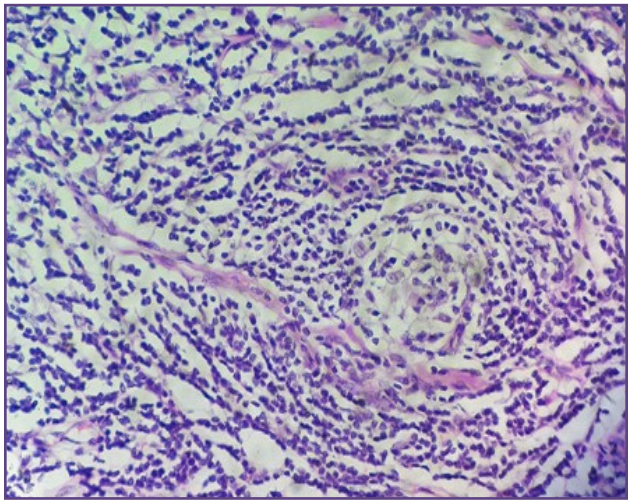

Fig. 1e: Lollipop appearance.

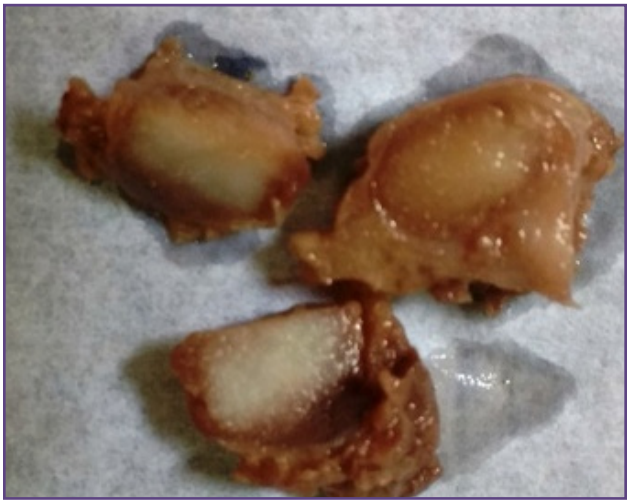

Fig. 2a: Enlarged lymph nodes measuring 2x2x1cm.

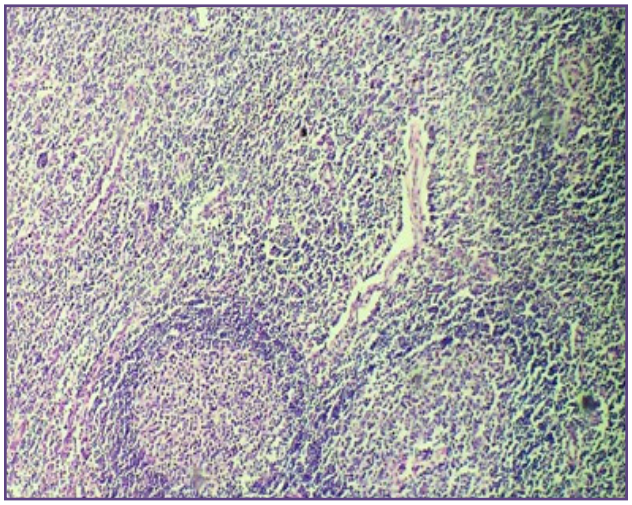

Fig 2b: Hyperplastic lymphoid follicles with prominent germinal centres.

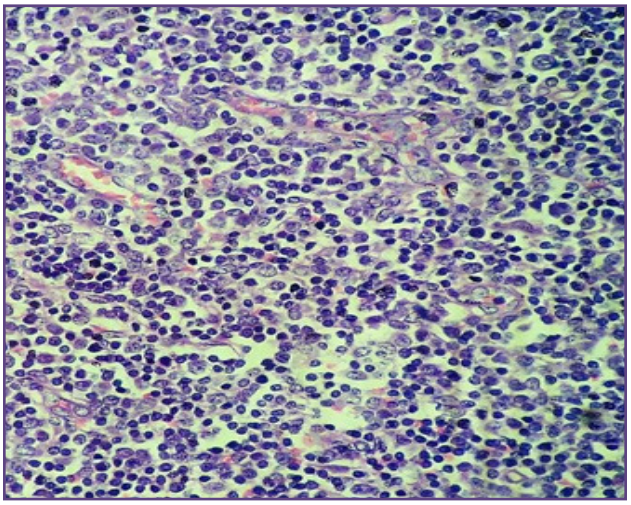

Fig. 2c: Vascular proliferation.

