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### Case Report

# ROSAI DORFMAN DISEASE WITH HAEMOLYTIC ANAEMIA IN AN ELDERLY PATIENT: A RARE PRESENTATION

Gupta N<sup>1</sup>, Fatima J<sup>2\*</sup>, Karoli R<sup>3</sup>, Shukla V<sup>4</sup>, Lal N<sup>5</sup> Mishra A<sup>6</sup>

<sup>1</sup>Assistant Professor, Department of Medicine, Era's Lucknow Medical College & Hospital, Lucknow, India

<sup>2</sup>Professor and Head, Department of Medicine, Era's Lucknow Medical College & Hospital, Lucknow, India

<sup>3</sup>Professor, Department of Medicine, Era's Lucknow Medical College & Hospital, Lucknow, India

<sup>3</sup>Associate Professor, Department of Medicine, Era's Lucknow Medical College & Hospital, Lucknow, India

<sup>4</sup>Professor, Department of Pathology, Era's Lucknow Medical College & Hospital, Lucknow, India

<sup>5</sup>Junior Resident, Department of Medicine, Era's Lucknow Medical College & Hospital, Lucknow, India

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\*Corresponding Author: **Fatima J**

Professor and Head, Department of Medicine, Era's Lucknow Medical College & Hospital, Lucknow, India, Mobil: 9956290759

## ABSTRACT

Rosai Dorfman disease (RDD) or sinus histiocytosis with massive lymphadenopathy (SHML) is a rare disorder that typically manifests as lymphadenopathy and systemic symptoms. The authors report a 56 year old man who presented with massive generalised lymphadenopathy with haemolytic anaemia. Histopathological examination demonstrated lymphophagocytosis (emperipolesis) consistent with a diagnosis of RDD. Clinicians need to be aware of this entity which can present as a rare differential diagnosis of benign lymphoproliferative disorders.

**Keywords:** Sinus Histiocytosis, Massive Lymphadenopathy, Haemolytic Anaemia, Emperipolesis.

## INTRODUCTION

Sinus histiocytosis with massive lymphadenopathy (SHML) also known as Rosai-Dorfman Disease (RDD), was first reported in 1969<sup>1</sup>. It typically manifests as massive lymphadenopathy and systemic features. Physicians frequently encounter patients with generalized lymphadenopathy with anaemia and they need to be aware of rare conditions which can present like this. Here we describe RDD disease as a rare differential diagnosis of benign lymphoproliferative disorders. Its association with haemolytic anaemia is even rarer.

## CASE REPORT

A 56 year old man presented with complaints of fever on and off and progressive bilateral cervical lymphadenopathy since 6 months. He had progressive weakness since 6 months but no history of weight loss or loss of appetite. He had no addictions and no significant past history. General examination was unremarkable except significant pallor, mild icterus and multiple bilateral cervical, axillary and inguinal lymphadenopathy (Fig 1&2). Lymph nodes were 3-4 cm, firm, smooth, nontender, mobile and discrete. Haematological investigations revealed Hb -7.0gm%, TLC-8000/ mm<sup>3</sup>, Platelets count -2.10 lakhs/mm<sup>3</sup>. Erythrocyte

sedimentation rate (ESR) 105mm/hr, Reticulocyte count-8%, LDH-900 mg/dl, GBP- schistocytes and fragmented and nucleated RBC's. Bone marrow examination- erythroid hyperplasia Other investigations showed Total bilirubin- 3.8 mg/dl, Indirect bilirubin -2.8 mg/dl, Direct bilirubin -1.0 mg/dl, SGOT, SGPT, Alkaline Phosphatase -normal, Direct coomb's test -positive. Chest X-ray was normal. Ultrasound abdomen showed mild splenomegaly. Serological test for HIV - Negative.

Histopathological examination of a left cervical lymph node biopsy displayed dilated sinuses in the parenchymal region with extensive infiltration consisting of histiocytes and chronic inflammatory cells. A large number of lymphocytes could be seen in cytoplasm of histiocytes suggesting lymphophagocytosis - emperipolesis (Fig.3). Lymphoid follicles were hypertrophied and showed germinal activity. Immunohistochemical staining of histiocytes was positive for S-100 gene product expression.

