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CASE REPORT

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Histocytopathological diagnosis of Rosai–Dorfman disease: Case report

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Abstract

Sinus histiocytosis with massive lymphadenopathy (Rosai–Dorfman disease) being a rare benign proliferative self-limiting disease of the cells of macrophage-histiocyte family is of unknown etiology and presents with massive lymphadenopathy. We are hereby reporting a case of RDD presenting with massive bilateral cervical and submandibular lymphadenopathy, diagnosed by histocytopathology.

KEYWORDS

histocytopathology, massive lymphadenopathy, Rosai–Dorfman, Tanzania

1 | INTRODUCTION

Sinus histiocytosis with massive lymphadenopathy (SHML) also known as Rosai–Dorfman disease is a benign, self-limiting disease that commonly involve lymph nodes.[1-6] The disease was first described by Rosai and Dorfman in 1969[7,8] and since then, there has been some many more cases reported from the available literatures.

In terms of age and sex predilection, RDD commonly affect children and young adult in their second decades of life and shows slight male preponderance.[9-12]

RDD may show an extra nodal disease pattern (23%) particularly by having predilection to the head and neck region (75% of cases)[4,13,14] and involvement of ≥1 extranodal site has been identified in 43% of cases.[13] The tendency of RDD to have simultaneous involvement of nodal and extranodal sites remains to be rare, and its diagnosis may be challenging.[12]

SHML being a newly recognized and distinct pseudolymphomatous benign entity has distinctive microscopic features, though its histocytomorphology has been documented in relatively few cases.[15,16]

Misdiagnosis sometimes may be encountered in patients with massive lymphadenopathy since they may be labeled to be having lymphomas or other neoplasms depending on the affected anatomical sites such as involvement of the nose and paranasal sinuses by sinus histiocytosis.[10,12,17]

We report such a case of Rosai–Dorfman disease diagnosed by fine needle aspiration cytology (FNAC) and open lymph node biopsy with emphasis on clue to histocytopathological interpretation.

2 | CASE PRESENTATION

We are presenting a 58-year-old Tanzanian female patient who presented at our outpatient otorhinolaryngology clinic at Benjamin Mkapa Hospital with a 6-month history of low-grade fever and bilateral cervical and submandibular lymph nodes.

On physical examination, the patient was found to have bilateral cervical and submandibular lymphadenopathy and occasional low-grade fevers. Local examination revealed multiple nodes with the largest one measuring 5 × 5 cm, ovoid, mobile in all directions, and non-tender. Laboratory results showed hemoglobin 11 g/dl and elevated ESR (30 mm/h) and a diagnosis of probable lymphoma was made. FNAC was ordered that revealed a smear (hematoxylin and eosin stain used) showing histiocytes with emperipolesis, scattered lymphoglandular bodies, and also atypical histiocytes with dense inflammatory infiltrates were noted suggestive of RDD (Figures 1-3).

Open lymph node biopsy was then done, and the smear revealed a fragment composed of dilated sinuses filled with large histiocytes with intact lymphocytes and plasma cells (emperipolesis and lymphophagocytosis) with large round, vesicular nuclei with delicated nuclear membrane and prominent nucleoli, and some histiocytes showed multinucleation. Elsewhere, mixed inflammatory cells noted. Confirmatory diagnosis of RDD was made (Figures 4 and 5).

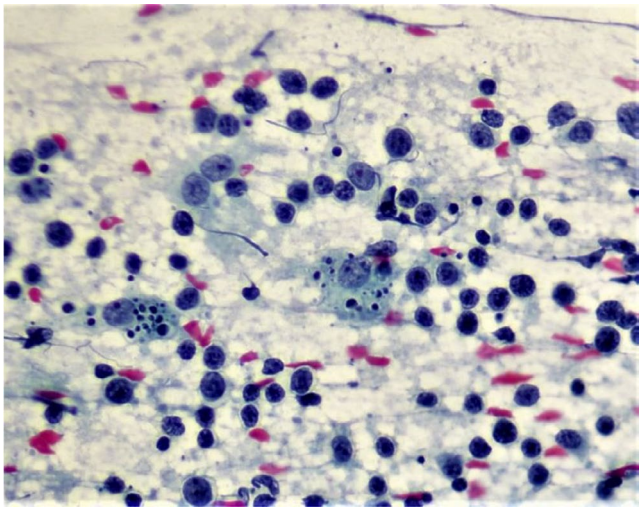

FIGURE 1 Cytological smear showing histiocytes with emperipolesis, lymphocytes, and scattered lymphoglandular bodies

The patient was kept on steroids for 3 weeks with no residual disease and recurrence after 3 months of follow-up. She was kept on intramuscular injection. Betamethasone sodium (diprofos) 7mg stat and then tabs prednisolone 20 mg once daily for 5 days, then 10mg once daily for the next 5 days, and then 5mg once daily for the next 5 days.

