Indian Journal of Pharmacy Practice., 2024; 17(1):75-77.
https://www.ijopp.org

Case Report

Case Report on Presentation of Castleman's Disease in a Patient with Mixed Connective Tissue Disorder

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ABSTRACT

Castleman disease is also known as Angio follicular lymph node hyperplasia or giant lymph node hyperplasia. It is an uncommon benign B-cell lymphoproliferative condition which involves a hyperactive immune system. A 56-years-old female patient presented to the Emergency department with complaints of generalized tiredness, abdominal pain and fever for two weeks. She had a history of burning micturition, vomiting, black coloured stools and bilateral axilla pain. PET CT WHOLE BODY SCAN showed multiple enlarged hypermetabolic bilateral axillary and subpectoral lymph nodes with surrounding fat stranding. Left axillary lymph node excision biopsy was done under general anaesthesia and histopathology report showed both hyaline and plasmacytic variant of Castleman's disease. The final diagnosis of mixed variant Castleman disease was made based on histological findings. MCTD is a rare autoimmune systemic disease whose features overlap with at least two connective tissue diseases like Rheumatoid Arthritis, Systemic Lupus Erythematosus and systemic sclerosis. With the patient's diagnosis of MCTD considered, the patient was on steroid therapy (Prednisone 40 mg/day) to which the patient responded well. The individual did not develop any adverse effects and no symptoms developed despite the steroid therapy.

Keywords: Castleman's disease, Mixed Connective Tissue Disorder, Mixed variant, Multicentric, Histopathology.

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Received: 11-09-2023;
Revised: 02-10-2023;
Accepted: 18-10-2023.

INTRODUCTION

Castleman disease is also known as Angio follicular lymph node hyperplasia or giant lymph node hyperplasia. It is an uncommon benign B-cell lymphoproliferative condition which involves a hyperactive immune system.[1] Castleman disease has the potential to affect any organ system and it presents with different systemic manifestations. There are three histopathological variants which are hyaline type, plasma cell type and the mixed type. The hyaline type accounts for 90% of the cases of Castleman disease and this type is usually localized to a single lymph node and is asymptomatic. This is known as the unicentric form. Contrast to this, the plasma cell type accounts for less than 10% of the cases and is frequently associated with systemic manifestations and immunological abnormalities.[2] The exact etiology of the disease has not been completely understood because of its rare presentation. Even though different therapeutic approaches are available for the diagnosis and treatment of Castleman disease Immunohistochemical (IHC) evaluation of the lymph node specimen in addition to routine H&E histopathological evaluation becomes the gold standard in arriving at a definitive diagnosis.[3]

CASE PRESENTATION

A 56-years-old female patient with a previous medical history of hypothyroidism and Type 2 Diabetes Mellitus was presented to the Emergency department with complaints of generalized tiredness, abdominal pain and fever for two weeks. She had a history of burning micturition, vomiting, black coloured stools and bilateral axilla pain. Her blood tests revealed that her hemoglobin was reduced (9.5 g/dL) along with the packed cell volume (30%). Her urine culture report showed probable significant growth of Enterococcus faecium. CT KUB showed minimal bilateral perinephric fat stranding with thickening of pararenal fascia and mild urothelial thickening in the right pelvis. When the ANA profile was done, it came back positive for nRNP/Sm thereby diagnosing the patient with Mixed Connective Tissue Disorder (MCTD). PET CT WHOLE BODY SCAN showed multiple enlarged hypermetabolic bilateral axillary and subpectoral lymph nodes with surrounding fat stranding. Left axillary lymph node excision biopsy was done under general anaesthesia and histopathology report showed both hyaline and

DOI: 10.5530/ijopp.17.1.11

plasmacytic variant of Castleman's disease. The final diagnosis of mixed variant Castleman disease was made based on histological findings as shown in Figures 1, 2 and 3.

The patient was started on steroid therapy concomitant with anti-pyretic and antibiotic therapy. The patient became symptomatically better and did not develop another episode of fever or chills while on the prescribed therapy.

DISCUSSION

Castleman disease is rare lymphoproliferative which was first discovered in the year 1956 by Benjamin Castleman. Castleman disease is also termed as localized nodal hyperplasia, angiomatous lymphoid hamartoma, or giant lymph node hyperplasia.[4] The pathogenesis of CD is not clear, but elevation of IL-6 levels is recognized. The increased levels of IL-6 and its overproduction can stimulate B lymphocytes proliferation. This can decrease the expression of vascular endothelial growth factor which can result in systemic symptoms like fever, proteinuria and anemia.[5]

MCTD is a rare autoimmune systemic disease whose features overlap with at least two connective tissue diseases like Rheumatoid Arthritis, Systemic Lupus Erythematosus and systemic sclerosis. The etiology of the disease is not clear but genetic predisposition is thought to play a role. It affects all races, and it is diagnosed by the presence of anti-U1-RNP antibody.[6]

CD may occur in any part of the body where the lymph nodes are present such as mediastinum, lungs, neck, axilla, mesentery, pelvis, or retroperitoneum. Unicentric CD patients are usually present with enlarging mass in one region without any significant symptoms whereas Multicentric CD is characterized by generalized lymphadenopathy in multiple regions with clinical symptoms like fever and night sweats. The final diagnosis is based on histopathological findings. The occurrence of CD can be at any age. In this particular case, the patient was found to have mixed variant of Castleman disease. The mixed type variant is the rarest variant as it consists of both hyaline-vascular and plasma variant in it. Some known causes of MCD are Human Immunodeficiency Virus (HIV) and Human Herpesvirus 8 (HHV-8) but 50-90% of patients with MCD test negative for HIV AND HHV-8 which is defined as idiopathic MCD which was diagnosed in this case.[7]

