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Sinus Histiocytosis (Rosai-Dorfman's Disease) With Massive Lymphadenopathy with Neoplastic Proliferation: A Rare Two Case Reports.

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ABSTRACT:
Background: Rosai-Dorfman disease (RDD) or sinus histiocytosis with massive lymphadenopathy is a rare, idiopathic, benign histiocytic proliferation of unknown etiology typically presenting with massive cervical lymphadenopathy with or without systemic involvement. Most commonly seen in children and young adults but it may occur at any age. **Case/Result:**We reported 2 cases, **1st case** in a 7-year-old male child. The child had multiple large cervical and submental lymph nodes for 2 years associated with low-grade fever. The child was finally diagnosed with a case of sinus histiocytosis with massive lymphadenopathy. The clinical examination and cytomorphological findings wereconsistent with Rosai-Dorfman disease with massive lymphadenopathy with anongoing neoplastic process.
2nd case in 9 years old male who presented with massive bilateral cervical lymph nodes swelling for 4 months associated with fever on & off for 4 months, hepatomegaly 2cm. The patient was finally diagnosed with a case of Rosai-Dorfmann syndrome (Sinus histiocytosis with massive lymphadenopathy).
Conclusion: It is concluded that FNAC is a rapid, reliable, and useful tool for the diagnosis of sinus histiocytosis with massive lymphadenopathy. This disease's etiology is unknownand progresses with a benign prognosis only when an early diagnosis and treatment are made. A delayed diagnosisofgeneralized lymphadenopathy contributes to a bad outcome.

I. INTRODUCTION:

Sinus histiocytosis is also known as Rosai-Dorfman Disease, it is a rare and benign histiocytic proliferative disorder of unknown etiology and can occur in any age group but is most commonly seen in children and young adults. It was first described by Rosai and Dorfman in 1969. It is usually associated with lymph node enlargement in various superficial or deep sites but most often those of the neck (cervical lymphadenopathy). Other non-specific findings include fever, skin pallor, unintended weight loss, malaise, rhinitis, elevated ESR, and hypergammaglobulinemia. This disease must be differentiated from lymphoma with extranodal involvement, Langerhans cell histiocytosis, granulomatous and reactive conditions. The histiocytes showed strong positivity for S100, and CD68 was negative for CD1a staining. This disease is so-mostly complete spontaneous remission in some cases long-standing-clinical disease for years in other cases [1, 2].

II. METHOD & MATERIAL:

Report of two cases of Rosai-Dorfman Disease, 1st of the case a 7 years old male child with unilateral cervical and submental lymph nodes was studied, 2nd case 9 years old male presented with massive bilateral cervical lymph nodes swelling. Clinical details of all patients are given below. 22-gauge biopsy needles and the standard technique of aspiration were used to make the cytology smears. Smears were fixed with alcohol and stained with Papanicolaou stain; air-dried smears were stained with May-Grunwald-Giemsa stain.

III. CASE REPORT:

Case-1: A 7-year-old male child presented with unilateral progressive multiple cervical and submental, soft to firm, non-tender, massive lymphadenopathy of two years' duration associated with fever, gradually increasing in size since 1 year. The patient received a 3-month Anti tubercular treatment (ATT) before coming here. There was no history of weight loss. Clinical examination revealed multiple enlarged unilateral

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cervical and submental lymph nodes, ranging in size from 4 × 4 cm to 3 × 3 cm and the lymph nodes were non-tender, discrete, soft to firm, and mobile. The complete blood count showed leucocytosis (16,400/cu. mm). Ultrasonography of the abdomen was within normal limits; the patient was clinically diagnosed with a case of Hodgkin's lymphoma.

Fine needle aspiration cytology of the submental and cervical lymph nodes was done from multiple sites. Microscopic examination revealed the predominantly polymorphous population of small lymphocytes and follicular centrocytes admixed with diffusely distributed histiocytes which showed emperipolesis. These histiocytes had reniform nuclei with abundant pale cytoplasm containing numerous intact lymphocytes (figure-1). Some scattered large mononuclear atypical cells were also noted which had irregular nuclear contours and small basophilic nucleolus. Atypical histiocytes (figure-2). Fine needle aspiration cytology done from cervical lymph nodes showed similar morphology.

