# Sinus Histiocytosis with Massive Lymphadenopathy (Rosai Dorfman Disease) - Diagnosis of a Masquerader on Fine Needle Aspiration Cytology of Lymph Node - A Case Report

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## INTRODUCTION

Sinus histiocytosis with massive lymphadenopathy (SMHL) was first described by Destombes in 1965.[1] Rosai and Dorfman later identified this disorder as a clinicopathologic entity and labelled it as sinus histiocytosis with massive lymphadenopathy and it since then came to be also known as Rosai Dorfman disease.[2,3] Rosai and Dorfman described SHML as massive lymphadenopathy affecting mostly cervical group of lymph nodes in young black children.[2,3] Later various reviews involving larger number of cases showed a much broader spectrum of the entity.[4] The age of patients varied from new born to eighth decade of life. A worldwide distribution with male predominance was noted. The most common site of involvement is lymph node followed by extra-nodal sites such as head and neck region, soft tissue, breast, gastrointestinal tract, central nervous system and bones.[5] We report an interesting case of a young male who presented with low grade fever for 2 weeks and cervical lymphadenopathy which was clinically suggestive of tuberculous; however, on fine needle aspiration cytology (FNAC) it was diagnosed as Rosai Dorfman disease.

## PRESENTATION OF CASE

A 21years old male patient presented to the FNAC clinic with low grade fever for 2 weeks, neck swelling of two months duration which was progressively increasing in size. There was no history of cough or weight loss. He gave history of positive Mantoux test in childhood for which he had received and completed a course of anti-tubercular therapy. On examination, he was moderately built and nourished. Multiple cervical lymph nodes were palpable more on the left side of the neck, the largest one measuring approximately 2.0 x 2.0 centimetre which were firm in consistency, non-tender, discrete. No other regional lymph nodes were palpable. Systemic examination was normal.

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## CLINICAL DIAGNOSIS

Tuberculous lymphadenitis was the most likely clinical diagnosis.

## DIFFERENTIAL DIAGNOSIS

Lymphoproliferative disorders, Kikuchi's disease.

## PATHOLOGICAL DISCUSSION

**Investigation**

Haemoglobin was 14 grams / dL, total leukocyte count was 7,800 cells per dL, platelet counts were 2.5 lakhs / dL. peripheral smear was normal. Liver function test, renal function tests, urine routine, chest Xray film were within normal limits. Mantoux test was negative. Ultrasound of the lymph node showed altered echogenicity of the lymph nodes.

Fine needle aspiration was done from left posterior cervical group of lymph nodes which yielded blood mixed aspirate. Smears were made and stained with Haematoxylin and Eosin (H & E), Papanicolaou and Ziehl- Neelsen stains. Smears revealed a highly cellular aspirate which showed small and large lymphoid cells, numerous histiocytes and plasma cells (Figure 1). The histiocytes were large, with one to three large vesicular nuclei and abundant cytoplasm (Figure 2). The histiocytes exhibited emperipolesis or engulfed intact lymphocytes, plasma cells and occasional neutrophils (Figure 3). There was no evidence of any granuloma or areas of necrosis. Smears stained by Ziehl-Neelsen showed no acid-fast bacilli. The differential diagnosis considered were SHML, sinus histiocytosis, lymphoproliferative disorder and Langerhans cell histiocytosis. Absence of eosinophils and a polymorphous lymphoid background, absence of coffee bean shaped grooved histiocytes reduced the possibility of lymphoproliferative disorder and Langerhans cell histiocytosis respectively. Sinus histiocytosis was excluded due to presence of emperipolesis in the numerous histiocytes seen. A presumptive diagnosis of the lymph node fine needle aspiration cytology suggestive of SHML or Rosai Dorfman disease was given and lymph node biopsy with immunohistochemistry (IHC) studies was suggested to confirm the diagnosis. Cartridge based nucleic acid amplification technique (CBNAAT) for *Mycobacterium tuberculosis* on the lymph node was found to be negative. The patient underwent excision biopsy of the lymph node which was suggestive of SHML.

## DISCUSSION OF MANAGEMENT

The patient was started on systemic corticosteroids for two weeks and then tapered over two weeks. The patient had clinical improvement and there was complete resolution of cervical lymph nodes.