3 | DISCUSSION

Rosai–Dorfman Disease is a rare disease of lymph nodes often associated with extranodal pattern, and it is characterized by benign histiocytic proliferation.[1,4-6,10,13,17]

RDD is commonly encountered in children and young adults, and the trend is marked in those at their first to second decades of life with slight male preponderance.[5,9,12,13]

The disease tend to present with various clinical features such as painless massive enlargement of cervical lymph nodes that may be accompanied by leukocytosis and elevated ESR, fever, and hypergammaglobulinemia.[4,5,8,10,16]

Patients with RDD may present with concurrent involvement of extranodal and nodal sites and such phenomenon may be challenging in terms of establishing its diagnosis, and thus RDD may be missed during the first encounter.[3,12]

To date, the exact etiopathogenesis of RDD has remained to be idiopathic, though an aberrant exaggerated immune response to infectious agents especially viral etiology may lead to proliferation of the histiocytes.[8,12,13]

Available studies have depicted the presence of human herpesvirus 6 genome through in situ hybridization as well as the relationship with Klebsiella, Epstein–Barr virus, Brucella, or cytomegalovirus as the possible underlying etiology.[10,12,13]

The pathognomonic histocytopathological feature of RDD is the presence of a phenomenon known as emperipolesis which is characterized by numerous large histiocytes with abundant, pale cytoplasm having variable number of intact lymphocytes within the cytoplasm.[3,7,15,17-19]

Histocytopathologically, in patients with RDD, the background is polymorphous comprising of lymphocytes, plasma cells, and occasional neutrophils, and all these features were present in the collected cytology and histopathology specimens.[3,7,18,19]

Although the histocytomorphological features are typical, diagnostic difficulties may sometimes arise. The major differential diagnosis of RDD upon FNAC of the lymph

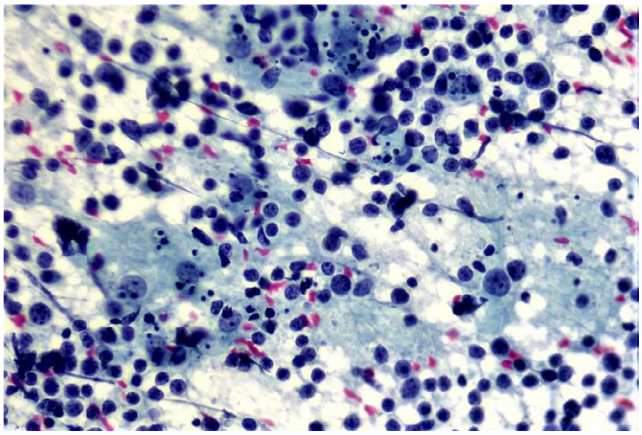

FIGURE 2 Cytologic smear showing histiocytes with emperipolesis, and some histiocytes showed multinucleation

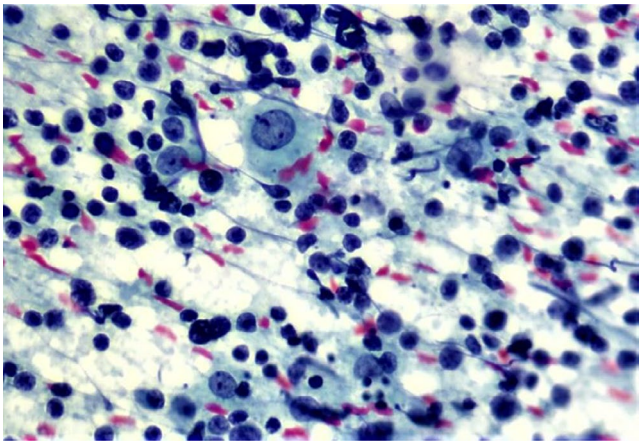

FIGURE 3 Cytologic smear showing histiocytes with dense inflammatory infiltrates in a cytologic smear

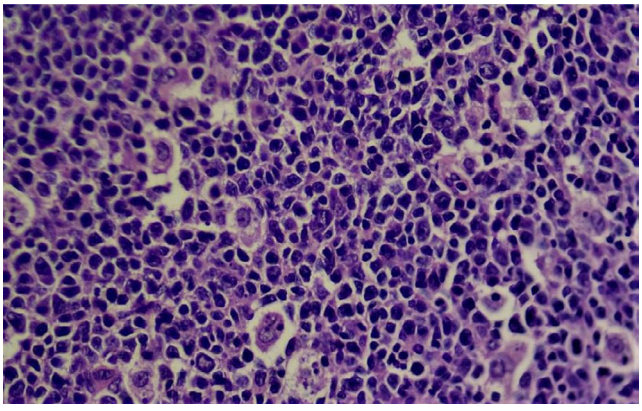

FIGURE 4 Atypical histiocytes with inflammatory infiltrates in histological section

nodes or open lymph node biopsy include reactive lymphoid hyperplasia with sinus histiocytosis, Langerhans cell histiocytosis (LCH), tuberculosis and lymphoma which may be Hodgkin's or non-Hodgkin's lymphoma.[3,7,17-19]

