Open Access Journal

Indian Journal of Medical Research and Pharmaceutical Sciences

June 2018;5(6) ISSN: ISSN: 2349-5340

DOI: 10.5281/zenodo.1302974 Impact Factor: 4.054

CASTLEMAN DISEASE – A RARE CASE REPORT

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Keywords:

Castleman disease, giant lymph node hyperplasia,angiofollicular lymph node hyperplasia.

Abstract

Castleman disease (CD) is a rare disease of lymph nodes and related tissues.It was first described by Dr. Benjamin Castleman in the 1950s. It is also known as Castleman's disease, giant lymph node hyperplasia, and angiofollicular lymph node hyperplasia (AFH). CD is not cancer. Instead, it is called a **lymphoproliferative disorder**. This means there is an abnormal overgrowth of cells of the lymph system that is similar in many ways to lymphomas .Even though CD is not officially a cancer, one form of this disease (known as **multicentric Castleman disease**) acts very much like lymphoma.The exact etiology of CD is unknown. Signs and symptoms CD are often nonspecific, may include fever,weight loss,fatigue,night sweats, enlarged lymph nodes,nausea and vomiting; and an enlarged liver or spleen. Treatment may involve immunotherapy, chemotherapy, corticosteroid medications and/or anti-viral drugs.

Introduction

Castleman disease is a group of uncommon lymphoproliferative disorders characterized by lymph node enlargement. Castleman disease includes at least 3 distinct disorders—unicentric Castleman disease (UCD), human herpesvirus 8 associated multicentric Castleman disease (HHV-8-associated MCD), and idiopathic multicentric Castleman disease (iMCD).[1]

Unicentric Castleman disease (UCD) one or more enlarged lymph nodes are present in a single region of lymph nodes. It is the most common subtype of Castleman disease.Human herpesvirus 8 associated multicentric Castelman disease (HHV-8-associated MCD), enlarged lymph nodes are present in multiple lymph node regions and infection with human herpesvirus 8 (HHV-8, also known as Kaposi sarcoma-associated herpesvirus) is present. It is less common than unicentric Castleman disease (UCD) and diagnosed most frequently in patients infected with human immunodeficiency virus (HIV). In idiopathic multicentric Castleman disease (iMCD), enlarged lymph nodes are present in multiple lymph node regions and no known cause for the disease is identified. It is less common than unicentric Castleman disease (UCD)[2,3]

Multicentric Castleman disease can be further classified as:1)Multicentric Castleman disease without POEMS syndrome2)Multicentric Castleman disease with POEMS syndrome that involves areas of abnormal bone (osteosclerotic lesions)3)Multicentric Castleman disease with POEMS syndrome without osteosclerotic lesions. Exact underlying cause of multicentric Castleman disease (MCD) is poorly understood. Increased production of interleukin-6 (IL-6) by the immune system may contribute to the development of MCD. Increased production of IL-6 may result in an overgrowth of lymphatic cells. [4,5]

People with unicentric Castleman disease usually do well . Castleman disease may increase risk of lymphoma. Complications of multicentric Castleman disease can be life-threatening and may include:

- Infection leading to the failure of multiple organs
- Cancer, such as lymphoma or Kaposi's sarcoma

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Other conditions associated with MCD include amyloidosis, POEMS syndrome, autoimmune disease, hemolytic anemia, and immune thrombocytopenic purpura (ITP).[5]

Case presentation

A 11 yr old hindu male child,product of non-consaguinous marriage from lower middle socioeconomic status presented to our hospital with high grade ,documented fever for for 20 days associated with intermittent pain abdomen.No history of loose stools/vomiting/burning micturition/cough & cold.Child was neurodevelopementally normal and fully immunised as per NIS.Family and sibling history nothing suggestive.O/E-child was conscious,oriented,febrile.HR-110/min,RR-28/min,spo2-96%.Anthropometric measurements were within normal limit.On head to toe examination,no abnormality detected.No pallor,icterus,cyanosis,clubbing or edema with enlarged right inguinal lymphnode measuring 3*3cm single,nontender,firm and mobile was found [Fig.1]. On systemic examination of abdomen:inspection-normal contour,umbilicus central,few visible superficial veins over right side,no mass or visible peristalsis.Palpation-soft,tenderness over right hypochondriac area,liver enlarged 5cm firm,tender with smooth surface and sharp border.spleen not palpable,no other mass palpable.percussion and auscultation findings being normal.All other systemic examination being normal. On investigation:CBC and PS comment within normal limit,MPICT and CRP negative,urine routine and culture with blood culture negative,ICTC non-reactive,chest-x-ray normal, ANA,anti CCP,serum rheumatoid factor,IgM scrub and monospot negative.LFT with PT/INR normal.USG abdomen shows hepatosplenomegaly and multiple enlarged retroperitoneal,inguinal and iliac nodes. FNAC from right iliac lymphnode suggestive of Castleman disease(plasma cell type) multicentric variant[Fig.2].