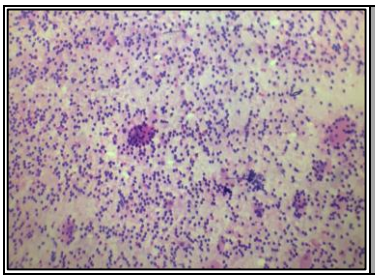

***Figure 1.***
***Smears Revealed a Highly Cellular Aspirate Which Showed Small and Large Lymphoid Cells, Numerous Histiocytes and Plasma Cells***

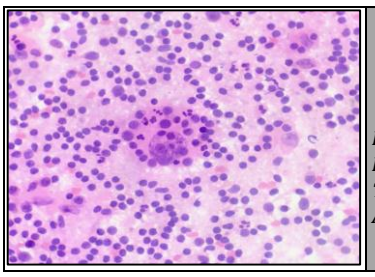

***Figure 2.***
***Large Histiocytes with One to Three Vesicular Nuclei and Abundant Cytoplasm***

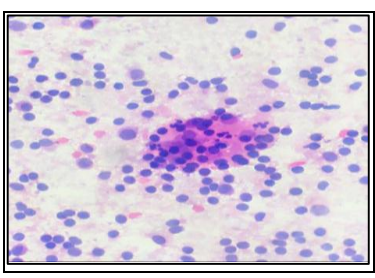

***Figure 3.***
***The Histiocytes with Emperipolesis or Engulfed Intact Lymphocytes, Plasma Cells and Occasional Neutrophils***

## FINAL DIAGNOSIS

Sinus histiocytosis with massive lymphadenopathy (Rosai Dorfman Disease).

## DISCUSSION

SHML or Rosai Dorfman disease is a potential masquerade due to its varied clinical manifestations. A short prodrome of nonspecific fever with or without pharyngitis and night sweats may be seen in some patients before palpable lymphadenopathy sets in. In most of the patients the disease initiates with and limits to painless cervical lymphadenopathy lasting for several years before receding by itself.[6] Outcome is fatal only in patients with generalized lymphadenopathy and immune dysfunction.[6,7] Exact pathogenesis of the disease is still not known. Theories implicating an infectious cause and immunodeficiency state have been suggested. The relationship with klebsiella / brucella genera of bacteria, Epstein-Barr, human herpes virus 6 or cytomegalovirus have been suggested.[8] A rare genetic syndrome, known as Faisalabad histiocytosis, which encompasses sensorineural deafness, joint contractures and short stature is associated with lymphadenopathy that very closely mimics SHML.[9] SHML is rarely associated with haematological and lymphoid neoplasms. Follicular lymphoma and nodular lymphocyte predominant Hodgkin lymphoma, respectively, are more commonly associated with SHML compared to others.[10,11] FNA smears are typically highly cellular with many histiocytes showing emperipolesis (wandering in and around) in a

reactive background of lymphocytes and plasma cells.[12] Most histiocytes have a bland nucleus and abundant pale cytoplasm. Some histiocytes are huge and may show hyperchromatic nuclei with prominent nucleoli.[13] The 'halo' around the engulfed lymphocyte seen in histopathological sections of the lymph node biopsy is a fixation artifact and hence is absent in FNA smears which could lead to difficulty in differentiating lymphocytes overlapping the histiocyte from phagocytosed lymphocytes. In early SHML lesions, prominent germinal centre yields many lymphocytes and occasional immunoblasts, whereas in later stages, numerous plasma cells, with some containing Russell bodies can predominate.[13] The common differential diagnoses include, infectious lesions, reactive lymphoid hyperplasia with sinus histiocytosis, Langerhans cell histiocytosis, hemophagocytic syndrome and malignant lymphoma. The cytomorphological features such as emperipolesis, absence of eosinophils and atypical grooved histiocytes help in diagnosing SHML over the other conditions listed above. Due to the indolent nature most patients are followed up with symptomatic treatment with or without corticosteroids.

## CONCLUSIONS

This case highlights the need for clinical consideration, careful cytopathological examination of the lymph node FNA smears in patients with minimal to moderately enlarged lymph nodes followed by histopathological examination of the excised lymph node along with specific IHC (like S - 100 protein) for confirmation - all of which, would help in the early detection and timely management of the disease.

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