Case Report

Multicentric Plasma Cell Variant of Castleman Disease: A Case Report

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Abstract

Castleman disease (CD) is a lymphoproliferative disorder with markedly different presentations and clinical courses. The manifestations of this rare disease depend on the distribution and pathologic subtype. The histological variants of CD include the hyaline vascular variant and the plasma cell variant, with the former constituting about 90% of cases. Clinically, the unicentric form of CD is associated with a better prognosis, while multicentric CD is linked to a long-term poor outcome with an increased risk of second malignancies. Histopathologic examination of the involved lymph nodes remains the mainstay of diagnosis due to the clinical heterogeneity of the disease.

We present the case of a 64-year-old male who was evaluated for bilateral inguinal lymphadenopathy, with a PET scan showing multiple hypermetabolic intra-abdominal lymph nodes. In view of a strong clinical suspicion of lymphoma, excision biopsy of the left inguinal lymph node was performed and sent for histopathological examination.

Keywords:

inguinal lymphadenopathy, iMCD, CD138, plasma cell variant

Introduction

Castleman Disease (CD) is a rare lymphoproliferative disorder with diverse clinical presentations, often mimicking many benign and malignant diseases. The morphological subtypes of this entity include the hyaline vascular variant and the plasma cell variant, with the latter constituting less than 10% of cases. Clinically, the entity is divided into unicentric and multicentric forms. The disease has varied outcomes and prognosis, and many of the subtypes require long-term follow-up due to the risk of developing a second lymphoproliferative disorder. Histopathology remains the mainstay of diagnosis.

Case Report

A 64-year-old male presented to the outpatient department with complaints of incidentally detected bilateral inguinal swellings. There was no history of fever, night sweats, or weight loss. He has been a known case of diabetes for 15 years and coronary artery

disease for 12 years. He also has mild chronic kidney disease with borderline creatinine levels for 5 years. On examination, he had bilateral firm, mobile inguinal lymph nodes measuring 4 × 3 cm on the left side and 1 × 1 cm on the right side.

His investigations showed a hemoglobin level of 8.6 g/dL with an elevated erythrocyte sedimentation rate of 133 mm in the 1st hour. Serum protein electrophoresis showed an M band of 2.3 g/dL in the gamma region. His bone marrow examination was inconclusive, and the serum-free kappa-lambda ratio was also normal. A PET scan revealed multiple hypermetabolic enlarged lymph nodes in the portocaval, paraaortic, aortocaval, retrocaval, bilateral common iliac, left internal iliac, left external iliac, and left inguinal regions, which were reported as likely neoplastic etiology (possibly lymphoma). An excision biopsy of his left inguinal lymph node was performed and sent for evaluation.

Gross examination revealed a pale white, firm lymph node measuring 4 cm in greatest dimension. Histopathological examination showed partial effacement of the lymph node architecture with sheets of plasma cells, including binucleate forms in the interfollicular region, with some showing intracytoplasmic Russell bodies. There were also areas showing retained follicles traversed by sclerotic and hyalinized blood vessels. With a differential diagnosis of lymphoplasmacytic lymphoma, plasmacytoma, and plasma cell variant of CD, we proceeded with immunohistochemistry. CD20 was negative in the neoplastic cells, but CD138 was strongly positive, with polyclonal expression of kappa and lambda light chains. Correlating the histopathology and immunohistochemistry findings, a diagnosis of plasma cell-rich variant of Castleman Disease was rendered.

The patient is under regular follow-up and is currently not receiving any chemotherapy. No recurrences have been reported so far.