Case-2: A 9-year-old male presented with massive bilateral cervical lymph node swelling ranging from 2x2cm to 3x2cm for 4 months associated with fever on & off for 4 months, firm, movable, and non-tender swelling. Laboratory examination showed anemia, leucocytosis, and a high erythrocyte sedimentation rate. Ultrasonography of the abdomen showed hepatomegaly 2cm. The provisional suspected diagnosis was a probable lymphoma. FNAC was performed on a bilateral cervical swelling. Cytological smears showed reactive polymorphous population lymphoid cells admixed with many histiocytes, many of the histiocytes have intact lymphocytes within their cytoplasm (emperipolesis) (figure-3).

IV. RESULT:

Final diagnosis Sinus histiocytosis with massive lymphadenopathy was made by cytomorphological findings and emperipolesis often presents with multiple, painless lymph nodes. The case report highlights, multiple, unilateral/bilateral lymph nodes in the cervical and submental regions. Clinically and Cyto-morphologically it was suggestive of Rosai- Dorfman disease with massive lymphadenopathy with an ongoing neoplastic process in one case, which is rare and mimics malignant lymphoma.

V. DISCUSSION:

Rosai-Dorfman disease was first described by Rosai and Dorfman in 1969 as sinus histiocytosis. It is a rare, benign disease. The Rosai-Dorfman disease is of unknown etiology and is commonly seen in the first and second decade of life however, it may occur in any age group. The patients presented with bilateral or unilateral, massive, painless cervical lymphadenopathy associated with fever, joint pain, weight loss, leucocytosis, and elevated ESR. Clinically the symptoms and signs of the patient may often mimic lymphoma. 25% of cases, maybe extranodal involvement of RDD, and the disease includes the salivary gland, eye, bone, and skin. Extranodal involvement of sinus histiocytosis is associated with massive lymphadenopathy [2, 3]. The exact pathogenesis of the disease is still unknown, some theories suggest an infectious cause or immunodeficiency state have been suggested. The presence of the human herpes virus 6 genomes was demonstrated by in-situ hybridization technique and relationships with Klebsiella, Epstein-Barr virus, Brucella, or Cytomegalovirus were also suggested [4]. Cytological features of SHML usually reveal a polymorphous population of lymphoid cells with numerous large histiocytes having abundant, pale cytoplasm, and phagocytosed lymphocytes (emperipolesis). Large mononuclear atypical cells with irregular nuclear contour and basophilic nucleolus were also noted as probably atypical histiocytes. The background shows occasional plasma cells and neutrophils, which were also noted in this case report. Histiocytes show positive immunostaining for CD68, CD11c, CD14, CD33, and S100 antigens in cytological smears.

In India, cervical lymph node enlargement in children is very common and is commonly suspicious of tuberculosis and reactive condition. Lymphomas and other reactive conditions may present with similar findings, SHML is a rare benign disorder presenting with similar morphology, due to its clinical features and cytological findings that form a distinct entity. Other conditions with a predominance of histiocytes in cytology smears may resemble SHML, and should be excluded before a diagnosis of SHML is made. The common conditions showing histiocytic proliferation are reactive lymphadenitis, tuberculous lymphadenitis, granulomatous lymphadenitis, and Hodgkin's disease. Less common are histiocytic lymphoma, hemophagocytic syndrome, histiocytosis, and related disorders. One condition that is very important in India is granulomatous lymphadenitis due to tuberculosis. The non-cohesive singly dispersed histiocytes with round to oval nuclei seen in SHML can easily be differentiated from the cohesive clusters of epithelioid histiocytes with slipper-shaped, elongated nuclei, finely granular

chromatin, and pale cytoplasm seen in tuberculosis. Langhan's giant cells and a caseous necrotic background may also be seen in tuberculous lymphadenitis. Reactive sinus histiocytosis shows loose clusters of histiocytes, accompanying which are reactive lymphocytes, germinal center cells, immunoblasts, and tingible body macrophages. The increased number of histiocytes in SHML is higher than in reactive lymphadenitis. Most reactive lymphadenopathies showed a greater spectrum of nuclear sizes and prominent germinal center cells, and also lack emperipolesis. Smears from patients with Hodgkin's disease show lymphocytes, plasma cells, histiocytes, and eosinophils, along with Reed-Sternberg cells. In SHML, Reed-Sternberg cells and eosinophils are not seen [5]. Rosai-Dorfman's disease involving the upper aero-digestive tract is uncommon, and few cases have been reported in young patients. Diagnosis of sinus histiocytosis with massive lymphadenopathy at this unusual location is challenging for its close mimicry of malignancy. Emperipolesis is a non-phagocytic engulfment of hematopoietic cells, where a cell enters a histiocyte stays for some time and then exits. We noted in this case report, a single case of sinus histiocytosis with massive lymphadenitis in a 7 years male child displaying lymphocytes in histiocytes [6]. The mainstay of management is supportive and symptomatic as there is no ideal treatment. However, various treatment modalities include surgery, radiotherapy, steroids, and chemotherapy. The usual course of this disease is benign with 50% of the patients showing a complete resolution without squeale and one-third of the patients having persisting asymptomatic lymphadenopathy. Very few (17%) continue to be symptomatic after 5 to 10 years [7].

