CASE REPORT

# Rosai-Dorfman Disease

**Sindhu Sharma, Subhash Bhardwaj, Deepa Hans**

**Abstract**

Rosai-Dorfman Disease (RDD) or Sinus Histiocytosis with massive lymhadenopathy (SHML) is a rare, benign proliferative disorder of histiocytes, sometimes showing familial incidence. It is mainly characterized by painless bilateral cervical lymph node enlargement and is often associated with fever and leucocytosis. It presents in the first or second decades of life, though any age group can be affected. Without the awareness about RDD, the diagnosis of RDD is unexpected especially in South East Asian Countries where certain lymphadenopathies such as tuberculosis, metastatic nasopharayngeal carcinoma and lymphomas are common. RDD is commonly missed and so its revision would seem worthwhile, this case illustrating the disappearance of the lymphadenopathy without treatment.

**Key Words**

Sinus histiocytosis with massive lymphadenopathy (SHML), Lymphophagocytosis. Emperipolesis, Rosai-Dorfman disease (RDD)

## Introduction

Sinus histiocytosis with massive lymphadenopathy (SHML), is a benign self limiting condition of unknown etiology which presents as massive bilateral cervical lymphadenopathy (1). In 1969, Rosai and Dorfman described 4 cases of a disease which they called Sinus histiocytosis with massive lymphadenopathy (SHML). Later in 1972, they analyzed 30 additional cases, establishing SHML as a clinicopathologic entity (2). RDD generally occurs in first and second decades of life with a peak incidence at twenty years of age. It presents as a chronic, massive enlargement of cervical lymph nodes accompanied by fever, leucocytosis, elevated erythrocyte sedimentation rate (ESR) and hypergammaglobulinemia (3). Other lymphatic groups, such as mediastinal, axillary and inguinal lymphnodes can also be affected. In about 25 to 40 % of cases, extranodal sites such as eyes and ocular adnexa, head and neck, upper respiratory tract, skin, subcutaneous tissue, bone, skeletal muscle, central nervous system, gastrointestinal tract, salivary glands, thyroid, breast, liver, heart, uterine cervix etc are also affected (4). The concomitant involvement of one or more sites in the same individual is observed in upto 44.7 % of cases (5).

## Case Report

A five year old boy presented in the FNAC section of the Post Graduate Department of Pathology, Government Medical College Jammu with multiple bilateral soft to firm nontender, cervical and submandibular lymphadenopathy of six months duration. To begin with he had fever of short duration followed by neck swellings on the left side. There was no history of pain, respiratory tract infections or any symptoms related to ear, nose or throat. There was no family history of tuberculosis. Clinical examination showed multiple, enlarged, bilateral, cervical and submandibular lymphnodes ranging in size from 1 X 1 cm (on right side) to 3 X 3 cms (on left side ) (*Fig 1*). They were nontender, discrete firm and mobile.

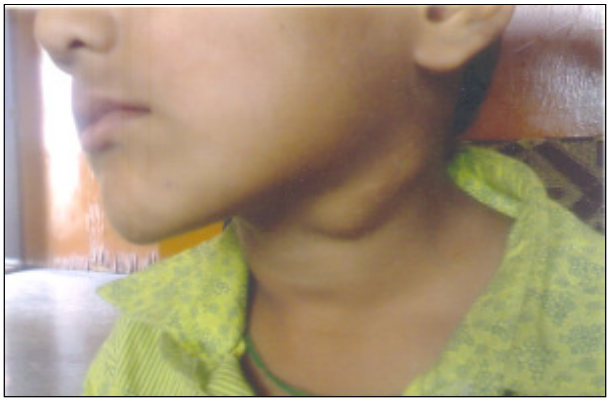

***Fig. 1 Clinical Photograph of a Child Showing Massive Cervical Lymphadenopathy( more on left side )***

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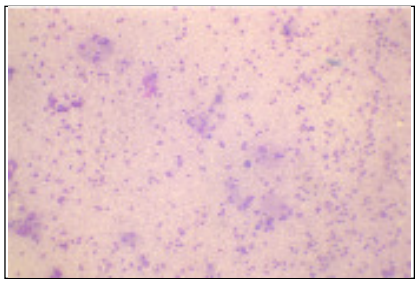

