

## Case Report

# Idiopathic multicentric Castleman disease -a case report

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## Introduction

Castleman disease (CD), which is also known as angiofollicular lymph node hyperplasia or giant lymph node hyperplasia, is a rare disorder occurring in the elderly. CD is divided into 3 main subtypes, unicentric CD, human herpes virus-8 [HHV-8] associated multicentric CD and HHV-8 negative/ idiopathic multicentric CD (iMCD). There are 3 subtypes of iMCD, POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes) associated iMCD, TAFRO syndrome (thrombocytopenia, anasarca/ascites, reticulin fibrosis in bone marrow, renal dysfunction, organomegaly) iMCD and 'not otherwise specified' iMCD [1]. Patients usually present with fever, night sweats, weight loss, symptoms of fluid overload, lymphadenopathy and hepatosplenomegaly [2].

Here we report a case of a 55-year-old male who presented with bilateral lower limb swelling and symptomatic anaemia. He was diagnosed as having, 'not otherwise specified iMCD'. His symptoms improved following treatment with corticosteroids and chemotherapy. Cases of 'not otherwise specified iMCD' are rare in the literature.

## Case presentation

A 55-year-old male, with a past history of hypertension, presented with bilateral lower limb swelling over two weeks. He complained of significant loss of appetite and loss of weight over 3 weeks associated with exertional dyspnoea, generalized fatigability and palpitations. He denied any skin rashes, oral ulcers, high risk sexual behavior or past history of blood transfusion. There was no family history of autoimmune diseases, renal diseases or malignancy.

On examination, he had pallor, periorbital oedema and bilateral ankle oedema. There was left sided cervical and axillary lymphadenopathy. Abdominal examination revealed a non-tender moderate hepatomegaly. There was no splenomegaly. Other systems examination was normal.

Full blood count revealed a total white cell count of  $6.83 \times 10^9$  /L [ N-40.2%, L-23.4%], haemoglobin of 5.4 g/dl and a platelet count of  $15 \times 10^9$  /L. Blood picture was reported as a reactive film with severe thrombocytopenia and severe anaemia of chronic of disease and iron deficiency anaemia. Erythrocyte sedimentation rate was 65mm/hr. Lactate dehydrogenase level was 265U/L. Reticulocyte count was 6.1%. Urine full report revealed proteinuria 2+ without red cells. Urine protein to creatinine ratio was 2717.83 mg/mmol. Serum creatinine was 120.49micromol/L while serum electrolytes were normal. Liver function tests revealed a alanine transaminase level of 119 U/L [ $<45$ ], aspartate transaminase level of 164.5 U/L [ $<35$ ],total protein of 6.2 g/dL [6.6-8.3], albumin of 3.1 g/dL [3.5-5.3], globulin of 3.2 g/dL, alkaline phosphatase of 139.7 U/L [30-120],total bilirubin of 8.22 micromol/L [2-21], direct bilirubin of 4.46 micromol/L ( $<5$ ) and gamma glutamyl transpeptidase of 26.1 U/L ( $<49$ ).Electrocardiography, 2D-echo and chest X-ray were normal. Anti-nuclear antibodies were positive but anti-double stranded DNA antibodies and rheumatoid factor were negative. Retroviral serology was negative. Ultrasound scan abdomen and contrast enhanced computed tomography of chest, abdomen and pelvis revealed moderate hepatomegaly, increased cortical echogenicity in bilateral kidneys with altered cortico-medullary demarcation along with para-aortic lymphadenopathy. Cervical lymph node biopsy features were consistent with plasma cell type Castleman disease. Bone marrow biopsy revealed bone marrow involvement by Castleman disease. Serum protein electrophoresis revealed a monoclonal band in the gamma region with a paraprotein concentration of 4.66g/L. Urine Bence-Jones proteins were negative and skeletal survey was normal. Nerve conduction studies did not reveal any evidence of polyneuropathy.

A diagnosis of idiopathic MCD was made. This was not associated with POEMS syndrome or TAFRO syndrome. Therefore, the patient was diagnosed to have 'not otherwise specified' idiopathic MCD.

Since the patient presented with symptomatic anaemia, three units of packed red cells were transfused. He was started on chemotherapy with cyclophosphamide and vincristine along with prednisolone. Following 6 cycles of chemotherapy, his symptoms and cytopenias improved over the next three months.

## Discussion

Castleman disease is a heterogenous group of lymphoproliferative disorders, which were first described by Dr. Benjamin Castleman in 1954. Depending on the number of groups of lymph nodes involved, there are two main types, unicentric CD and multicentric CD. In unicentric CD only a single group of lymph nodes are involved whereas in multicentric CD multiple regions of lymph nodes are involved. Multicentric disease is further divided into HHV-8 associated disease and idiopathic MCD. According to the available literature, MCD is more common than UCD and HHV-8 associated disease is rare [3]. A study done by Talat *et al* among HIV negative patients revealed that the median age CD is diagnosed is 37 years with UCD at 30 years and MCD at 52 years [4].There are 3 histological sub-types of CD, hyalinevascular, plasma cell and mixed [5].

UCD usually presents with a single enlarged lymph node. Over 50% of cases are asymptomatic. MCD is a systemic disorder presenting with constitutional symptoms, generalized lymphadenopathy, hepatosplenomegaly, anaemia, hypoalbuminaemia and hypogammaglobulinaemia [5]. The 3 subtypes of iMCD present differently. POEMS- associated iMCD presents with polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder and skin changes including acrocyanosis, hypertrichosis, plethora, telangiectasia and hyperpigmentation [6]. TAFRO syndrome iMCD presents with thrombocytopenia, anasarca, myelofibrosis, renal dysfunction, and organomegaly. 'Not otherwise specified' iMCD presents with thrombocytosis, hypergammaglobulinemia, and mixed or plasmacytic histopathologic features.

The exact aetiology of UCD is not known. HHV-8 is known to cause HHV-8 associated MCD. The etiology of iMCD is not known. But several autoimmune, inflammatory, neoplastic and infectious mechanisms are known to contribute. All three subtypes have cases with elevated levels of human interleukin 6 (IL-6) or viral IL-6.

Diagnosis is challenging since there are no recognized diagnostic criteria and since there is overlap with other infectious, autoimmune and malignant disorders [7]. In our case, even though HHV-8 serology was not available, since retroviral serology was negative the patient was diagnosed as having idiopathic multicentric CD.

Even though CD clinically mimics lymphoma, it is different from malignant lymphoproliferative disorders histologically as well as prognostically. UCD has good prognosis and the definite treatment is surgical excision of involved lymph nodes. MCD has a variable prognosis and there are no clinical trials regarding standard treatment. A wide variety of treatment including surgery, steroids, rituximab and chemotherapy have been suggested [8]. A literature review revealed that 24 (19%) of 128 patients with iMCD were diagnosed with separate malignant diseases. Of these 11 had haematological malignancies and 13 had solid organ tumors [9].

## Conclusion

This case emphasizes the importance of considering CD as a differential diagnosis in patients presenting with systemic symptoms and lymphadenopathy. Histological diagnosis is important to differentiate from lymphoma since the prognosis is different.

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