Case report

Mutlicentric Castleman's disease presenting in a young patient

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Abstract

Multicentric Castleman's disease (MCD) is a rare lymphoprofilerative disease and Its presentation in a young age population is unusual. Here, we report the case of a 28 year old Sri Lankan, male who was evaluated for lower limb edema and sensory type neuropathy along with skin thickening and pigmentation. He was found to have generalized lymphadenopathy and hepatosplenomegaly. His investigations revealed evidence of demyelinating type sensory- motor polyneuropathy, pulmonary hypertension, hypothyroidism. However studies conducted for HIV viruses and monoclonal gammopathy were negative. An excision biopsy of an Inguinal lymph node of his right side axila revealed changes supportive of a diagnosis of multicentric Castleman's disease. Despite being a rare disease and even rarer in a young population, diagnosis of MCD/POEMS syndrome should be suspected in patients' presenting with similar features described above. MCD is associated with many malignancies and has poor prognosis.

Key words: Castleman disease, Neuropathy, Edema, Pulmonary hypertension, Skin sclerosis

Funding: None
Competing interest: None
Received: 20 May 2019 **Accepted revised version:** 24 July 2019 **Published:** **23** September 2019
DII: http://doi.org/10.4038/amj.v12i1.7654

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Introduction

Castleman's disease (CD) is a rare group of lymphoproliferative disorders of unknown aetiology and pathogenesis. CD has no established clinical trials for treatment of the disease. Here, we report an unusual case of multicentric Castleman's disease presenting in a young Sri Lankan patient.

Case Presentation

A 28-year-old male from Rathnapura, Sri Lanka was investigated for bilateral lower limb swelling and numbness for two years duration. He also complained of worsening breathing difficulty along with progressive skin changes of increased pigmentation and thickening.

His clinical examination revealed generalized lymphadenopathy that was non tender, firm, non-matted with average size of 2-3 cm. He had increased skin thickening extending proximally up to mid arm. He had no evidence of acrosclerosis, hand edema, digit loss or features of Raynaud's type phenomena. Abdominal exam revealed hepatosplenomegaly.

Among the extensive investigation workup that was performed on this patient, he was noted to have a persistently elevated erythrocyte sedimentation rate but negative results for anti nuclear, anti double stranded DNA, anti centromere and anti SCL 70 antibodies.

Nerve conduction study revealed demyelinating type sensory-motor polyneuropathy whilst serum protein electrophoresis studies revealed polyclonal hypergammaglobulinaemia. Examination of skin biopsy specimens was normal. He was also diagnosed with hypothyroidism.

Imaging studies with ultra sound scan and CT scan of the abdomen revealed hepatosplenomegaly and a haemangioma of the liver. There was evidence of pulmonary hypertension noted with echocardiography whilst normal results of imaging studies of the lung and spirometry study revealed only mild reversible obstruction. His bone marrow revealed normocellular active marrow, 2% plasma cells without evidence of malignancy infiltrating the bone marrow.

Table 1: Diagnostic criteria for POEMS syndrome

Mandatory major criteria
Monoclonal plasma cell proliferative disorder
Polyneuropathy
Other major criteria (one required)
Sclerotic bone lesions
CD
Vascular Endothelial Growth Factor level elevation
Minor criteria (one required) Organomegaly – Splenomegaly, Hepatomegaly, Lymphadenopathy Volume overload – Extravascular (Oedema, Pleural effusion, Ascities) Endocrinopathy – Adrenal, Thyroid, Gonadal, Parathyroid, Pancreatic Skin changes – Hyperpigmentation, Hypertrichosis, Plethora, Flushing, Acrocyanosis, White nails, Haemangioma
Papilledema
Thrombocytosis, Polycythaemia

An excision biopsy performed on a lymph node of the right axilla, revealed features supportive of a diagnosis of mulitcentric hyaline vascular variant of CD. The specimen revealed scattered large follicles (black arrowheads) showing vascular proliferation and hyalinisation of germinal centers surrounded by tight concentric layering of lymphocytes (onion skin appearance) but no evidence of dysplasia or malignancy (Figure 1). The patient however had undergone 3 separate biopsies of enlarged lymph nodes on separate sites that revealed non specific, reactive type changes prior to the above mentioned final fourth lymph node biopsy. He was thereafter referred to the oncology unit at National Cancer Institute Maharagama (NCIM) for further management but was recommended to be screened regularly for development of lymphoma or monoclonal gammopathy.

Discussion

CD may present with two types of disease states, namely, unicentric disease and multicentric disease (MCD). Both types of CD differ from their presentations and prognosis (1).

CD also has 3 different types of histological variants (2), namely, Hyaline vascular variant, Plasma cell variant and the HHV8 positive CD. Unicentric disease is associated with a benign lymphoproliferative disease of young adults.

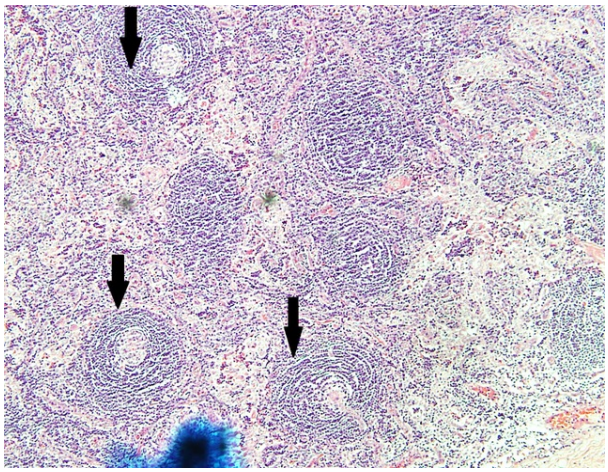

Figure 1: Histology of the lymph node-biopsy of the patient; note the scattered large follicles (black arrowheads) showing vascular proliferation and hyalinisation of germinal centers.

MCD commonly presents at an older age (50 -60 years) but HIV associated patients may present at a younger age. This patient was not found to have HIV infection. MCD universally presents with generalized lymphadenopathy, whilst hepatosplenomegaly is known to occur. It is also associated with anemia, high ESR, hypoalbuminaemia and hypergammaglobulinaemia (3). MCD is associated with POEMS syndrome. A diagnosis of POEMS syndrome requires the criteria showed in Table 1. However, further studies conducted including serum protein electrophoresis, urine protein electrophoresis and serum protein immunofixation electrophoresis along with bone marrow examination studies on this patient did not reveal evidence of monoclonal gammopathy. Therefore, this patient did not have POEMS syndrome. However, he may still be at a risk of development of monoclonal gammopathy and resultant POEMS syndrome in later years. Patients with MCD have poor prognosis, since they develop multiorgan failure due to progression of the disease or acquiring life threatening infections along with increased risk of development of malignancies such as non-Hodgkin lymphoma and Kaposi sacorma (4)

There are no randomized clinical trials supportive of the treatment. Treatment options include Anti-CD20 monoclonal antibody therapy (eg; Rituximab), cytotoxic chemotherapy, glucocorticoids, IL-6-directed therapy and antiviral drugs. Rituximab therapy is now emerging as the treatment of choice for most patients including HIV positive patients (5).

Conclusion

CD is a rare disease. Further knowledge is required about its etiology, pathogenesis and treatment along with establishment of a registry of patients with CD.

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