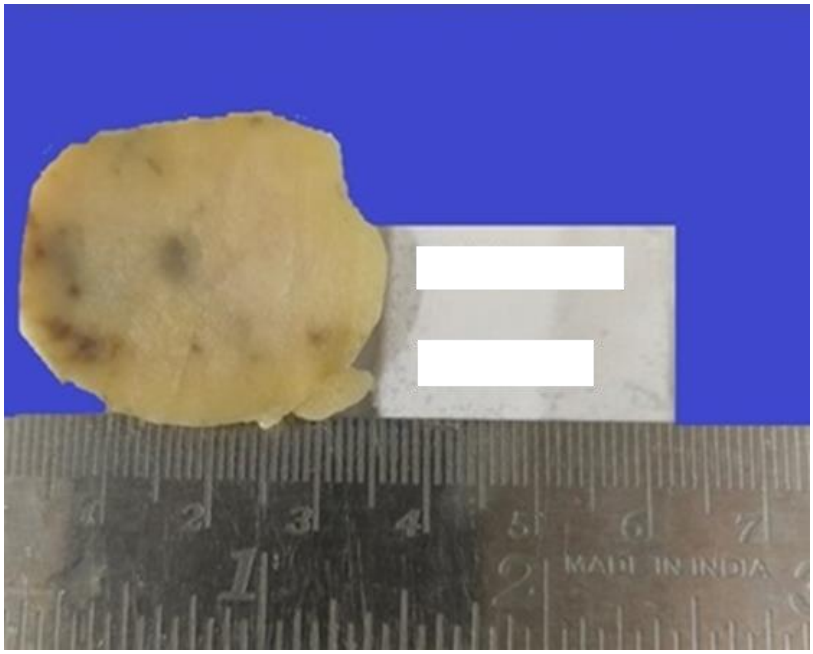

Figure 1: Firm pale white lymph node with specks of haemorrhage

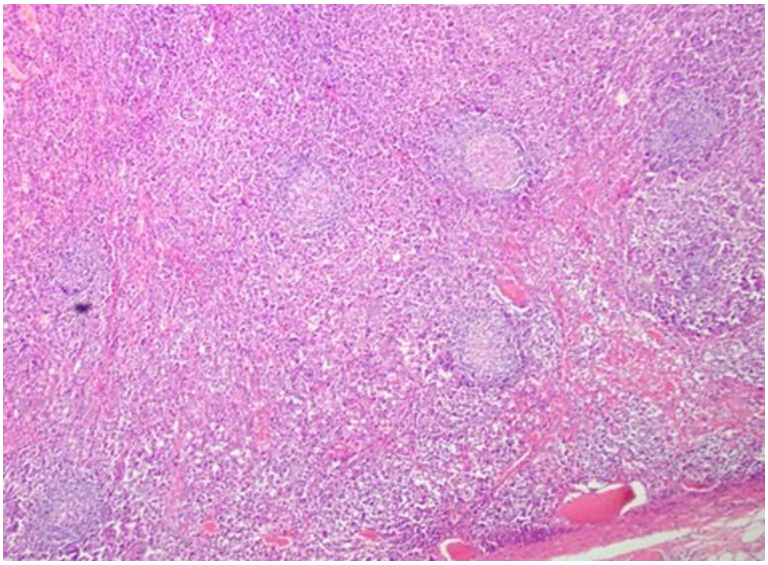

Figure 2: Partial effacement of lymph node architecture with few atretic retained follicles

