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Diagnosis of Multifocal Extranodal Rosai Dorfman Disease by Fine Needle Aspiration Cytology

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Authors' contributions

This work was carried out in collaboration between all authors. Author DP designed the study. Author ID wrote the protocol, and wrote the first draft of the manuscript. Author AK managed the literature searches, analyses of the study performed the spectroscopy analysis. Author MN managed the experimental process. Author DP took the photographs and author SN identified the entity. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Rosai-Dorfman Disease (RDD) or sinus histiocytosis with massive lymhadenopathy is a rare, non-neoplastic proliferative disorder of the cells of macrophage-histiocyte family having a self limiting course. Though it affects lymphnodes commonly, it can also involve many extranodal sites. These cases can often be misdiagnosed as lymphoma. Therefore, one has to be very careful not to interpret it as lymphoma or other causes of histiocytosis because of the difference in treatment protocol. Fine needle aspiration cytology (FNAC) is a simple, fairly accurate diagnostic tool in the evaluation of such lesions.

Although large numbers of RDD cases have been reported, review of the literature has revealed very few cases diagnosed by FNAC. Here, we report a case of RDD presenting with massive bilateral cervical and submandibular lymphadenopathy along with unilateral orbital involvement, diagnosed by FNA cytology, which was subsequently confirmed by excisional biopsy and immunohistochemistry.

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Keywords: Fine needle aspiration cytology; lymphadenopathy; orbital involvement; rosai-dorfman disease.

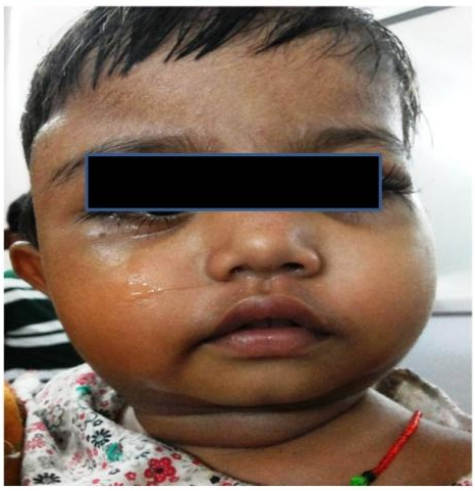
1. INTRODUCTION

Rosai-Dorfman Disease also known as Sinus histiocytosis with massive lymphadenopathy (SHML), is a rare, benign, idiopathic self-limiting disorder characterised by painless huge enlargement of the lymph nodes [1]. However, several extranodal sites such as eyes and ocular adnexa, upper respiratory tract, skin, subcutaneous tissue, bone, skeletal muscle, central nervous system, gastrointestinal tract, salivary glands, genitourinary tract, thyroid, breast, liver, kidney, heart, uterine cervix, etc., may also be involved [2]. Extranodal sites are involved in about 28% of cases. Simultaneous involvement of nodal and extranodal sites is still rare and can pose a diagnostic problem if multiple sites are affected. We report such a case of multifocal Rosai Dorfman Disease diagnosed by FNAC with emphasis on clue to cytologic interpretation.

2. CASE REPORT

A 2year 3month old female child presented with multiple bilateral cervical and submandibular lymphadenopathy since 2 months accompanied by low-grade fever. The lymph nodes had been gradually increasing in size and number during this period. She also had right sided peri-orbital swelling since 1 month (Fig. 1). She had no history of respiratory tract infection or weight loss. There was no family or contact history of tuberculosis. Clinical examination revealed multiple, enlarged, bilateral, cervical and submandibular lymph nodes which were non tender, discrete, firm, and mobile, largest measuring 3x3 cm in size. Orbital swelling was found to be firm, nodular and non-tender, measuring 2.5x2cm. The peripheral blood cell count showed leukocytosis ($18x10^9$\L) with neutrophilia. ESR was raised, 60 mm at the end of one hour. Chest X-ray showed no abnormality. Ultrasonography of the abdomen did not reveal any organomegaly. A clinical diagnosis of lymphoma was suggested.

FNAC of the cervical nodes was performed from multiple sites. Smears were stained with Giemsa and Haematoxylin & Eosin stain. Microscopic examination revealed cellular smears with diffusely distributed polymorphous population of cells comprising of plasma cells, histiocytes, mature lymphocytes, neutrophils and occasional eosinophils. The histiocytes had abundant pale to amphophilic, granular and foamy cytoplasm with single to multiple nuclei without any nuclear atypia or nuclear grooving. The nuclei showed fine chromatin and inconspicuous to prominent nucleoli. The cytoplasm of many histiocytes exhibited numerous intact plasma cells, lymphocytes and neutrophils (emperipolesis) (Figs. 2a, 2b). Stain for acid fast bacilli were negative. FNAC of the orbital swelling also revealed exactly similar picture (Fig. 2c). A cytological diagnosis of Rosai-Dorfman disease was suggested based on the characteristic cytomorphology.

