Case Report

Castleman Lymphadenopathy Presenting as Axillary Mass in a 69-Year-Old Male: A Case Report with Review of Literature

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Abstract

Castleman disease (CD), first described by Benjamin Castleman, is a rare and heterogeneous disorder of unknown aetiology, characterised by massive lymphadenopathy and a range of systemic inflammatory symptoms. It shows no specific predilection for age, gender, or ethnicity and exhibits distinctive histomorphological features. Depending on the extent of involvement, CD can be classified as either unicentric or multicentric, each with distinct clinical presentations. Unicentric CD (UCD) presents as localised lymphadenopathy, usually without any other symptoms. In contrast, multicentric CD (MCD) is a progressive, systemic inflammatory condition involving multiple lymph node stations and organ systems. Histologically, two main morphological variants are recognised: the hyaline vascular (HV) type and the plasma cell (PC) type.

We herein report a case of a 69-year-old male who presented to our hospital with a painless, gradually enlarging axillary swelling, which, on imaging, appeared as a conglomerate of enlarged lymph nodes. Radiological findings were non-specific, and aspiration cytology was suggestive of Rosai-Dorfman disease.

The diagnosis of CD is generally delayed and fraught with challenges since it is rare and can mimic a broad array of entities, encompassing lymphomas, granulomatous inflammation, autoimmune disorders, among others. Histopathological analysis of the excised lymph node is considered the best modality for diagnosing and distinguishing the various subtypes of CD.

Keywords:

Castleman disease, Lymphadenopathy, Lymph nodes, Lymphoproliferative disorders, Histopathology

Introduction

Castleman Disease (CD) is an eponym named after Benjamin Castleman, who first described it in a group of enlarged mediastinal lymph nodes during his time at Massachusetts General Hospital in the 1950s [1,2]. Later, its two morphological variants—Hyaline Vascular and Plasma Cell type—were identified [3]. CD, to this date, remains an unusual group of distinct disorders with no established aetiology, sharing among themselves a common histomorphology.

CD is not encountered in routine clinical practice, so experience with its diagnosis and management is limited, with histopathology being the best available diagnostic modality. Owing to its rarity and a lack of experience in

diagnosis, we herein report a case of a 69-year-old male with an axillary mass diagnosed as CD on histopathology.

Case Report

A 69-year-old male, chronic smoker and hypertensive, presented with a painless, gradually enlarging swelling in the left axilla for the past three months. There was no history of fever, weight loss, or other similar swellings, and a non-significant surgical and family history. The swelling was irregular, non-tender, not adherent to the overlying skin. No palpable organomegaly was found; blood counts, liver and kidney function tests were within normal limits; HIV serology was non-reactive.

USG left axilla revealed a large, ill-defined nodal mass comprising multiple, discrete nodes, the largest measuring 38 × 22 mm. Contrast-enhanced CT showed a lobulated, irregular mass comprising multiple, enlarged, discrete, homogeneously enhancing left axillary lymph nodes, the largest measuring 34 × 27 mm, with loss of fatty hilum [Fig. 1a]. The mass displayed increased peripheral vascularity with feeders from the left axillary artery. Few enlarged, homogeneously enhancing mediastinal lymph nodes, the largest measuring 12.4 mm in the subcarinal location, were also evident.

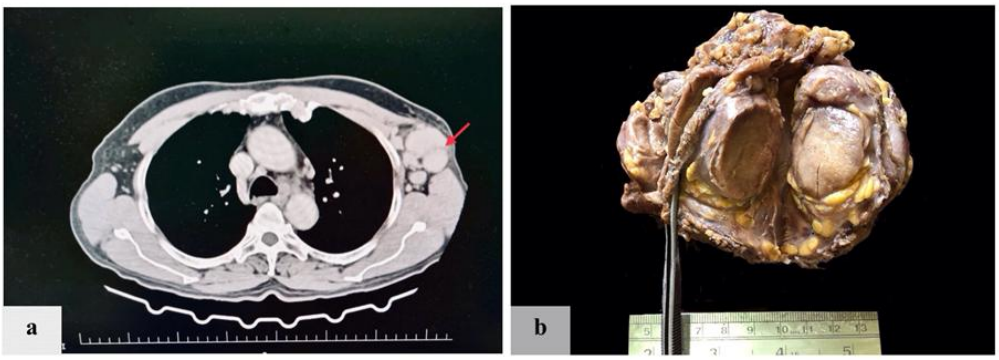

Figure 1: CECT chest radiograph showing multiple, enhancing, enlarged left axillary lymph nodes with a lobulated outline (red arrow) (a). Gross photograph of the excised axillary lymph node mass showing discrete, encapsulated lymph nodes. Cut section is greyish tan, firm (b).

Previous FNAC done elsewhere for the swelling showed a reactive lymphoid background and numerous scattered histiocytes exhibiting emperipolesis, suggestive of Rosai-Dorfman Disease. Following an uneventful surgery in our hospital, excision of the axillary mass was done and the specimen sent for histopathology.