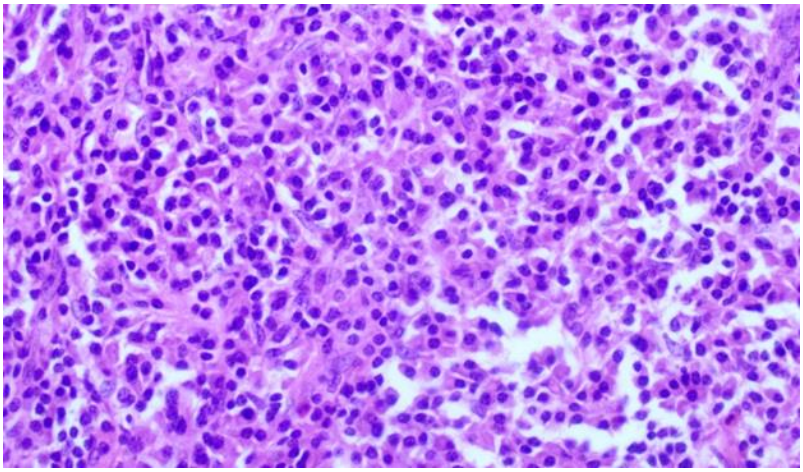

Figure 3:Expansion of interfollicular areas by sheets of plasma cells

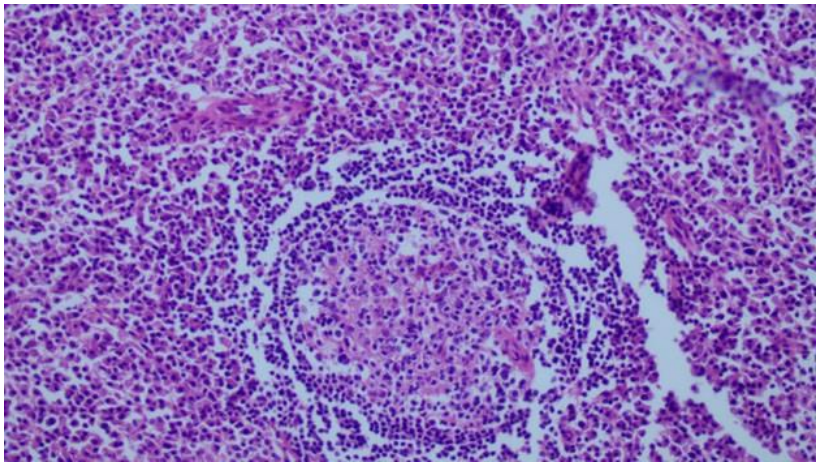

Figure 4: Follicles traversed by sclerotic vessels

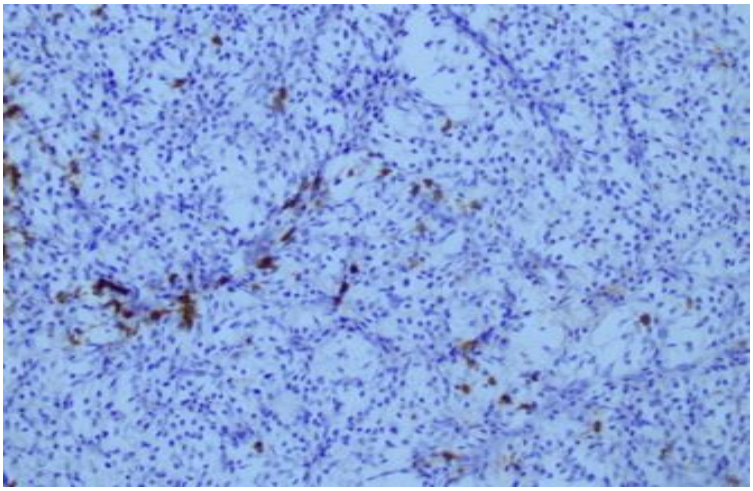

Figure 5: IHC CD 20 – negative in interfollicular area

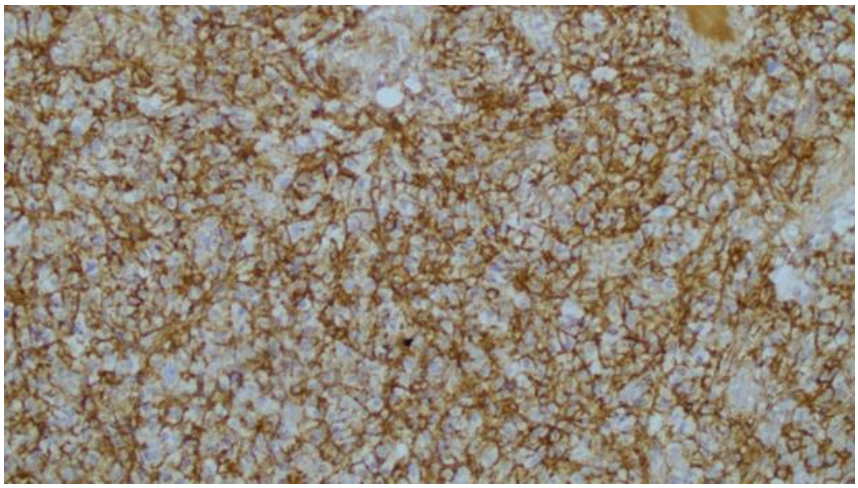

Figure 6: IHC CD 138 – strong and diffuse positivity

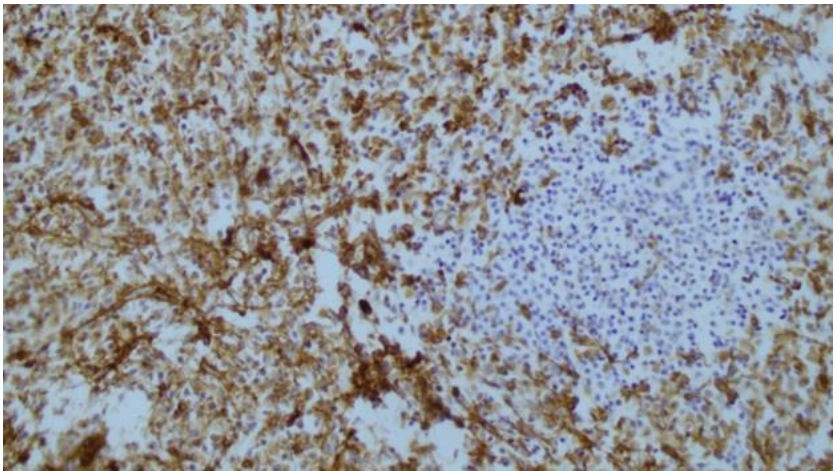

Figure 7: IHC Kappa - positive in 70% plasma cells

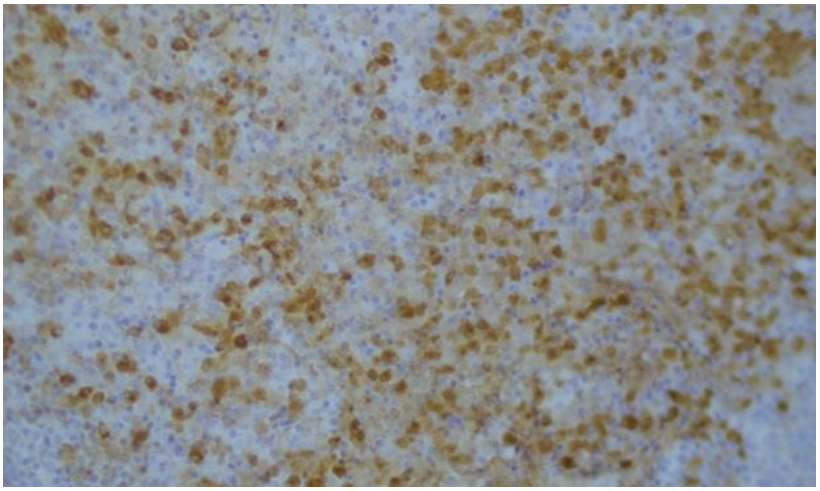

Figure 8: IHC Lambda - positive in 30 % plasma cells

Discussion

CD was so-termed in reference to a series of 13 cases of localized mediastinal lymph-node hyperplasia first described by Dr. Benjamin Castleman in 1956. This was followed by the identification of a plasma cell-rich variant by Flendrig and Schillings in 1969 [1]. The incidence of CD is unknown; however, it is mainly reported in adults, with a slight feminine predominance (60%) [2]. It can affect lymph nodes anywhere in the body, including the neck, chest, abdomen, and pelvis, imitating both benign and malignant diseases [3].

The histologic subtypes of CD include hyaline vascular, plasma cell, and mixed hyaline vascular plasma cell types. CD has been classified clinically as unicentric (localized, unicentric Castleman disease [UCD]) and multicentric (systemic, multicentric Castleman disease [MCD]). MCD has been etiologically classified by the Castleman Disease Collaborative Network (CDCN) as human herpesvirus 8 (HHV-8)-related; HHV-8-unrelated, also called idiopathic MCD (iMCD); POEMS (polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes) syndrome–related; and others [4]. The multicentric plasma cell subtype of CD is a relatively uncommon disease entity that can present as a diagnostic dilemma because of its overlapping clinicopathological presenting features similar to malignant lymphoma [5].

The major biologic factors involved in the disease pathogenesis include inflammatory mediators like IL-6, NF-kappa B, and VEGF. The interplay of these factors results in lymphovascular proliferation and systemic manifestations [6]. HHV-8 is the well-established etiologic cause of HHV-8–associated MCD, particularly in the setting of immunodeficiency. The virus infects plasmablasts and B cells, causing upregulation of the aforementioned biologic mediators. The pathogenesis of HHV-8 negative MCD is less well understood. The current understanding of POEMS-associated MCD is with respect to the role played by monoclonal plasma cells and VEGF. The other subcategory of MCD, iMCD, is thought to be driven by self-reactive antibodies, germline mutations in genes regulating inflammation, acquired oncogenic mutations, or an infection with a pathogen [7].

