

# Cytology of nodal Rosai-Dorfman disease: a case report

**Puvitha R. Duraisami\***

Department of Pathology, Coimbatore Medical College, Coimbatore, Tamil Nadu, India

**Keywords:** *Emperipolesis, Rosai-Dorfman disease, Cervical lymphadenopathy, Cytology.*

### Abstract

Rosai-Dorfman disease (RDD) or sinus histiocytosis with massive lymphadenopathy is a rare, benign, histiocytic proliferative disorder. It can be encountered in both nodal and extra nodal locations. Fine needle aspiration technique is a simple, accurate and most economic tool, being used widely. Fourteen year old male child presented with bilateral cervical lymphadenopathy. Fine needle aspiration of cervical node revealed RDD, which was later confirmed by histopathology and immunochemistry. Owing to the rarity, cytomorphological appearance of this disease and its mimics are considered here.

**\*Corresponding author:**

Dr. R. D. Puvitha, Assistant Professor, Department of Pathology, Coimbatore Medical College, Coimbatore, Tamil Nadu 641014. India  
Mobile no: 919843112163. Email: drrdpuvitha@yahoo.com

**Date of Submission: June 25, 2014**

**Date of Acceptance: Aug 7, 2014**

**Date of Publishing: Jan 28, 2015**

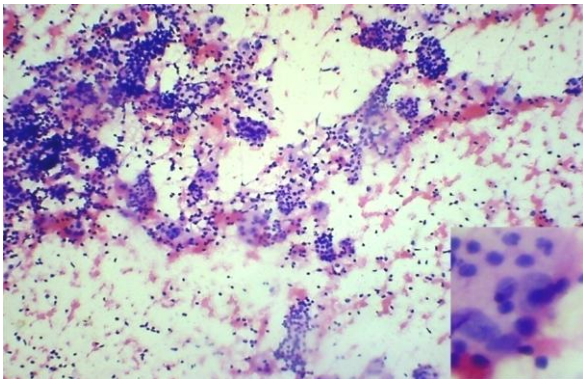


## Introduction

Rosai Dorfman disease (RDD) was first introduced in 1969 as Sinus histiocytosis with massive lymphadenopathy (SHML), a rare non-malignant histiocytic proliferative disorder, can occur in a wide span of age from newborn to older age.<sup>[1]</sup> It can present as nodal and extra nodal manifestation. Fine needle aspiration (FNA) is commonly used modality for the diagnosis of superficial and deep-seated lesions, is simple, inexpensive and relatively painless outpatient procedure.<sup>[2]</sup> Choice of final diagnosis and differential diagnosis from other lesions are very important because of different plan of therapy. Spontaneous regression of enlarged node and improvement of illness without chemotherapy is common in RDD.<sup>[2, 3]</sup>

## Case Report

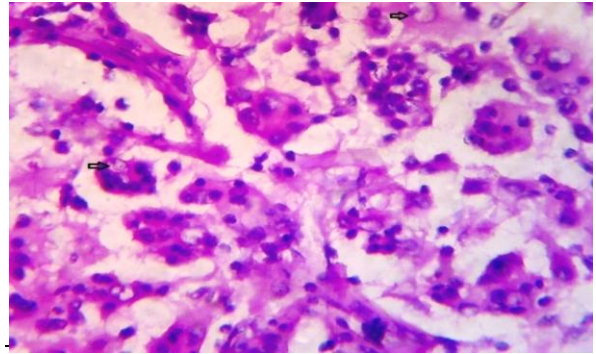
A Fourteen year old male child presented with bilateral neck swellings for the past one month. He also had fever, malaise and night sweats. On examination he had bilateral, enlarged, matted cervical and post auricular lymph nodes. No other lymph node enlargement or organomegaly were noted. Biochemical parameters including hemoglobin, ESR were within normal limits. A fine needle aspiration of cervical node was done as a preoperative, pretreatment investigation. It revealed highly cellular smear composed of many lymphocytes, plasma cell and histiocytes with lymphophagocytosis (Fig. 1). Provisional diagnosis of RDD was considered, which was confirmed further by histopathology and Immunohistochemistry.



