

## Case Report

### Rosai Dorfman disease : A rare association of sero positive rheumatoid arthritis

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#### Abstract

Rosai-Dorfman disease (RDD) is a rare self-limiting histiocytic proliferative disorder that mostly presents with cervical lymphadenopathy with constitutional symptoms. It is associated with connective tissue disease in 10% of cases. Here we present a case of 14-year-old boy who presented with a prolonged fever, arthralgia and generalize lymphadenopathy. Eventually the diagnosis of RDD associated with early Rheumatoid arthritis was made.

#### Key words:

Rosai Dorfman, Sero-positive rheumatoid arthritis

#### Introduction

In 1969, Sinus histiocytosis with massive lymphadenopathy (SHML) was first described by Rosai and Dorfman (1). Marked dilatation of the lymph node sinuses containing histiocytes was the striking histopathological characteristic feature of SHML (1). This rare disease has unknown aetiology and commonly presented with fever, elevated inflammatory markers such as ESR, cervical lymphadenopathy and increased globulin level (2). This rare disorder said to be isolated or associated with malignancy and auto immune conditions (3). SHML is associated with autoimmune disorders such as systemic lupus erythematosus, idiopathic juvenile arthritis, and autoimmune haemolytic anaemia in 10% of patients (3). We report a case of Rosai-Dorfman syndrome with early manifestations of Rheumatoid arthritis.

#### Case report

A 14-year-old boy, presented with two months history of intermittent fever which was associated with arthralgia, involving small and large joints symmetrically. He did

not have any features to suggest systemic infections. He did not have photosensitive rashes, oral ulcers nor alopecia. He was on carbamazepine since childhood for epilepsy. There was no travel history in recent past. He did not have known allergy to neither food nor drugs.

On examination, he was febrile, pale and had generalised lymphadenopathy. He had multiple papules on extensor surfaces of his forearms and legs. There were no signs of inflammation over the joints. Examination of other systems were unremarkable.

Laboratory tests revealed that he had microcytic hypochromic anaemia (Hb 8.4g/dl, MCV 71, MCH 21.2), with normal range of white cell and platelet count, and elevated inflammatory markers (ESR 120 mm1st hour, CRP 54). His peripheral blood smear showed reactive white cells, and hypochromic microcytic red cells with marked rouleaux formation. His liver transaminases, bilirubin, serum creatinine, and electrolytes were normal. His serum protein level was high and showed reversed albumin globulin ratio (albumin 23g/l, globulin 60g/l) as well. His serum LDH was 339 U/l, and serum ferritin was 231 µg/l.

Further, his cultures and gram staining of blood and urine were negative. Tests for HIV, syphilis, tuberculosis, toxoplasma, CMV and EBV were negative.

His chest x-ray showed bilateral hilar lymphadenopathy. The ultrasonography of neck revealed cervical lymphadenopathy with preserved fatty hilum. Computed tomography of chest and abdomen revealed multiple lymph node enlargement involving para-tracheal, subcarinal, hilar, para oesophageal and both axillary regions. The largest lymph node was 36mm. Mild hepatomegaly was seen. Electrocardiogram and 2D Echocardiography were normal.

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Because of the poor response to broad spectrum antibiotics and negative results for infective focus, extensive investigations were arranged for pyrexia of unknown origin associated with arthralgia and lymphadenopathy. Axillary lymph node biopsy revealed reactive lymphoid hyperplasia and distended sinuses with histiocytosis. Immunohistochemistry highlighted histiocyte antigens S-100 and CD68. Bone marrow biopsy shows normal reactive marrow. Skin biopsy was normal. (Figure 1)