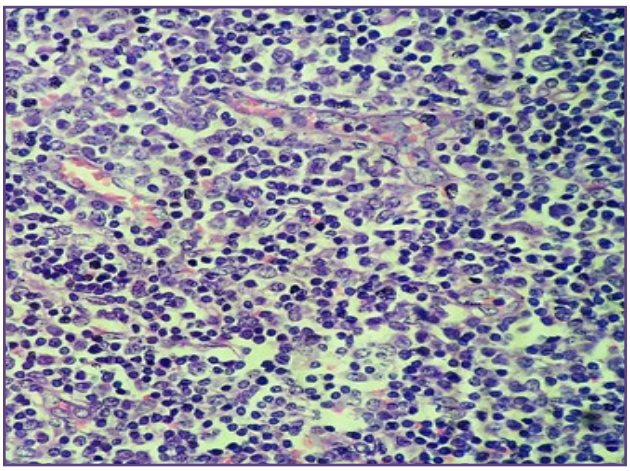

Fig. 2d: Plasma cells in clusters.

or are two ends of the same spectrum of disease. CD has an increased prevalence in HIV infection.[13] It is also seen with POEMS syndrome.[9] Castleman disease can progress to or may be associated with lymphoma complicating both the diagnosis and treatment.[14]

Computerised tomography in unicentric hyaline vascular CD shows a localized mass and homogeneous intense contrast enhancement, suggesting that the lesion is hypervascular. Occasionally, calcification and central necrosis are seen, especially if the lymph node size is large.[9] In the plasma cell multicentric type, multiple lymph node involvement is seen along with splenomegaly. Radiologically contrast enhancement varies and is histopathologically related to vascular proliferation and plasma cell infiltration.[9]

On histology, CD is divided into four types, hyaline vascular, plasma cell, mixed type and the plasmablastic variant.[6] 1] The hyaline vascular pattern subtype is the most common, is usually asymptomatic, localised and unicentric and accounts for 80-90% of the cases. Majority of these patients present as a slow growing mass and are treated by surgery alone. The hyaline vascular variant (HVV) is characterized by small atrophic or "regressively transformed" germinal centers surrounded by widened mantle zones composed of small lymphocytes in an onion ring-like arrangement. The germinal centres have small hyalinized vessels and prominent follicular dendritic cells. The interfollicular region shows small T lymphocytes and vascular proliferation including many high endothelial venules.

The plasma cell type, usually multicentric, accounts for 10 to 20% of cases. These patients have systemic symptoms and laboratory findings of inflammatory activity and show higher morbidity and mortality. The plasma cell variant usually presents in elderly males with systemic symptoms like fever, fatigue, anemia, bone marrow plasmacytosis and polyclonal hypergammaglobulinemia. Also multicentric CD can progress into lymphoma or vascular neoplasms such as Kaposi's sarcoma, follicular dendritic cell tumor and plasmacytoma.[7] The plasma cell variant (PCV) is characterized by hyperplastic instead of regressively transformed germinal centres and a massive accumulation of polyclonal plasma cells in the interfollicular region. Marked vascular proliferation in the interfollicular region is present.

The mixed variant shows both hyaline vascular and plasma cell elements.

The plasmablastic variant is less common and is associated with human immunodeficiency virus (HIV) infection.[6] It is characterized by large plasmablasts (immunoblasts) in the mantle zone harboring HHV-8 latent nuclear antigen. This variant can undergo progression to frank plasmablastic monoclonal lymphoma and is clinically very aggressive.[6]

Castleman disease is treated by multimodality approach which includes surgery, localised radiotherapy, corticosteroids, chemotherapy and immune modulators.[3]

Unicentric CD has an excellent prognosis with surgery having 5 year survival rate close to 100%. Radiotherapy is considered if there is residual disease or unresectable lesion. Multicentric CD is treated by chemotherapy, monoclonal antibodies and glucocorticoids and has poor prognosis with a median survival of 2 to 3 years.[2,3]

Conclusion

Castleman disease is a rare disorder which can mimic lymphoma clinically and histologically. The aim of this discussion was to emphasize the importance of histology which clinches the diagnosis and differentiates it from other lymphoproliferative disorders.

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