Grossly, the specimen was a 12 × 10 × 3 cm fibrofatty mass of multiple discrete, well-encapsulated lymph nodes ranging in size from 2 cm to 5.4 cm, with a greyish-tan, firm cut section [Fig. 1b]. Extensive sampling was done and representative sections from multiple nodes were microscopically examined.

H&E stained sections of lymph nodes showed capsular thickening and numerous lymphoid follicles with atretic germinal centres and expanded mantle zones [Fig. 2]. Some of the follicles exhibited twinning of germinal centres [Fig. 2b], radially coursing hyaline blood vessels forming ‘lollipop’ lesions, and deposition of eosinophilic hyaline material [Fig. 2c, d]. Interfollicular zones contained sheets of plasma cells [Fig. 2e]. Sinuses were congested with lymphoid cells. No evidence of any granuloma or malignancy was found, and a diagnosis of Mixed type Castleman Disease was made.

After complete excision of the swelling, the patient is under follow-up and is so far asymptomatic with no new lesions.

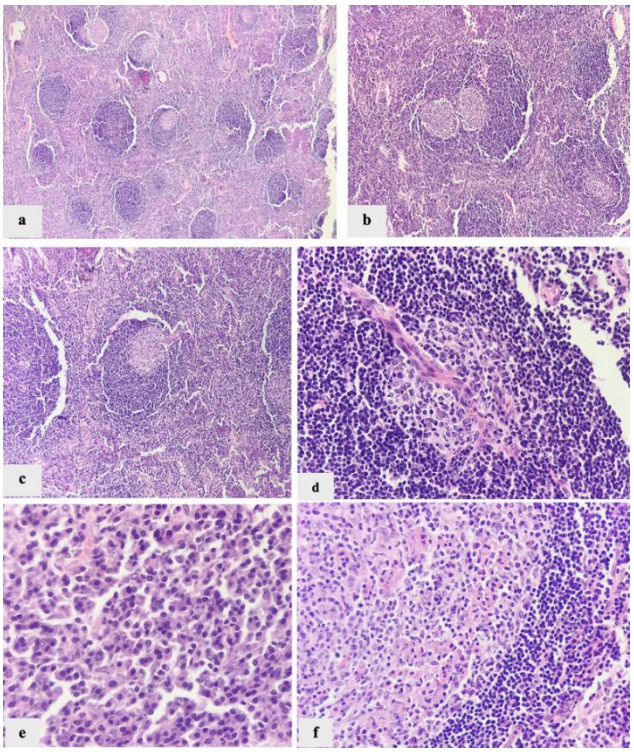

Figure 2: H&E microphotographs of Castleman disease showing increase in lymphoid follicles (a) [4x], twinning of germinal centres (b) [10x], radially transgressing vessels forming 'lollipop lesions' (c, d) [10x, 40x], inter follicular areas with sheets of plasma cells (e) [40x], concentric layering of lymphocytes in the mantle zone (f) [40x].

Discussion

Castleman Disease is a rare, reactive lymphadenopathy first described by Benjamin Castleman in an enlarged group of mediastinal lymph nodes. The initial accounts were published in the 1950s as part of New England Journal of Medicine's weekly Case Records of the Massachusetts General Hospital [1,2]. Later, in the year 1972, its two morphological variants, Hyaline Vascular and Plasma Cell type, were defined by Keller et al. [3].

Depending upon the extent of involvement, CD can be Unicentric or Multicentric; more recently, an Oligocentric variant has also been proposed [4]. When enlargement is restricted to a single lymph node or a single nodal group, it is termed as Unicentric CD (UCD). UCD is understood to be a clonal neoplastic disorder of follicular dendritic cells, which is clinically asymptomatic or associated with a painless bulky nodal mass with or without compressive symptoms. There is no gender predilection, and the mean age of diagnosis is in the fourth decade of life; however, any age group can be affected [5].

Multicentric CD (MCD), on the other hand, is a polyclonal lymphoproliferative, progressive, systemic inflammatory condition which involves multiple lymph node stations. In contrast to UCD, the mean age of presentation of MCD is in the sixth decade, with a predilection for the male gender [5,6]. Association with Human Herpes Virus-8 (HHV-8), also called Kaposi Sarcoma Herpes Virus (KSHV), and HIV is seen in most cases of MCD, while no such relation exists for UCD [6].

As per the classification proposed by the Castleman Disease Collaborative Network (CDCN), MCD is further segregated on the basis of causation into idiopathic MCD (iMCD), KSHV-associated MCD (KSHV-MCD), and polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes (POEMS)-associated MCD (POEMS-MCD) [7]. Surgical excision is

usually curative for UCD, whereas MCD requires a more aggressive approach using immunomodulatory or chemotherapeutic agents [6,8].