Case discussion

Castleman disease is a rare disorder that involves an overgrowth cells of lymphatic system . Also known as giant lymph node hyperplasia and angiofollicular lymph node hyperplasia.Multicentric.Other associated conditions with Castleman disease are cancer of the lymphatic system (lymphoma), Kaposi's sarcoma and POEMS syndrome

Castleman disease is defined by a range of characteristic features seen on microscopic analysis (histology) of tissue from enlarged lymph nodes.[6] Histologically Castleman disease are categorized into common patterns:

- Hyaline vascular - regressed germinal centers, follicular dendritic cell prominence hypervascularity in interfollicular regions, prominent zones with an “onion-skin” appearance.[7]
- Plasmacytic – increased number of follicles with large hyperplastic germinal centers and sheetlike plasmacytosis .[6,7]
- Hypervascular - similar to hyaline vascular features, but seen in iMCD rather than UCD.[7]
- Mixed - presence of a combination of hyaline vascular, plasmacytic, and/or hypervascular features

The clinical utility of subtyping Castleman disease by histologic features is uncertain, as histologic subtypes do not consistently predict disease severity or treatment response.[6]
Diseases other than Castleman disease can present with similar histologic findings in lymph node tissue, includes following :[8]

- Infectious causes - Epstein-Barr virus, human immunodeficiency virus, tuberculosis
- Autoimmune diseases - Systemic lupus erythematosus, rheumatoid arthritis
- Lymphoproliferative disorders - lymphoma, autoimmune lymphoproliferative syndrome

Although the exact underlying cause of multicentric Castleman disease is unknown, it is thought to occur sporadically in people with no family history of the condition[9]The signs and symptoms of multicentric Castleman disease (MCD) are often nonspecific. However, if MCD is suspected, the following tests may be recommended to help establish the diagnosis and rule out other conditions that cause similar features:[4,5]
Blood tests can be ordered to evaluate the levels of Interleukin-6 (IL-6) and other substances in the body, which can be elevated in people with MCD. Imaging studies (such as a CT scan, PET scan, MRI scan, and/or ultrasound) can help identify enlarged lymph node(s) and other health problems.A biopsy of affected tissue, often a lymph node, is usually recommended to confirm the diagnosis

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Possible treatment options include:[4,5]

- Immunotherapy can be used to block the action of the interleukin-6 (IL-6), a protein that is produced in excess by the immune system of people with MCD
- Chemotherapy may be recommended to slow the growth of lymphatic cells
- Corticosteroid medications can reduce inflammation
- Anti-viral drugs can block the activity of HHV-8 or HIV (in people who are infected by these viruses)

Rituximab is often effective in the treatment of HHV-8–associated MCD. The IL-6 inhibitor siltuximab is often effective for the treatment of iMCD and is approved by the US Food and Drug Administration. See Treatment and Medication.

The Castleman Disease Collaborative Network is "a global initiative dedicated to accelerating research and treatment for Castleman disease." Its goals include the following:

- Facilitating collaboration among the global physician and researcher community
- Mobilizing resources to fund research
- Strategically investing in high-impact research
- Supporting patients and their loved ones

Patients, physicians, and researchers can contact the Castleman Disease Collaborative Network with questions.

Conclusion

In our setting we rarely found castleman disease.In this case on USG abdomen and pelvis ,we found Hepatosplenomegaly with multiple enlarged retroperitoneal, ingunal and iliac lymhpnodes.On FNAC of right iliac lymhnode suggests our diagnosis.Child was referred to higher centre for further management.

Any child presents with single group lymphadenopathy,1st of all a focus in the draining zone has to be searched.In India particularly in cervical nodes one has to rule out Tuberculosis.Before heading towards lymphoma one has to keep benign entity like Castleman disease as a possibility.Early diagnosis and timely management will have best outcome and certainly prevent progression to Lymphoma.

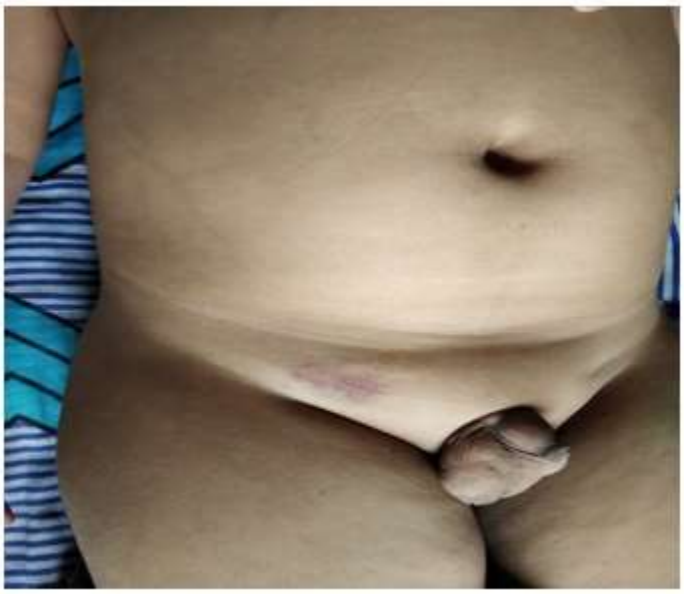

Fig-1

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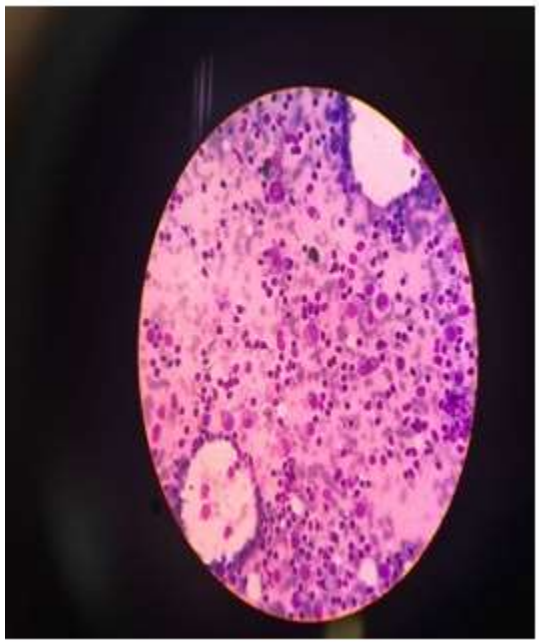

Fig 2

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