Unicentric CD can be treated by surgical excision of the affected node which allows full recovery without relapse in almost all cases. However, MCD variant requires multimodal therapies like monoclonal antibodies, cytotoxic chemotherapy and corticosteroids. Aggressive chemotherapy combination like cyclophosphamide, vincristine, doxorubicin and prednisone is recommended for patients with a good performance state. Steroid therapy or single agent chemotherapy is given for patients with a poor performance state to manage and improve their symptoms. Studies showed that a common feature among patients receiving steroid therapy was that they showed recurrence of the disease upon tapering or stopping steroid administration. With the patient's diagnosis of MCTD considered, the patient was on steroid therapy (Prednisone 40 mg/day) to which the patient responded well. The individual did not develop any adverse effect and no symptoms developed despite the steroid therapy. Anti-interleukin-6 antibodies have been successful in alleviating

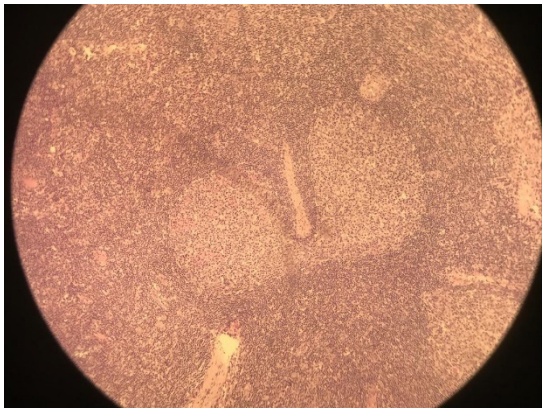

Figure 1: Histology slides-Twinning of germinal centres.

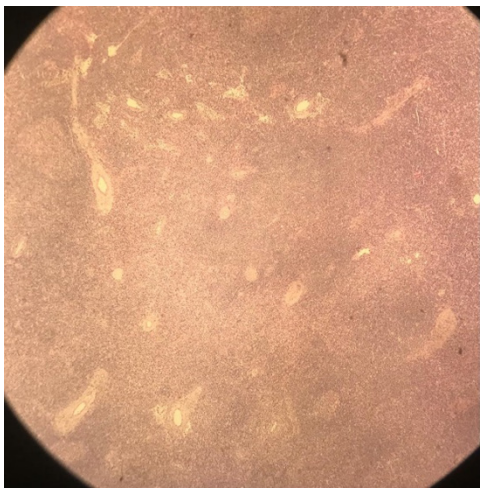

Figure 2: Low power view showing stretch atretic germinal centres and hyalinised blood vessels.

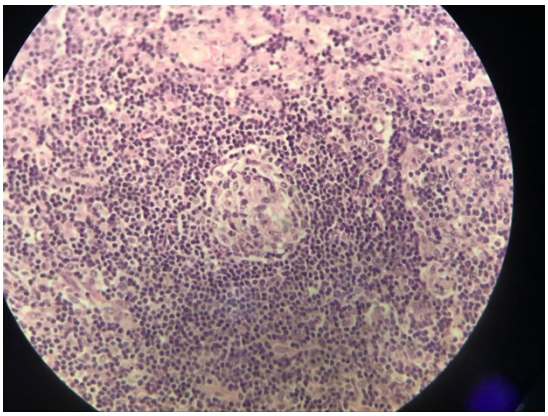

Figure 3: High power view showing atretic germinal centre with hyalinised blood vessels and hyalinised material.

the systemic manifestations of MCD. Siltuximab which is monoclonal antibody acting against IL-6 was evaluated in a randomized controlled trial in idiopathic MCD and has been approved for the same by US FDA, EMA and more than 30 other regulatory agencies.[1,3]

CONCLUSION

Multicentric mixed variant of CD is a very uncommon disease which can present as various diseases like Kaposi's sarcoma or malignant lymphomas. This is because of their similar features. MCTD with Castleman's Disease is rare association. Hence this case report brings forth the importance of Immunohistochemistry evaluation of lymph node biopsy specimens in addition to other routine tests to make a definitive diagnosis. This will be in consideration as a differential diagnosis when the presenting complaints include lymphadenopathy with systemic involvement.

ABBREVIATIONS

PET: Positron emission tomography; **CT:** Computed tomography; **CD:** Castleman disease; **MCTD:** Mixed connective tissue disease; **IHC:** Immunohistochemistry; **CT KUB:** Computed Tomography of Kidneys, Ureters and Bladder; **ANA:** Antinuclear Antibody; **HIV:** Human immunodeficiency virus; **HHV:** Human Herpesvirus; **MCD:** Multicentric Castleman's disease.

ACKNOWLEDGEMENT

We take this opportunity to show our deepest gratitude and thanks to Dr. Ashwin Karuppan, Senior Consultant Physician and Diabetologist, General Medicine, Gleneagles Global Health City, for guiding us through the case and helping us do our very best in finishing this case report.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

SUMMARY

- Presentation of Castleman's disease in a 56-years-old female patient with mixed connective tissue disorder.
- Histopathology report confirmed the diagnosis as mixed variant of Castleman's disease.
- Castleman's disease is an uncommon benign B-cell lymphoproliferative condition which involves a hyperactive immune system

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Cite this article: Karuppan AV, Ganesh D, Jayaseely CPS. Case Report on Presentation of Castleman's Disease in a Patient with Mixed Connective Tissue Disorder. Indian J Pharmacy Practice. 2024;17(1):75-7.