Histopathological examination of an excised lymph node is the modality of choice for the diagnosis of CD. Morphologically, lymph nodes of CD show prominent changes both in the follicular and interfollicular regions, characterised by follicular hyperplasia and prominent mantle zones exhibiting concentric layering of lymphocytes (Fig. 2). Germinal centres are depleted of small lymphocytes and contain residual follicular dendritic cells (FDCs), some of which may be dysplastic. Hyaline blood vessels can be seen radially transgressing into the follicles forming 'lollipop lesions'. Occasional follicles show fusion of their outer zones with a resultant follicle containing two or more germinal centres, called 'twinning of germinal centres'. Interfollicular zones in Hyaline Vascular type (HV) show proliferation of high endothelial venules and occasional plasma cells, immunoblasts, or eosinophils, whereas the presence of sheets of plasma cells is a characteristic feature of the Plasma Cell type (PC) of CD [3,7].

Immunohistochemical staining with FDC markers like CD21 and CD23 highlights the FDC meshwork in B cell-depleted germinal centres, while expanded mantle zones are positive for CD20, IgD, and BCL-2. Increased blood vessels in the interfollicular areas can be identified using CD31 staining. Cells infected with HHV-8, generally localised to mantle zones, show positive immunostaining for viral encoded latency-associated nuclear antigen-1 (LANA-1). In suspected cases, clonality analysis by immunoglobulin gene rearrangement studies and flow cytometry can be done to exclude lymphomas [4].

Diagnosis of CD on FNAC remains challenging, as the cytomorphology is nonspecific and can generate a wide range of differentials including reactive hyperplasia, autoimmune disorders, Rosai-Dorfman disease, or Hodgkin lymphoma, amongst others. Smears show a polymorphous population of lymphocytes, occasional neutrophils, eosinophils, hyalinised blood vessels, and clusters of FDCs, some of which may also exhibit emperipolesis [9]. FDCs can be confused with histiocytes because of their ample pale cytoplasm, which could have possibly led to the diagnosis of Rosai-Dorfman on cytology in our patient, particularly given the presence of emperipolesis.

Our patient presented with a localised enlargement of the unilateral axillary group of lymph nodes, and highly likely clinical possibilities included tubercular lymphadenopathy or a metastatic or lymphomatous process. Radiology and FNAC findings were also nonspecific, with histopathology proven to be the best diagnostic modality in this situation. Clinical information and data on CD are limited, primarily derived from various case reports across different countries [10–12]. A case series from India, stated as the largest from the region, has documented 50 cases of CD over a period of 11 years [13]. Since the incidence of this disease is low and experience with the diagnosis and management is limited, this case report aims to highlight the possibility of CD in cases of unexplained or massive lymphadenopathies, which can have a bearing on the future course of patient management.

Conclusion

CD is rare and underreported in literature. Diagnosis can be challenging, as radiological and FNAC findings could be non-specific. Histopathology, therefore, becomes the best diagnostic modality. CD must be considered as a possibility in cases of massive, unexplained lymphadenopathies.

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References

1. Castleman B, Towne VW. Case records of the Massachusetts General Hospital: Case No. 40011. N Engl J Med. 1954;250:26–30.
2. Castleman B, Iverson L, Menendez VP. Localized mediastinal lymph-node hyperplasia resembling thymoma. Cancer. 1956;9(4):822–30.
3. Keller AR, Hochholzer L, Castleman B. Hyaline-vascular and plasma-cell types of giant lymph node hyperplasia of the mediastinum and other locations. Cancer. 1972;29(3):670–83.
4. van Rhee F, Oksenhendler E, Srkalovic G, et al. International evidence-based consensus diagnostic and treatment guidelines for unicentric Castleman disease. Blood Adv. 2020;4(23):6039–50.
5. Simpson D. Epidemiology of Castleman disease. Hematol Oncol Clin North Am. 2018;32(1):1–10.
6. Carbone A, Borok M, Damania B, et al. Castleman disease. Nat Rev Dis Primers. 2021;7(1):84.
7. Fajgenbaum DC, Uldrick TS, Bagg A, et al. International, evidence-based consensus diagnostic criteria for HHV-8-negative/idiopathic multicentric Castleman disease. Blood. 2017;129(12):1646–57.
8. Dispenzieri A, Fajgenbaum DC. Overview of Castleman disease. Blood. 2020;135(16):1353–64.
9. Murro D, Agab M, Brickman A, Loew J, Gattuso P. Cytological features of Castleman disease: a review. J Am Soc Cytopathol. 2016;5(2):100–6.
10. Murakami M, Johkoh T, Hayashi S, et al. Clinicopathologic characteristics of 342 patients with multicentric Castleman disease in Japan. Mod Rheumatol. 2020;30(5):843–51.
11. Oksenhendler E, Boutboul D, Fajgenbaum D, et al. The full spectrum of Castleman disease: 273 patients studied over 20 years. Br J Haematol. 2018;180(2):206–16.
12. Gopal S, Liomba NG, Montgomery ND, et al. Characteristics and survival for HIV-associated multicentric Castleman disease in Malawi. J Int AIDS Soc. 2015;18(1):20122.
13. Singh A, Purkait S, Mallick S, et al. Clinicopathological profile of Castleman's disease in Indian population: experience from a tertiary care center. Indian J Hematol Blood Transfus. 2020;36:254–9.