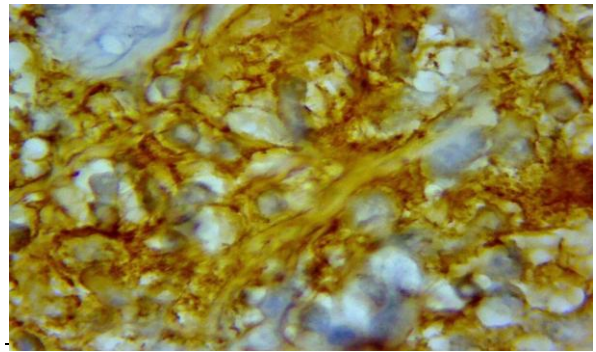
**Fig 1.** Cytosmear show cellular smear with many multinucleated cells in the background of lymphocytes and plasma cells (H&E, 10x). Inset show emperipolesis (H&E, 40x).

Histopathological examination of node revealed marked dilatation of the sinuses with a mixed population of lymphocytes, plasmacytoid lymphocytes and histiocytes with emperipolesis (Fig.2). Immunohisto-

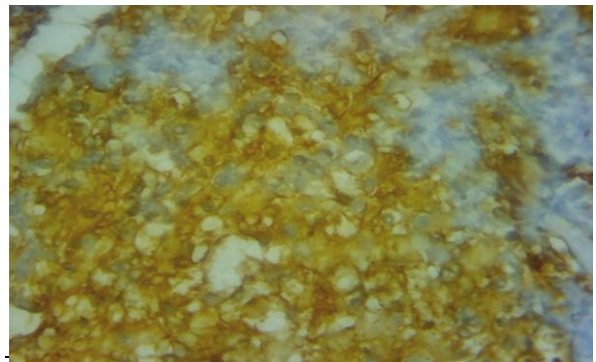
chemistry showed CD 68 (Fig.3) and S100 (Fig.4) diffuse membrane positivity, hence the histiocytic nature the lesion was confirmed.



**Fig 2.** Section showing dilated sinuses with histiocytes. Arrows show emperipolesis cell. (H&E, 40x).



**Fig 3.** Immunohistochemistry show intense membrane positivity in CD68.



**Fig 4.** Immunohistochemistry show intense membrane positivity S-100 protein.

## Discussion

In 1965, Destombes initially described Sinus histiocytosis with massive lymphadenopathy.<sup>[2]</sup> Later in 1969, Juan Rosai and Ronald F Dorfman recognized this disease as a separate clinicopathologic entity and coined the term sinus histiocytosis with massive lymphadenopathy.<sup>[1]</sup> Sinus histiocytosis with massive lymphadenopathy (SHML), also known as Rosai Dorfman disease (RDD), is a rare non-malignant his-

tiocytic proliferative disorder, can occur in a wide span of age from newborn to older age, commonly in the second to third decades.<sup>[2, 4]</sup> Males outnumber with a ratio of 3:2. It can present as nodal and extra nodal manifestation. Classically, it presents as prominent bilateral, painless cervical lymphadenopathy. Relatively common extranodal sites involved with this disease include the soft tissue, skin, upper respiratory tract, gastrointestinal tract, breast, bones and central nervous system.<sup>[5]</sup> Extranodal involvement of at least one site is identified in half of the cases and in one fourth cases have exclusive extranodal presentation.<sup>[4, 5]</sup> Clinically it presents with low-grade fever, weight loss, leukocytosis, elevated erythrocyte sedimentation rate and hypergammaglobulinemia.<sup>[2-5]</sup> In our case it has presented in a young adolescent male as bilateral cervical, post auricular lymphadenopathy along with low grade fever, malaise and night sweats.

The etiology of RDD is unknown.<sup>[4, 5]</sup> Two theories have been put forth to describe the pathogenesis of the disease. The first theory states that it is caused by a specific infectious process which can be even an acute infection, causing histiocytic proliferation, Second theory states that the disease is due to an aberrant exaggerated immune response to an infectious agent.<sup>[6, 10]</sup> In our case, patient was suffering from low grade fever and lymphadenopathy for the past six months, probably fits into first theory.

FNA smears are typically highly cellular; many histiocytes with phagocytosed lymphocytes in a reactive background of lymphocytes and plasma cells. Histiocytes are large cell and show emperipolesis.<sup>[6, 7]</sup> This process whereby cells enter and transit through a cell, evading cellular degradation is known as emperipolesis, it differs from phagocytosis, in that engulfed cells remain viable within the cell.<sup>[1, 6]</sup> This is the key morphological feature of RDD. In smear preparations, phagocytosed lymphocytes are not surrounded by a "halo," as they often do in tissue sections which are a fixation artifact.<sup>[4, 10]</sup>

