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Case Series

Castleman's disease: a diagnostic and therapeutic quandary, case series from a tertiary cancer centre in South

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ABSTRACT

Castleman's disease (CD) is a rare, nonclonal lymphoproliferative disorder which was first described by Dr Benjamin Castleman. It can affect lymph nodes of any part of body, imitating both benign and malignant diseases. Co-occurrence and overlap in significant number of cases can be seen with lymphomas, amyloidosis and POEMS syndrome making its diagnosis and treatment challenging. We present a case series of four cases of CD, registered from January 2017 to August 2024.The mean age of presentation was 27 (13 - 42) years. There was male preponderance in the study with male to female ratio of 3:1. All the patients were immunocompetent. One patient belonged to pediatric age group where as other three were adults. Two patient was initially misdiagnosed out of which one received erroneous treatment for tuberculosis. In patients with multicentric CD, one was diagnosed with POEMS syndrome. Complete surgical excision was offered for unicentric CD. All the multicentric CD patients were treated with chemotherapy +/- immunotherapy. All the patients were alive on last follow up. Castleman's disease is a rare disease having outcomes ranging from a benign to potentially fatal course. CD possesses a diagnostic challenge, as lack of specific features makes it difficult to distinguish it from other diseases often leading to inaccurate diagnosis and superfluous treatment. POEMS syndrome is frequently associated with CD. Surgical excision remains the mainstay treatment for unicentric CD, whereas patients with multicentric disease chemoimmunotherapy remains an acceptable option however owing to multiple complexities and association with other concomitant diseases, the overall prognosis of MCD remains abysmal.

Keywords: Castleman's disease, Unicentric, Multicentric

INTRODUCTION

Castleman's disease (CD) is a rare, nonclonal lymphoproliferative disorder having distinct subtypes based on its etiological, pathological, and clinical features.[1] It can have varied presentations affecting lymph nodes of any part of body, imitating both benign and malignant diseases. Co-occurrence and overlap in significant number of cases can be seen with lymphomas, amyloidosis and POEMS syndrome.[2,3] Due to its rarity, limited information is available about the clinical and pathological variations and associations of this entity. Currently CD has been categorized into unicentric (UCD) and multicentric (MCD) forms based on the extent of lymph node involvement, along with other clinical features.

Systemic symptoms, generalized lymphadenopathy, and multiple organ involvement is hallmark of MCD. In contrast UCD has paucity of systemic symptoms, and is associated with younger age group. Histopathologically CD can be classified into: hyaline-vascular (HV), plasma cell (PC), and mixed types.[4-7] HV morphology is significantly more common in UCD, whereas the majority of MCD cases show PC morphology. Due to lack of

consensus on optimal therapeutic approach, the present study was conducted to analyse the clinical, pathological characteristics and treatment responses in patients with CD from a single medical institution.

CASE SERIES

Clinical details, radiological findings, pathological features, immunohistochemistry results and treatment outcomes were noted and analyzed for the four CD cases, who presented to our OPD from January 2017 to August 2024.

Case 1

A 13-year-old male from West Bengal, presented with complaints of swelling in left side of neck gradually increasing in size since the past 1 year. No history of B symptoms. No past medical history. Clinically 4×4 cm conglomerated mass was palpable on left cervical level IV. Investigations: CBC, LFT, RFT–normal. Viral markers-negative, bone marrow aspiration and biopsy-normal.

Whole body pet CT scan s/o–multiple enlarged lymph nodes seen in left level V of neck largest measuring 2.5×3.6 cm, increased uptake of b/l tonsil. Biopsy from the left cervical lymph node was s/o low grade NHL.

IHC was s/o NLPHL. Simultaneously second opinion was taken which revealed diagnosis of unicentric castlemans disease Hyaline vascular type. Patient was then referred to department of surgical oncology where the lymph nodal excision was done.

Case 2

A 27-year-old male from West Bengal presented in September 2023 with painless bilateral neck swelling since last 8 years. No history of B symptoms. Clinically bilateral cervical lymphadenopathy was present involving level 1b to level IV on both sides measuring 12×10 cm on right side and 10×9 cm on left side. Left axillary 2×2 cm node was palpable, mobile and firm in consistency. Routine blood investigations normal.

Viral markers-negative. Biopsy from lymph node was consistent with CD PC type. PET CT scan showed Multiple FDG avid enlarged level IA, bilateral level IB, bilateral level II-VI, bilateral axillary, retro pectoral lymph nodes. In view of the above report's patient was diagnosed with multicentric CD and was planned for 6 cycles of rituximab and prednisolone. Post 6 cycles he was symptomatically better. Size of the nodes decreased and patient was kept on Thalidomide maintenance. Last PET was suggestive of stable disease.