## DISCUSSION

Sinus histiocytosis with massive lymphadenopathy is a rare disorder characterized by a non-malignant proliferation of histiocyte within lymph node sinuses and lymphatics in extranodal sites. There is no evidence to support

immunodeficiency, autoimmune disease or a neoplastic process for the etiology of the disorder. An association with Epstein-Barr virus (EBV), cytomegalovirus (CMV), Brucella, Klebsiella, or human herpes virus 6 has been suggested but not proven.<sup>2-4</sup> Usually presents in young adults. Hepatosplenomegaly is uncommon. Frequently accompanied by fever, elevated ESR, neutrophilia, polyclonal gammopathy. The classic histology is characterized by effacement of nodal architecture and dilatation of lymph node sinuses by lymphocytes, plasma cells and numerous characteristic histiocytes with large vesicular nuclei and abundant clear cytoplasm. Many of these histiocytes, also known as RDD cells, contain intact lymphocytes, and sometimes plasma cells and red blood cells, within their cytoplasm. Emperipolesis (the process whereby cells enter and transit through a cell evading

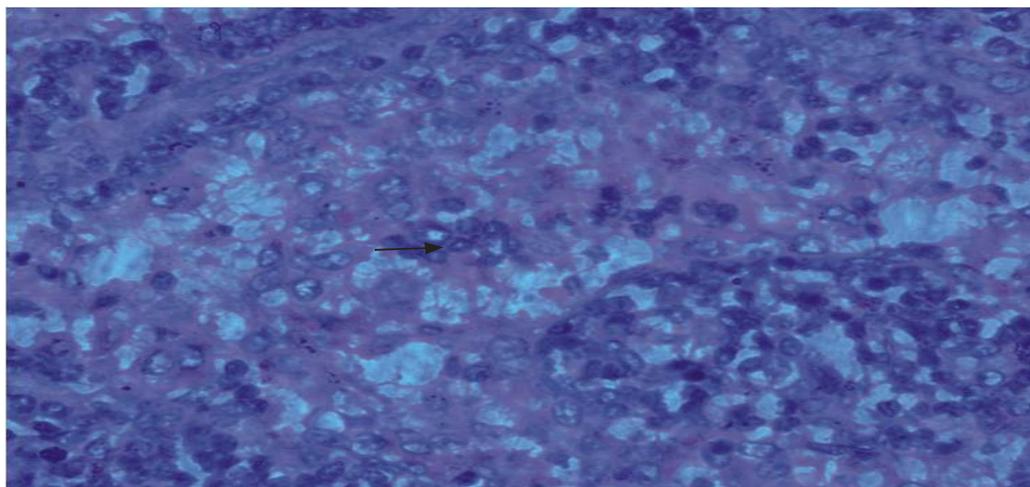
cellular degradation) is a classical finding and it differentiates it from other diseases. It was first described by Humble *et al.*<sup>5</sup> The differential diagnosis of a chronic inflammatory infiltrate containing numerous large histiocytes includes granulomatous diseases such as Wegener's granulomatosis, sarcoidosis, Hodgkin's disease, and Langerhans' cell histiocytosis (LCH). When extranodal sites are involved, similar morphologic features to the nodal counterpart are seen although with more fibrosis, fewer typical RDD histiocytes, and less prominent emperipolesis.<sup>6</sup> The most useful immunohistologic marker for SHML histiocytes is the expression of the S-100 protein.<sup>7,8</sup> In addition, SHML histiocytes stain for CD68, CD64, alpha-1 antitrypsin, and interleukin-2 receptor and are negative for CD1a.



Figure 1: Massive cervical lymphadenopathy



Figure 2: Bilateral inguinal lymphadenopathy



Histopathological examination of a left cervical lymph node biopsy displayed dilated sinuses in the parenchymal region with extensive infiltration consisting of histiocytes and chronic inflammatory cells. A large number of lymphocytes could be seen in cytoplasm of histiocytes suggesting lymphophagocytosis - emperipolesis (Fig.3)

The clinical course of SHML is characterized by spontaneous resolution without any specific treatment in most cases. Treatment is required when the condition is organ threatening or life threatening. For patients with high fever without other symptomatology steroid therapy may be instituted. Surgical debulking may be used in cases where vital organ function is

compromised. The role of additional therapies, such as chemotherapy or radiation therapy, is minimal. However all patients deserve long-term follow-up, since the natural history of the disease is quite variable, usually alternating periods of exacerbations and resolutions or, rarely, pursuing a progressive course.

Our patient was elderly, though the disease commonly presents in young<sup>9</sup>. Autoimmune haemolytic anaemia is a recognized complication of Non Hodgkin's lymphoma or Chronic lymphocytic leukaemia due to which a differential diagnosis of these disorders was made until we received the report of lymph node biopsy showing sinus histiocytosis. Autoimmune haemolytic anaemia in Rosai Dorfman Disease has been reported but is an uncommon association.<sup>10</sup>

### CONCLUSION

SHML is a rare disease of unknown etiology. Clinicians need to be aware of this entity which can present as massive generalized lymphadenopathy clinically resembling lymphoma, malignancy, hemophagocytic syndrome, infection, langerhans histiocytosis. The presence of autoimmune hemolytic anaemia which is a rare association of this disorder makes the clinical picture more complex. Lymph biopsy is a useful tool for diagnosis.

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