FNA can at times be misinterpreted due to limited or non-representative sampling and as FNA does not permit examination of the tissue architecture, diagnosis can be further confounded. The pathologic assessment is pivotal in making the diagnosis.<sup>[3, 7]</sup> Histopathological examination of the node reveals marked dilatation of the sinuses (henceforth referred as SHML) with a mixed population of lymphocytes, plasmacytoid lymphocytes and emperipolesis, further

confirmed by immunohistochemistry with positive S100 and CD68.<sup>[8, 11]</sup>

RDD is notable for its varied clinical presentations which evoke many differential diagnoses which includes Langerhans histiocytosis, various other reactive processes, hemophagocytic syndrome, lymphoma and other malignancies. Langerhans cell histiocytosis presenting as lymphadenopathy alone is very uncommon. Typically in this condition, histiocytic nucleus has contorted shapes with grooves and Immunohistochemically, both S100 and CD1a positive. Whereas in RDD, histocytes with emperipolesis is very specific and CD1a negative, rules out the differential diagnosis of Langerhans cell histiocytosis.<sup>[7, 8]</sup>

In non specific sinus hyperplasia, there is lack of emperipolesis and negative S100protein.<sup>[6]</sup> In hemophagocytic syndrome other blood cells like red blood cells, granulocytes and platelets are seen inside the histiocytes. In contrast, in RDD the phagocytosed cells are rather lymphocytes, again emperipolesis is very specific.<sup>[7, 8]</sup>

In lymphoma, monomorphic population of lymphoid cells are very specific, where in, our patient smears and sections show polymorphous population of cells with typical emperipolesis favours the diagnosis of SHML, which is further confirmed by immunohistochemistry.<sup>[8]</sup>

Histiocytic sarcoma (malignant histiocytosis) can occur in both nodal and extra nodal regions, cytologically, the neoplastic cells show marked pleomorphism, atypia with necrosis and increased mitotic activity. Emperipolesis can occur in a subset of cases. In RDD typical cytomorphological picture of emperipolesis in a bland histiocytic background rules out the other malignant association as well.<sup>[8, 9]</sup>

## Conclusion

FNA represents an efficient, minimally invasive, cost-effective and reliable though not infallible technique for the diagnosis of RDD. RDD must be included as a differential diagnosis in all young patients with chronic generalized lymphadenopathy. The diagnosis of RDD is made by histopathology. RDD is not a malignant illness and lymph node size most often decreases without special treatment. However, awareness of this entity and consideration of it as a differential diagnosis in the review of histiocytic and lymphocytic pathologies is of utmost importance.

## Acknowledgements

None

## Funding

None.

## Competing Interests

None declared.

## References

1. Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy. *Arch Pathol* 1969;87: 63-70.
2. Destombes P. Adenitis with lipid excess, in children or young adults, seen in the Antilles and in Mali (4 cases). *Bull SocPatholExotFiliales* 1965; 58:1169-75.
3. Adrienne YS, Griffin C, Zhang PJL, Palmer JN, Gupta P. Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman Disease): A case report and review of 49 cases with fine needle aspiration cytology. *Cyto Journal* 2011; 8:3.
4. Deshpande MH, Nayak S, Munshi MM. Cytology of Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman Disease) Diagnosis by fine needle aspiration. *DiagnCytopathol* 2000; 22: 181-5.
5. Bist SS, Bisht M, Varshnev S, Pathak VP. Rosai Dorfman syndrome with extranodal manifestation. *J Assoc Physicians India*. 2007; 55:445-7.
6. Humble JG, Jayne WH, Pulvertaft RJ. Biological interaction between lymphocytes and other cells. *Br J Haematol*. 1956;2: 283-94.
7. Middle P, Hemmerlein B, Fayyaz. Evidence for its relationship to macrophages and for a cytokine disorder. *Histopathology* 1999;35: 525-33.
8. Snehalatha R, Senthilnathan R, Ramani P, Herald SJ. The Rosai Dorfman Syndrome: the report of a rare case. *J ClinDiagnRes*. 2013;7:1519-21.
9. Vos JA, Zo SA, Barekmann CL, Jo Ann W, Andriko, Markku Miettinen, et al. Histiocytic sarcoma; a study of five cases including the histiocyte marker CD163. *Modern pathology* 2005;18:693-704.
10. Li S, Yan Z, Jhala N, Jhala D. Fine needle aspiration diagnosis of Rosai-Dorfman disease in an osteolytic lesion of bone. *CytoJournal* 2010;7:12.
11. Biswas M, Sarkar T, Das A, Naskar S. Refractory Extra nodal Rosai-Dorfman disease of cheek and upper eyelid: A rare case. *Annals of Pathology and Laboratory Medicine*, 2014;1:24-27