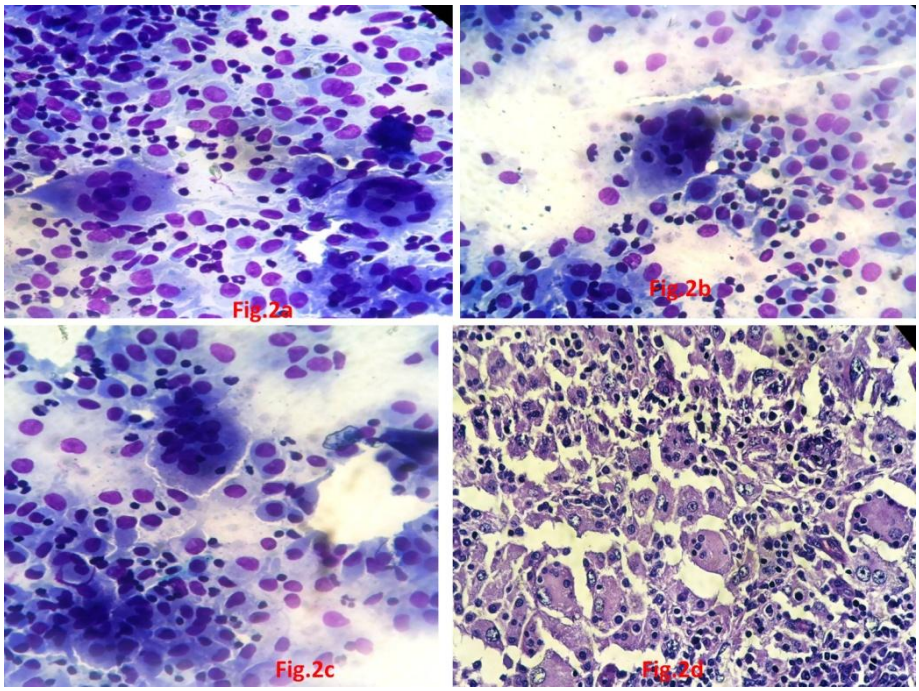


RDD

Fig. 1. Child is having bilateral cervical, submandibular and right side orbital swelling

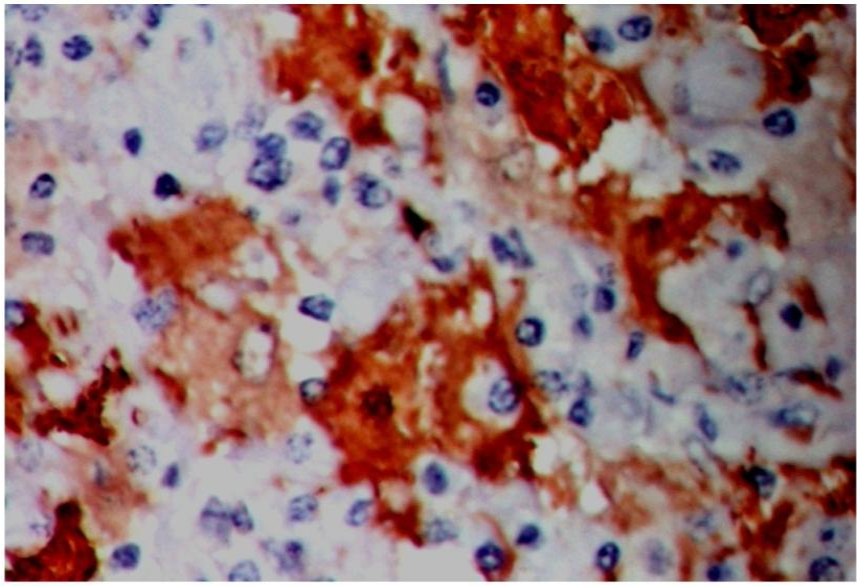
Subsequently, excisional biopsy of a cervical lymph node was done, which showed thickened capsule and nodal architectural distortion. The sinuses were dilated and packed with large histiocytes having abundant pale eosinophilic to amphophilic, granular, foamy cytoplasm and phagocytosed lymphocytes (emperipolesis), plasma cells and occasional neutrophils (Fig. 2d). The nuclei were vesicular without any lobation, indentation or longitudinal grooving.

Immunohisto chemistry using S-100 marker showed diffuse cytoplasmic positivity in the histiocytes (Fig. 3). Thus the diagnosis of RDD was confirmed.