The clinical presentation of unicentric CD is usually as an isolated lymphadenopathy and is rarely associated with symptoms. Multicentric CD may present with varied symptoms, ranging from multiple enlarged lymph nodes, flu-like symptoms, organomegaly, elevated inflammatory markers, anasarca, low hemoglobin, renal dysfunction, and hypergammaglobulinemia. iMCD-TAFRO is characterized by thrombocytopenia, anasarca, fever or elevated C-reactive protein, reticulin fibrosis, and

organomegaly. iMCD-NOS typically involves thrombocytosis and elevated immunoglobulins with a less intense disease course. MCD has been diagnosed in some patients with POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, and skin changes) syndrome as well [8].

Histologically, the hyaline vascular variant is characterized by follicles with regressed germinal centers surrounded by widened mantle zones comprised of small lymphocytes in an onion ring–like arrangement. The atretic germinal centers are traversed by sclerotic penetrating vessels and show hyalinization, which are described as lollipop follicles. The plasma cell variant is characterized by hyperplastic germinal centers and sheet-like accumulation of polyclonal plasma cells in the interfollicular region. Vascular proliferation in the interfollicular region is present in both CD variants. Mixed forms demonstrate the presence of both hyaline vascular and plasma cell elements. The plasmablastic variant is less common and is associated with HHV-8 and/or HIV infection.

Conclusion

CD is a great mimicker of benign and malignant diseases, in view of its diverse manifestations and ability to affect any body region. Because of its nonspecific characteristics and the fact that it can mimic other neoplasms, it is often misdiagnosed [9]. The most reliable way to establish a definitive diagnosis is by surgical resection and histopathologic confirmation. A timely and accurate diagnosis of CD aids in further management and follow-up, as these patients are at a high risk for developing lymphoma. This case is presented to stress the significance of histopathological examination in the diagnosis of this rare entity, which can have overlapping clinicopathological features.

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Ethical Clearance: Not applicable

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