VI. CONCLUSION:

Rosai-Dorfman's disease is an uncommon benign disease. The present case study concluded with the following;

1: Sinus histiocytosis with massive lymphadenopathy is a rare condition that is indolent.

2: Many atypical histiocytes were seen mimicking Reed-Sternberg cell so it was excluded from malignant lymphoma.

3:

Rosai-Dorfman's disease has a good prognosis and a self-limiting course.

Although SHML commonly undergoes resolution in a period of months to years, regular follow-up of patients is necessary because of the rare development of lymphoma after some years in some of these patients. Overall FNAC is a rapid, reliable, and sensitive means to establish a conclusive diagnosis, obviating the need for biopsy and immunohistochemistry examination.

ABBREVIATION: FNAC-Fine needle aspiration cytology; RDD- Rosai-Dorfman's disease; SHML-Sinus histiocytosis with massive lymphadenopathy; ESR- Erythrocyte sedimentation rate; CD- Clusters of differentiation; ATT- Anti-tubercular treatment.

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CONFLICTS OF INTEREST:
There are no conflicts of interest

CONSENT:
Informed consent was obtained.

ETHICAL APPROVAL:
It is not applicable.

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FIGURES:
Number of figures- 3

Figure-1: Cytological smears showing reactive lymphoid cells with emperipolesis (Black arrow), **40x, MGG, (Case-1).**