*Fig 2. Giemsa Stained FNA Smears from Cervical Lymph Node Showing Numerous Histiocytes (10X)*

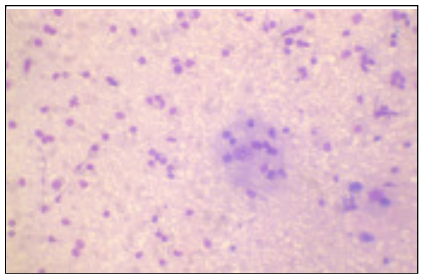

*Fig 3. Giemsa Stained FNA Smears from Cervical Lymph Node Showing Emperipolesis (40X)*

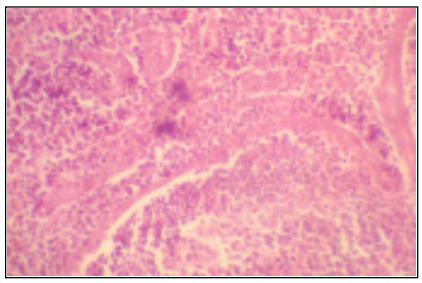

*Fig 4. H&E Stained Sections of Node Showing Dilated Sinuses and Multiple Giant Cells (10X)*

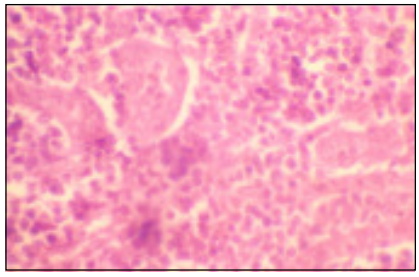

*Fig 5. H&E Stained Sections of Cervical Lymph Node Showing Emperipolesis*

Investigations showed Hb- 10 gm/dl, total leucocyte count - 16,000/cmm with neutrophilia and erythrocyte sedimentation rate 40 mm at the end of one hour by Westergrens method.

FNA of the cervical lymph nodes on the left side was performed from multiple sites and blood stained aspirate was obtained. Smears were stained with giemsa and pap stain. On microscopic examination, smears revealed presence of diffusely distributed histiocytes throughout the smears (*Fig 2*). These cells had abundant pale cytoplasm with single to multilobated or multiple nuclei but no nuclear atypia or nuclear grooving. The nuclei showed fine chromatin and inconspicuous to prominent nucleoli. The cytoplasm of these histiocytes exhibited numerous intact lymphocytes (emperipolesis) as well as presence of neutrophils. In some histiocytes the phagocytosed cells were so numerous that they obscured the nucleus (*Fig 3*). The background had mature lymphocytes, plasma cells, neutrophils and tingible body macrophages. Based on this characteristic cytomorphology, a diagnosis of Rosai- Dorfman Disease was made.

Subsequently, the biopsy of one of the cervical lymph node was done. Microscopic examination of the sections cut from paraffin embedded blocks showed fibrous thickening of the lymph node capsule and prominent dilatation of lymph sinuses resulting in partial architecture effacement. The primary lymphoid follicles were present mostly at the cortical areas. The sinuses were occupied by numerous histiocytes having abundant pale cytoplasm and phagocytosed lymphocytes ( emperipolesis ), plasma cells and occasional neutrophils (*Fig 4& 5*). Patient was not given any treatment and his neck nodes had decreased in size in the follow up period at the end of 6 months.

