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Pathology

A RARE CASE REPORT- CASTLEMAN'S DISEASE IN LYMPH NODE IN 41 YEAR MALE

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ABSTRACT Castleman disease, also known as angiofollicular lymph node hyperplasia is a group of uncommon lymphoproliferative disorders that share common lymph node histological features. It was first described by Dr. Benjamin Castleman in the 1950s. Castleman's disease has two main forms: localized to a single lymph node (unicentric) or occur systemically (multicentric). Even though CD is not officially a cancer, one form of this disease (known as multicentric Castleman disease) acts very much like lymphoma. In fact, many people with this disease eventually develop lymphomas. And like lymphoma, CD is often treated with chemotherapy or radiation therapy. We present a case of 41 year old male who presented with right inguinal lymphadenopathy which was excised and sent for histopathology. On histopathological examination, lymphoid follicles show hyalinised blood vessels and prominent interfollicular stroma with large number of plasma cells and fair number of Russell bodies. Thus, diagnosis of Castleman disease was made.

KEYWORDS : Castleman disease, angiofollicular, lymphoproliferative, Unicentric and Multicentric Castleman disease.

Introduction:

Castleman disease (giant lymph node hyperplasia) represents a morphologically distinct form of lymph node hyperplasia rather than a neoplasm or a hamartoma. It occurs most commonly in adults but can also affect children. [1] It is a rare disease of lymph nodes and related tissues. The incidence of Castleman Disease is estimated at 21-25 cases per million person-years, with 23% of those cases potentially representing Multicentric Castleman Disease. [2] The median age at presentation for Unicentric Castleman Disease is 30-34 years, for HIV-negative Multicentric Castleman Disease is 49-66 years and HIV-positive Multicentric Castleman Disease is between 36-40 years. The sex distribution is approximately equal, though some series have reported a male predominance, generally in the HIV-positive population and a slight female predominance (1.4:1) in Unicentric Castleman Disease. [3]

It is sometimes associated with human herpesvirus 8 (HHV-8) infection in immunocompromised individuals, such as those with human immunodeficiency virus (HIV) infection. Although it is not cancerous, it may also be associated with malignancies such as Kaposi sarcoma, non-Hodgkin lymphoma, Hodgkin lymphoma, and POEMS syndrome. The disease is non-clonal, with no *IgH* or *TCR* gene rearrangements.

A variety of laboratory tests and imaging studies are indicated for the assessment, but the diagnosis is confirmed by histologic examination of a needle biopsy specimen from an involved lymph node. [4]

Case report:

A 41 year old male presented to the surgery OPD at LLR Hospital, Kanpur in May, 2017 with right inguinal lymphadenopathy. Patient was asymptomatic. His past medical and family history was non-specific. On examination a non-tender, firm mass was palpated in right inguinal region but there was no generalised lymphadenopathy or organomegaly. Hemogram showed normocytic normochromic anaemia and mildly raised ESR. Tests for HIV and HHV 8 were done, both of which were negative. Excision of the lymph node was done and specimen was sent for histopathological examination in Department of Pathology, GSVM Medical College, Kanpur.

Gross:

Specimen consist of one globular firm to hard tissue piece measuring 4x2.5x1.8 cm. Outer surface is irregular with fibrofatty adhesions. Inner surface is homogenous greyish white. [Fig. 1]

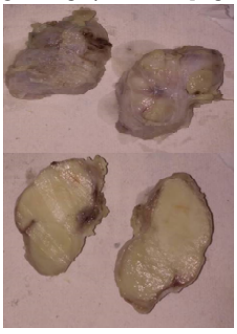

Fig 1 Outer surface and inner surface

Microscopic findings:

Sections from lymph node show few lymphoid follicles. Most of them show regressed germinal centres. Few follicles show hyalinised blood vessels. Prominent interfollicular stroma is seen with large number of plasma cells and fair number of Russell bodies along with proliferation of hyalinised blood vessels resembling Hassall corpuscles.[Fig. 2(a),(b), and (c)]

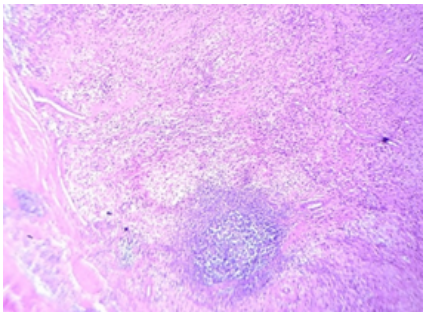

Fig 2(a) low power 10x showing regressed follicle centres.

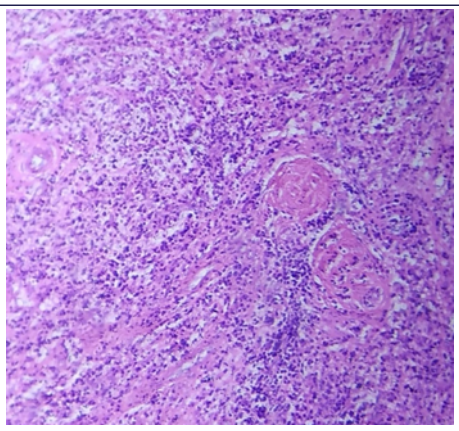

Fig 2(b) Low power 10x showing hyalinised blood vessels resembling Hassall's corpuscles.