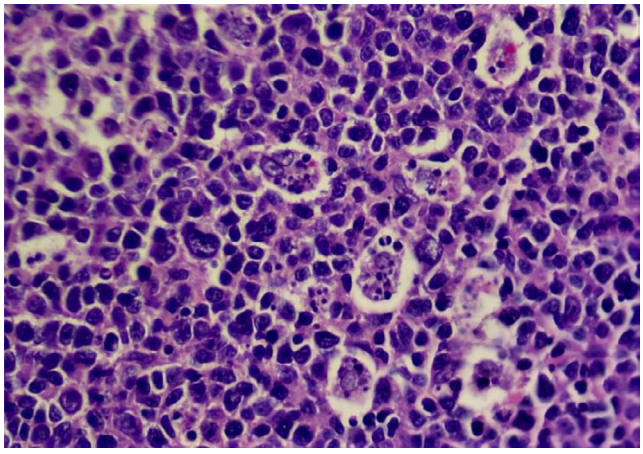

FIGURE 5 Slide section shows histiocytes exhibiting emperipolesis

Regarding the differentials of RDD, reactive sinus histiocytosis tend to show loose clusters of histiocytes, accompanied by germinal center cells, reactive lymphocytes, immunoblasts, and tingible body macrophages without emperipolesis. Such cytologic findings may sometimes mislead the cytologist for a simple diagnosis of reactive lymphadenopathy.[3,10,11,18,19]

Cytologically, Langerhans cells have grooved nuclei and the background shows eosinophilic microabscess and immunoreactivity with CD1a tends to be positive and thus can differentiate RDD.[3,18,19] Tuberculous lymphadenitis shows epithelioid cell granuloma with or without caseous necrosis which are absent in Rosai–Dorfman disease.[3,15,19] Hemophagocytic syndromes should be differentiated from Rosai–Dorfman disease on the basis of the presence of hemophagocytosis, the absence of emperipolesis, and the presence of pancytopenia and hepatosplenomegaly.[3,7]

Hodgkin's disease and some variants of non-Hodgkin's lymphoma show lymphocytes, plasma cells, histiocytes, eosinophils, and Reed–Sternberg cells.[7,11,17]

Histologically, apart from the mentioned known differential diagnoses, Gaucher's disease, metastatic carcinoma and melanoma, and histiocytic sarcoma can add up to other differentials though the classical histomorphology of histiocytic proliferation inclusive of emperipolesis can lead to a definitive diagnosis.[19] Whenever a pathologist is in doubt then, immunohistochemistry with CD11, CD14, CD34, CD68, and S-100 protein[7,13,19] may be of help to support the diagnosis of RDD.

In our case, we established the diagnosis of RDD due to massive bilateral cervical and submandibular lymphadenopathy coupled with the presence of emperipolesis in histocytopathology.

Regarding the treatment of RDD, usually it has a self-limiting course in majority of the patients,[4,5,8,10,12] and therefore treatment is not necessary in majority of them.

Our patient was treated using steroids which were provided by tapering the dose over two weeks for relief of symptoms and to reduce lymphadenopathy. Surgery is usually not required in patients with RDD[4,5,8] unless the lymphadenopathy is too massive and causing discomfort to patient. It should generally be limited to biopsy for confirmation of the diagnosis similar to what was done to our patient where open lymph node biopsy was done for confirmation of the diagnosis.

Depending on the affected anatomical site, the treatment options include surgery, chemotherapy, steroids, and radiotherapy.[5,20] Medical therapy for RDD includes corticosteroids, cytotoxic agents, or both. Combination of corticosteroids (prednisolone) along with agents such as vinca alkaloids (vincristine and vinblastine), 6-mercaptopurine, methotrexate, or alkylating agent (cyclophosphamide) has shown promising outcomes.[5,20] Generally, RDD has an indolent course with approximately 50% of them resolving without any residual disease. However, in one-third of patients, residual adenopathy may be noted and remaining approximately 17% have unresolved symptoms even after 5–10 years.[5,21] In our case, the patient showed no residual disease or recurrence at 3 months of follow-up.

4 | CONCLUSION

While examining FNAC smears and biopsies of a lymph node, the possibility of RDD should always be kept in mind as one of the differential diagnoses. FNAC coupled by histopathology remains to be essential in establishing the diagnosis of RDD. However, FNAC is a reliable, minimally invasive, cost-effective, efficient, and sensitive means to establish a conclusive diagnosis of RDD obviating the need for biopsy.

ACKNOWLEDGMENTS

The patient is highly acknowledged for providing a written informed consent to publish the case report.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

ZSA performed open lymph node biopsy, collected information for the case and drafted the initial version of the manuscript. ZF and AIN both performed cytology and histopathology and also provided critical feedback of the manuscript. AAK drafted the initial version of the manuscript. FB performed open lymph node biopsy and provided critical feedback and edited the manuscript. All authors read and approved the final version to be published in Clinical Case Reports.

ETHICAL APPROVAL

This report is in accordance with the Declaration of Helsinki.

CONSENT

The patient gave a written informed consent prior to her inclusion in this report.

DATA AVAILABILITY STATEMENT

The data that support the findings of this report are available from the corresponding author upon reasonable request.

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