RDD

Fig. 2a and b. Numerous histiocytes, multinucleated giant cell with extensive emperipolesis (arrow) in a background of mixed inflammatory cells (Giemsa stain x 400)
2c. Multinucleated giant cells with emperipolesis in a lymphohistiocytic background, along with neutrophils, (Giemsa stain x 400)
2d. Section from lymph node showing dilated sinuses filled with histiocytes with abundant pale eosinophilic cytoplasm with evidence of emperipolesis (H&E, x 400)



RDD

Fig. 3. Histiocytes showing diffuse cytoplasmic positivity for S1oo immunostaining (x400)

The patient was put on oral steroids which resulted in marked clinical improvement with no residual lymphadenopathy.

3. DISCUSSION

Rosai-Dorfman Disease is a rare disease of lymph nodes often associated with extranodal involvement characterised by proliferation of histiocytes. It is commonly encountered in children and young adults usually in 1st to 2nd decades with a slight male predominance [2]. Painless massive enlargement of cervical lymphnodes is the usual presenting clinical feature in these patients though may be accompanied by fever, leucocytosis and elevated ESR. Polyclonal hypergammaglobulinemia can be demonstrated during detail investigation of such cases. The above said patient is of two and half years old and a female child. Also she presented with concurrent involvement of nodal and extranodal sites. However, widespread concurrent nodal and extranodal involvements have also been reported by other authors where the diagnosis of RDD can be a challenge and may be missed in first encounter [3].

The exact etiology of the disease is not known [4]. An aberrant exaggerated immune response to an infectious agent especially of viral cause may lead to proliferation of the histiocytes. Research has shown presence of human herpes virus 6 genome by in situ hybridization and relationship with Klebsiella, Epstein-Barr virus, Brucella, or Cytomegalovirus as the possible cause [2,5].

There are only a few case reports or small series of cases on the cytodiagnosis of this entity. The clue to diagnostic interpretation is the presence of a phenomenon known as emperipolesis characterised by numerous large histiocytes with abundant, pale cytoplasm having variable number of intact lymphocytes within the cytoplasm emperipolesis [1,6]. The background is polymorphous comprising of lymphocytes, plasma cells and occasional neutrophils. All these features are present in our case. This patient surprisingly was diagnosed as lymphoma and the possibility of a diagnosis of Rosai Dorfman disease could be rendered only after cytologic examination.

Although the cytomorphological features are typical, diagnostic difficulties can sometimes arise. The major differential diagnosis on FNAC of the lymph nodes include reactive lymphoid hyperplasia with sinus histiocytosis, Langerhans cell histiocytosis (LCH), lymphoma both Hodgkin's and Non-Hodgkin's type and tuberculosis [2].

In LCH, Langerhans cells have grooved nuclei and the background shows presence of numerous eosinophils. Immunoreactivity with CD1a is posiitive in LCH and can differentiate RDD [7,8]. Reactive sinus histiocytosis shows loose clusters of histiocytes, accompanied by reactive lymphocytes, germinal center cells, immunoblasts, and tingible body macrophages without emperipolesis. These cytologic findings sometimes may mislead the cytologist for a simple diagnosis of reactive lymphadenopathy [9]. The presence of hemophagocytosis, emperipolesis absence of, and the presence of pancytopenia with hepatosplenomegaly rules out hemophagocytic syndrome. Tuberculous lymphadenitis shows epithelioid cell granulomas commonly over a background of caseous necrosis, which are absent in Rosai–Dorfman disease. Hodgkin's disease and some variants of Non-Hodgkin's lymphoma show lymphocytes, plasma cells, histiocytes, eosinophils, and Reed–Sternberg cells.

Histologically, besides the above said entities, storage disorders like Gaucher's disease and metastatic carcinoma and melanoma and histiocytic sarcoma can come as differential diagnosis. But the classical histomorphology of histiocytic proliferation inclusive of emperipolesis in a proper clinical context can lead to a definitive diagnosis. In doubtful cases, immunohisto chemistry with S-100 protein, CD11, CD14, CD34 and CD68 can be of help. In the present case also we could arrive at a diagnosis due to presence of emperipolesis in cytology smears associated with bilateral cervical lymphadenopathy and orbital swelling. It was confirmed later by histomorphology and strong and diffuse cytoplasmic positivity with S-100 protein.

RDD usually has a self limiting course in most of the patients and so treatment is not necessary in majority of them. Surgery is not required unless the lymphadenopathy is too massive and causing discomfort due to obstruction to patient. It should generally be limited to biopsy for confirmation of the diagnosis. Steroids are given to the patients for relief of symptoms and to reduce lymphadenopathy which was done in above patient.

4. CONCLUSION

Therefore, the authors conclude that the possibility of RDD should always be kept in mind as a differential diagnosis while examining FNA smears of a lymph node. The cytological findings should be interpreted in the appropriate clinical context. Thereby FNA can be used as a reliable, minimally invasive, cost-effective and efficient tool to establish a diagnosis of RDD avoiding an unnecessary biopsy.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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