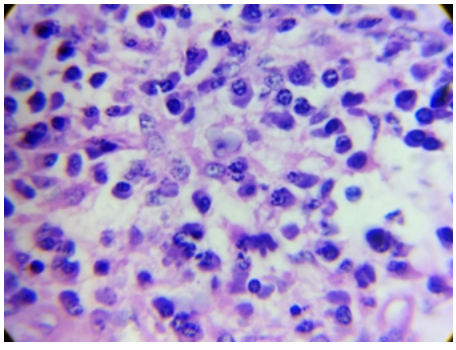

Fig 2(c) High power 40x show plasma cells and Russell Bodies.

Discussion:

Castleman Disease was first described as a pathological entity in 1954 and later defined by Castleman *et al*, in 1956 .[5] Flendrig and Schillings described two basic histopathological subtypes and one mixed variant which Keller *et al*. later designated hyaline-vascular, plasma cell, and hyaline-vascular plasma cell "mixed" types.[6,7] Clinical subtypes was proposed by McCarty *et al*. and Gaba *et al*. into unicentric and multicentric variants, respectively. [8,9] In general, hyaline-vascular type is commonly associated with a localized asymptomatic mass (76–91%), while plasma cell type is usually multicentric and symptomatic in 50% of patients.[3,9,10]

Four microscopic subtypes of Castleman disease have been stated.[16] First, the **hyaline vascular** type which is most common (approximately 90% in some studies). [3] It is mostly localized and rarely multicentric. Histologically, follicles show marked vascular proliferation and hyalinization of their abnormal germinal centers which are confused with Hassall corpuscles (thymoma) and splenic white pulp (ectopic spleen). Many of the large cells with vesicular nuclei present in the hyaline center are follicular dendritic cells (CD21 and CD35 positive). [11] Tight concentric layering of lymphocytes at the periphery of the follicles (corresponding to the mantle zone), resulting in an *onionskin appearance*. The interfollicular stroma is prominent, with numerous hyperplastic postcapillary venule vessels and an admixture of plasma cells, eosinophils, immunoblasts, and CD68 positive plasmacytoid dendritic cells.[12,13] Second, the **plasma cell** type is more likely symptomatic and multicentric, but it is sometimes localized. Histologically, there are sheets of mature plasma cells within interfollicular tissues that surround normal to large germinal centres, and the intense capillary proliferation seen in the hyaline vascular subtype is absent. Dysregulation of interleukin-6 (IL-6) has been implicated in the pathogenesis of plasma cell Castleman disease.[14,15] Third, the **mixed** subtype shows areas of both hyaline vascular and plasma cell types. It occurs less often. Fourth, the **plasmablastic** type was recognized more recently. Like the plasma cell type, it is usually multicentric, usually symptomatic, and has a less favorable outlook.[16]

From the point of view of clinical presentation, Castleman disease has been divided into a solitary and a multicentric form. [1] First, the **solitary** (mostly hyaline vascular type) form presents as a mass located most commonly in the mediastinum but also described in the neck, lung, axilla, mesentery, broad ligament, retroperitoneum, soft tissues of the extremities (including subcutis and skeletal muscle), nasopharynx, meninges, and several other sites. [1] Second, the **multicentric** or systemic form is nearly always of the plasma cell type, although occasional examples of the hyaline-vascular type (involving even the skin) are on record.[17] Basnayake et al (2017) presented a case of 36-year-old woman with generalized body swelling, foamy urine, multiple lymph nodes, hypertension, hepatomegaly and suggested that Castleman disease needs to be considered in the differential diagnosis when a patient presents with generalized lymphadenopathy and systemic manifestations. [18]

The long-term prognosis of systemic Castleman disease is poor; the disease tends to persist for months or years and to result sometimes in renal or pulmonary complications. [19] Furthermore, some of the patients have been found to have Kaposi sarcoma. Indeed, the coexistence of multicentric Castleman disease and Kaposi sarcoma in the same tissue sample is not an uncommon phenomenon. [20] O'Leary et al examined sixteen biopsies from lymph nodes of patients affected with Castleman's disease for the presence of HHV-8 (three HIV positive). Five multicentric Castleman's disease and two solitary Castleman's disease biopsies were positive for HHV-8. [21]Other cases have developed large cell lymphomas of immunoblastic type.[1]

It is sometimes associated with human herpesvirus 8 (HHV-8) infection in immunocompromised individuals, such as those with human immunodeficiency virus (HIV) infection. Although it is not cancerous, it may also be associated with malignancies such as Kaposi sarcoma, non-Hodgkin lymphoma, Hodgkin lymphoma, and POEMS syndrome. The disease is nonclonal, with no *IgH* or *TCR* gene rearrangements. [4]

In the present case the patient presented with inguinal lymphadenopathy without any other symptoms. On the basis of histopathological examination, diagnosis of Castleman Disease was made.

Conclusion:

This case report emphasizes the fact that Castleman Disease is an uncommon disease of lymph node with clinical presentation similar to malignant lymphoma but histologically and prognostically it is different entity. It should be considered as differential diagnosis of the lymphadenopathy specially if presented with symptoms of systemic involvement. This brings to light the importance of obtaining definitive histological diagnosis in patients presenting with lymphadenopathy.

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