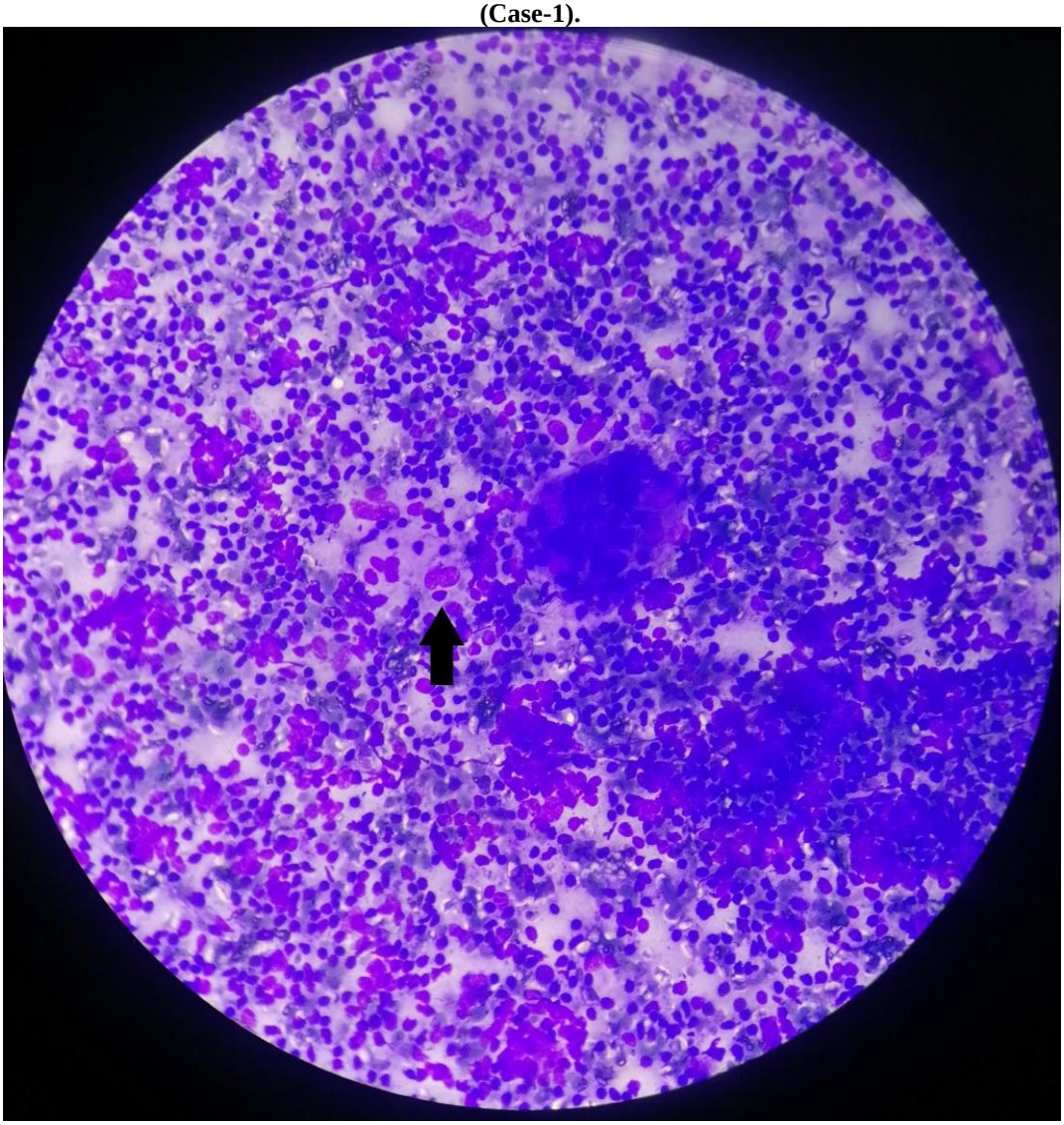

Figure-2: Cytological smears showing reactive lymphocytes with few atypical histiocyte (Black arrow), **40x, MGG, (Case-1).**

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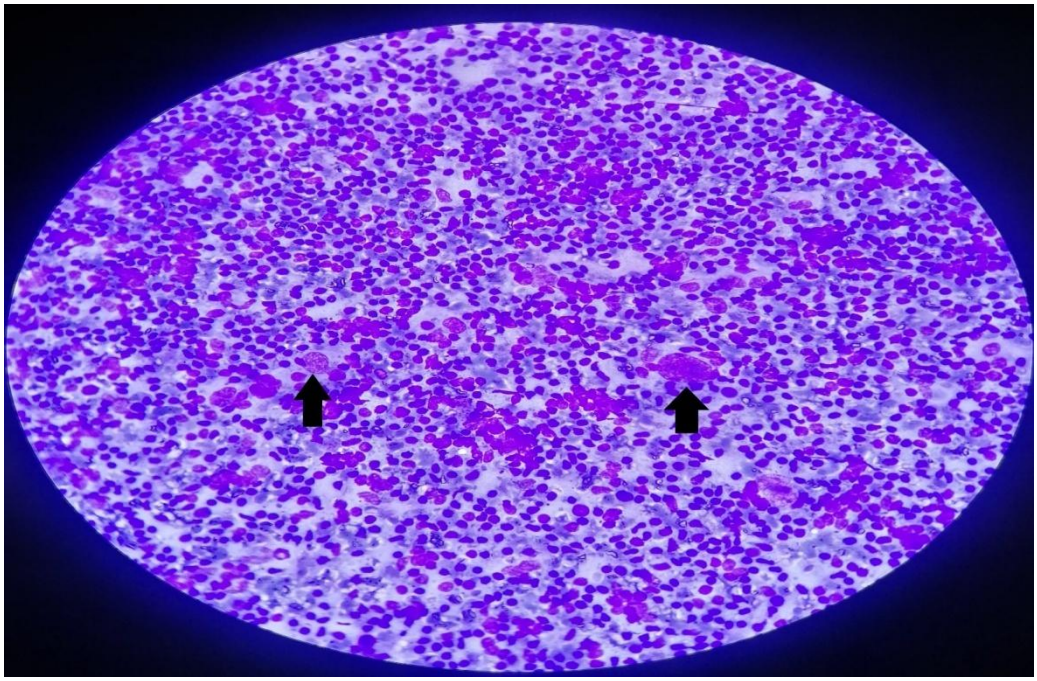

Figure-3: Figure-3: Smear showed many of the histiocytes have intact lymphocytes within their cytoplasm (emperipolesis)**, 40x, MGG, (Case-2).**