Case 3

A 42 years male accountant in a finance company presented to pulmonary medicine in January 2024 with c/o-cough since, 6 months, tingling and numbness in both hands and feet since last 5 months, breathlessness and fever since, 1 month. Patient has history of loss of appetite and weight loss of approximately 4 kgs in 4 months. He is a known case of diabetes and hypertension on medications. He was initially misdiagnosed with TB in December 2023 for which he took treatment for few months, defaulted thereafter.

PET CT was done s/o multiple lymph nodes in cervical and axillary region. Biopsy was s/o CD Mixed type. All other parameters of POEM'S syndrome were met, except for Monoclonal gammopathy. He was treated on the lines of POEMS syndrome.

Post 4 cycles of VTD, patient is symptomatically better. Repeat PET is suggestive of partial response. Patient is now planned for autologous stem cell transplant after completion of all 6 cycles.

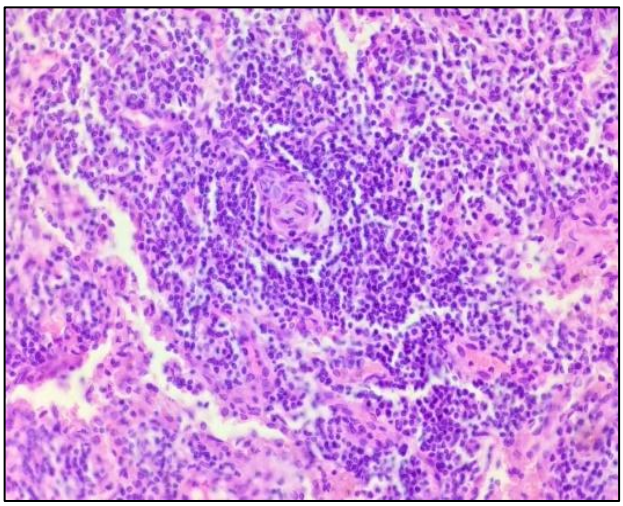

Figure 1: Showing an atretic follicle with onion skin ring pattern traversed by a vessel (10X).

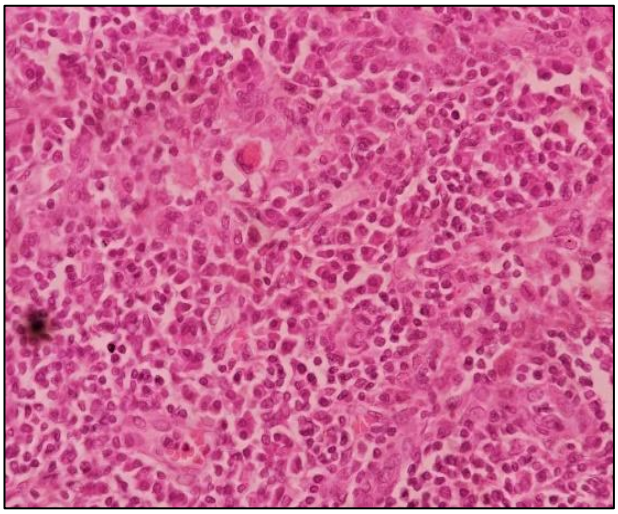

Figure 2: Showing plasma cells diffusely distributed in the interfollicular areas (10X).

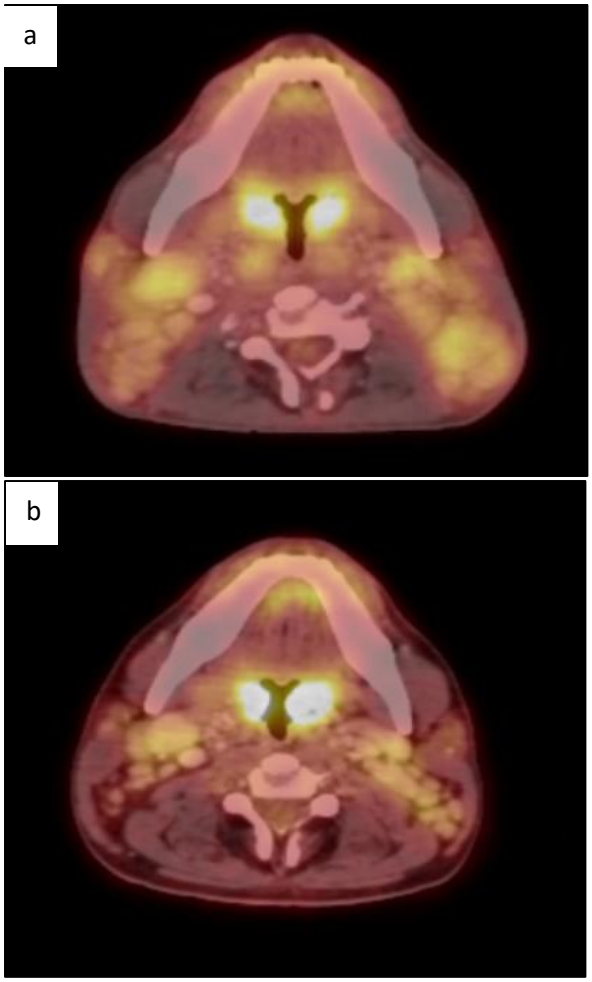

Figure 3(a, b): Showing pre and post treatment PET CT Scans of the patient diagnosed with MCD after 6 cycles of chemotherapy (PR).