**Discussion**

SHML or RDD is a rare but well defined, histiocytic proliferative disorder of unknown etiology characterized frequently by spontaneous remission. Some investigators consider it to be of bone marrow stem cell origin (1). It manifests mainly with an asymptomatic cervical lymphadenopathy, occasionally with extranodal locations. Literature reviews show about 600 cases of RDD had been reported till 2004, in all races but mainly in whites (43%), in any age group but mainly in first and second decades (81%), and more in males than females (2:1) (6,7).

More than 90% of patients with SHML present with massive bilateral mobile and nontender cervical lymphadenopathy. These nodes may at times be matted and prominent by periportal fibrosis. Forty percent of the cases may show extranodal involvement. Low grade fever is generally present along with, normochromic anemia, elevated ESR, leukocytosis and hyperglobulinemia (3).

Etiology of this disease is unclear. RDD may be of two types- either familial or infection induced. With respect to the latter, increased antibody titres to Epstein Barr virus and measles virus have been observed; however etiological evidence is lacking. Immune disturbances are likely to be a feature in some patients. Subtle undefined immunological defects are also considered as a casual

factor. Human Herpes Virus-6 DNA has been detected in biopsy specimens and is considered as a contributing factor. Also, a familial association has been observed in some cases (3). It has also been found that stimulation of monocytes / macrophages via macrophage colony stimulating factor (M-CSF) leading to immune suppressive macrophages may be the main pathogenetic mechanism of RDD (8).

Our case was a young male who presented with multiple cervical and submandibular lymphadenopathy, fever, leukocytosis, and an elevated ESR. However, the possibility of Rosai Dorfman Disease was not considered until FNAC was performed.

The cytological features of SHML usually reveal numerous large histiocytes with abundant, pale cytoplasm and phagocytosed lymphocytes (emperipolesis). The background typically shows lymphocytes, plasma cells and occasional neutrophil (4,9). These features were also present in our case.

Emperipolesis or lymphophagocytosis is the presence of intact lymphocytes wandering about within the cytoplasm of histiocytes; this is of great diagnostic significance. The internalized lymphocytes are usually located within cytoplasmic vacuoles (10). The histopathological features include progressive filling up of LN sinuses with normal histiocytes and lymphocytes leading to partial effacement of lymph nodal architecture as seen in our case too. Histiocytes showing similar phenomenon of emperipolesis. There may be pericapsular fibrosis and inflammation (8). Ultrastructurally, histiocytes lack Birbeck granules and viral particles. On Immunostaining show positivity for S100 protein, CD11C, CD14, CD33 and CD68 antigens and are CD1 negative (4).

The prognosis is excellent in most cases. Complete spontaneous regression is known to occur. The course of disease however may be protracted over three to nine months. Only two cases of progression, one to malignant lymphoma and another to amyloidosis have been documented (3). Complications are mostly due to pressure effects exerted by the enlarged cervical lymph nodes. The treatment modalities for RDD are nonspecific and include corticosteroids, chemotherapy with a combination of vinca alkaloids and alkylating agents, low doseinterferon, antibiotic therapy, radiation therapy and surgical treatment with partial or total resection (5).

Pathological differential diagnosis of RDD include reactive sinus hyperplasia ( in which cells lack emperipolesis and are S100 negative ), Langerhans cell histiocytosis ( positive for both S100 and CD 1a ), Hodgkin's disease, metastatic carcinoma, malignant melanoma and lymphoma. Perhaps the condition that resembles it most is the sinus histiocytosis induced by cobalt-chromium and titanium that occur in pelvic lymphnodes after hip replacement (8). In the case that we observed, most of the histological features were seen and a conservative approach was followed. After six months of follow up, the patient showed marked regression in the size of the lymph nodes inspite of not being put on any specific treatment.

## Conclusion

Massive cervical lympadenopathy is the hallmark of Rosai- Dorfman Disease. Head and neck region is the preferred site of the extranodal form of the disease. The diagnosis of RDD is made on the basis of clinical suspicion, confirmed by cytology and supported by histopathology. Clinicians and pathologists should always be aware of RDD in making a differential diagnosis of cervical lymphadenopathy.

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