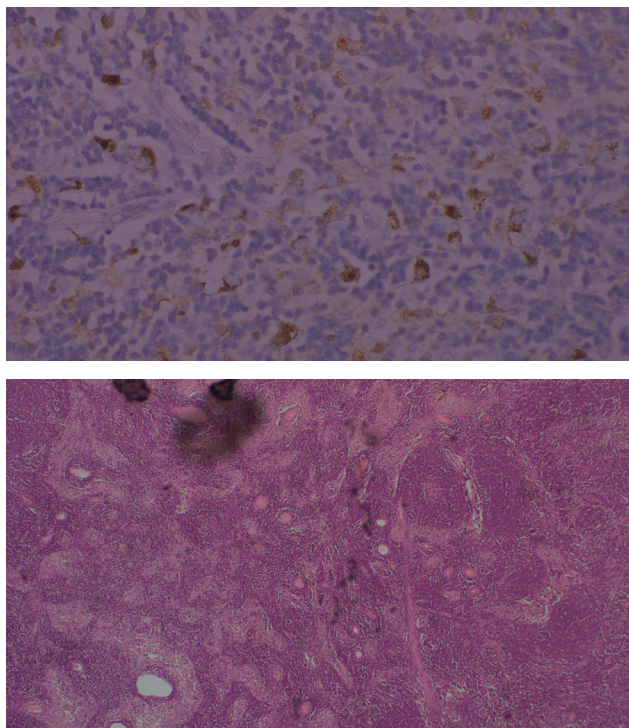


Figure 1 - Bone marrow biopsy and Skin biopsy

Serological studies revealed positive ANA titre 1:1280 which was fine speckled appearance. Both DsDNA and anti U1RNP antibodies were negative in this patient. Both rheumatoid factor and anti CCP antibodies were positive. Complement levels of C3 and C4 were normal.

Based on the clinical findings and investigations; the diagnosis of Rosai-Dorfman-Destombes disease was made. He was prescribed NSAIDs for joint pain and discharged after settling of fever.

After one month he came with inflammatory type of symmetrical polyarthritis involving large and small joints. Diagnosis of Rheumatoid arthritis was made according to 2010 ACR/EULAR classification criteria. He was started on prednisolone and methotrexate and, followed up in medical clinic. Arthritis gradually subsided and lymphadenopathy also resolved after 2 months.

## Discussion

RDD can occur as an isolated disease or in association with autoimmune, hereditary, and malignant diseases. (3) RDD is associated with autoimmune disorders in 10% of patients, such as systemic lupus erythematosus, idiopathic juvenile arthritis, and autoimmune haemolytic anaemia. The pathogenesis of the disease is not well established but various viruses such as HIV, EBV and CMV has been associated with disease. (3) Extra nodal involvement is seen around 43% of cases. (4)

Imaging features are nonspecific for RDD and may be resembles lymphoproliferative disease. Diagnosis of disease made by histology combined with clinical information. The diagnostic pathologic features of nodal RDD include the sinus expansion of large histiocytes and immunophenotype of the large RDD histiocytes is characterized by cytoplasmic and nuclear S100 positivity, with CD68 and variable CD163 and CD14 positivity. (3)

Our patient presented with pyrexia of unknown origin with lymphadenopathy and arthralgia. Rheumatoid factor and anti CCP antibodies were positive. An Axillary lymph node biopsy was taken for further evaluation as the rheumatoid arthritis is less likely to cause generalized lymphadenopathy. The biopsy revealed reactive lymphoid hyperplasia, distended sinuses with histiocytosis. Furthermore, the immunohistochemistry study highlighted the histiocyte antigen S-100 and CD68. RDD with early rheumatoid arthritis was made as final diagnosis. Our patient also had skin nodule, but skin biopsy didn't show evidence of cutaneous manifestations of RDD. Skin is the most common extra nodal site of RDD, but isolated skin RDD is very rare, only few reported in case reports. (5)

Management of RDD is mainly observation once autoimmune causes and malignancy ruled out. Spontaneous remission occurs in around 20 to 50 percent of cases. Surgery may be curative if it is large focal lesions. Immune therapy, chemotherapy, radiotherapy, corticosteroids and sirolimus have variable effect on disease. (3)

We have treated our patient with prednisone and DMARDS because of associated rheumatoid arthritis. No specific treatment given for RDD. Patient well responded to treatment, joint pain settled and lymphadenopathy also resolved.

## Conclusion

Rosai-Dorfman disease (RDD) should be considered as a differential diagnosis when patient presented with pyrexia of unknown origin with lymphadenopathy. Following diagnosis of this condition patient should be carefully assessed to exclude associated connective tissue disorder.

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