Case 4

A 25-year-old female with no known comorbidities came to OPD with history of painless swelling in right side of the neck since 3 months. There was no history of loss of weight, loss of appetite, night sweats. O/E -3×4 cm firm, mobile and non-tender mass was palpable in right neck. Whole body PET CT scan was s/o multiple enlarged right supraclavicular lymph nodes, along with multiple sclerotic lesions in musculoskeletal system.

Biopsy from the lymph node was suggestive of CD HV variant. Final diagnosis was made as UCD with multiple sclerotic bony lesions. Due to her poor financial condition, and unwillingness for surgery, she was then started on oral chemotherapy with prednisolone, Thalidomide and cyclophosphamide. Currently she is doing well on the treatment and repeat imaging is suggestive of partial response. The mean age of presentation was 27 (13-42) years. There was male preponderance in the study with male to female ratio of 3:1. All patients were immunocompetent. Majority of patients were found to have MCD (3:1). One patient belonged to pediatric age group where as other three were adults. Neck swelling was the most common symptom. Systemic symptoms were more common in multicentric CD. Two patient was initially misdiagnosed out of which one received erroneous treatment for tuberculosis. In patients with multicentric CD, one was diagnosed with POEMS syndrome. One patient with UCD had sclerotic bony lesions. Complete surgical excision was offered for unicentric CD. All the multicentric CD patients were treated with chemotherapy +/- immunotherapy. All the patients were alive on last follow up.

DISCUSSION

CD (also known as Angio follicular lymph node hyperplasia and giant lymph node hyperplasia) was first described by Dr Benjamin Castleman in 1956 while publishing records of 12 patients with mediastinal lymph nodes in Massachusetts General Hospital.8 Several hypotheses for occurrence of UCD and MCD have been proposed till date.

Although CD can manifest in any age, but the data available suggests the usual age of presentation for UCD in fourth and MCD in sixth decade.[9,10] In our study the two cases of UCD were diagnosed in First and second decade, and two cases of MCD were diagnosed in third and fifth decade. There is scarcity of data regarding paediatric CD in our country. One retrospective analysis done in a tertiary care hospital had 14 patients belonging to paediatric population-all the patients were of UCD subtype.[11] Our study has one paediatric case which is also of UCD subtype. Lymphomas can co-exist or can sequentially occur in patients with CD. NHL is more frequently associated with MCD whereas UCD is commonly associated with UCD. Larroche et al published a case series of 8 CD patients associated with lymphoma in which foci of CD and lymphoma were same in nearly half of cases, which can possibly explain cooccurrence of NLPHL and CD in one the cases of our study.[3]

Around 30% of CD are associated with POEMS syndrome.[2] Elevated levels of IL-6 is postulated to be one of the mechanisms of the disease spectrum. POEMS syndrome must be distinguished from its Castleman disease variant, which is a distinct entity which is characterised by little to no peripheral neuropathy and absence of plasma cell disorder, but can manifest several of the minor diagnostic criteria for POEMS syndrome.[12] One of our patient had normal monoclonal light chains, but other minor criteria in form of skin changes, extravascular volume overload (pleural effusion), and organomegaly were present at time of diagnosis. Sclerotic bone lesions are commonly associated in patients with MCD.[13] Rare case reports of patients with UCD have been published.[14] One of our patients with UCD had sclerotic bone lesion which is a rare event in literature. In the absence of randomised control trials, the optimal treatment approach for CD remains controversial. Current treatment approaches are based on experience of published case

series and reports. Complete surgical excision remains the standard of care for UCD with 5-year cure rates of more than 90 %. MCD on the other hand exhibits variable clinical course, and its outcome is dictated by various factors. Rituximab, Siltuximab, and Tocilizumab with or without other systemic agents remain the mainstay of treatment for patients with MCD.[15] However the cost of these drugs remains a significant challenge to the patients particularly in low-income countries, making their use limited.

CONCLUSION

Castleman disease is a rare disease having outcomes ranging from a benign to potentially fatal course. Castleman disease possesses a diagnostic challenge, as lack of specific features makes it difficult to distinguish it from other diseases often leading to inaccurate diagnosis and superfluous treatment. POEMS syndrome is frequently associated with CD. Surgical excision remains the mainstay treatment for unicentric CD, whereas patients with multicentric disease chemoimmunotherapy remains an acceptable option however owing to multiple complexities and association with other concomitant diseases, the overall prognosis of MCD remains abysmal. With the introduction of newer drugs there has been a considerable improvement in outcomes, but their cost still remains a major factor limiting their use in LMIC countries like India.

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