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IP Journal of Diagnostic Pathology and Oncology

Journal homepage: https://www.jdpo.org/

Case Report

Rosai-dorfman disease in pregnancy with rare presentations – A case report

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ARTICLE INFO

Article history:
Received 15-04-2023
Accepted 20-05-2023
Available online 22-06-2023

Keywords:
RosaiDorfman disease
Pregnant women
Unilateral cervical lymphadenopathy
Plasma cells

ABSTRACT

Rosai-Dorfman disease (RDD) also known as sinus histiocytosis with massive lymphadenopathy is a rare disorder of histiocytes characterized histologically by intracellular engulfment of lymphocytes. It may occur in any age group, but is most commonly seen in children and young adults. It is characterized by painless, bilateral massive cervical lymphadenopathy. In approximately one-third of patients it can occur in a variety of extranodal sites where it can have abundant plasma cells and sclerosis. We present a rare case of RDD in a pregnant women who presented with unilateral cervical lymph node with features of RDD showing increase in plasma cells and sclerosis as seen in extranodal sites.

1. Introduction

Rosai-Dorfman disease (RDD) also known as sinus histiocytosis with massive lymphadenopathy is a histiocytic disorder of unknown etiology recognized by Rosai and Dorfman in 1969.[1] RDD is a rare non-Langerhans cell histiocytosis characterized by accumulation of activated histiocytes within affected tissues. RDD now belongs to the R group of the 2016 revised histiocytosis classification.[2] It is a heterogeneous entity can occur in isolation or in association with autoimmune or malignant diseases.[2] It can occur at any age but appears to be more common in children and young adults and is characterized by painless, bilateral massive cervical lymphadenopathy.[1–3] In approximately one-third of patients, RDD can occur in a variety of extra nodal sites but the head and neck region is most common.[3] Other relatively commonly involved extra nodal sites include the soft tissue, skin, upper respiratory tract, gastrointestinal tract, breast, bones, and the central nervous system.[4–8] Histologically they are characterized by sinus lymphophagocytosis or emperipolesis. Extra nodal sites are known to be associated with abundant plasma cells and sclerosis.[4] RDD involving unilateral cervical lymph node in a pregnant women with increase in plasma cells and sclerosis in nodal site is a rare presentation.

2. Case Report

A 23 year old female in her 26 weeks of pregnancy presented with swelling in the right side of the neck for one month. There was no history of fever or other B symptoms. On examination was found to have a discrete mobile cervical lymph node measuring 5x3 cm. Fine needle aspiration cytology (FNAC) was done twice outside. First FNAC was reported as granulomatous lymphadenitis. Second FNAC showed polymorphous population of lymphoid cells with increase in histiocytes and plasma cells with large mononuclear and binucleate cells suggesting a diagnosis of lymphoma. FNAC attempted in our department showed polymorphous population of lymphoid cells with increase in histiocytes, plasma cells, eosinophils with few binucleate cells showing prominent nucleoli. The histiocytes showed prominent phagocytosis/emperipolosis of lymphocytes, plasma cells and neutrophils (Figure 1

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https://doi.org/10.18231/j.jdpo.2023.023

a,b). In view of increase in plasma cells a possibility of associated autoimmune disease was also considered and excision biopsy of lymph node and further evaluation was advised. The histopathological examination of the lymph node showed cluster of macrophages in the sinuses, which exhibited emperpolosis of lymphocyte, plasma cells and neutrophils suggesting the diagnosis of RDD (Figure 1 c,d). There was also increase in sclerosis and plasma cells (Figure 1c). No atypical cells / organisms/ foreign bodies seen. IHC done showed histiocytes positive for CD68, S100 (Figure 2a,b) and negative for CD1a which confirmed the diagnosis. The patient was kept on follow up as the patient was pregnant and she was lost to follow up for further treatment.

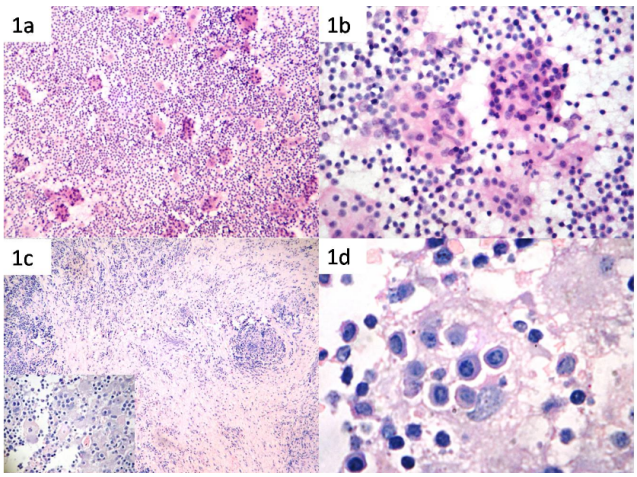

Fig. 1: a,b: Cytology showing lymph node with histiocytosis and emperipolosis(PAP, 100X, 400X); **c:** Histopathology showing increased sclerosis, inset shows sinus histiocytosis with emperipolosis (H&E,100X,400X); **d:** Sinus Histiocyte showing emperipolosis of lymphocytes and plasma cells(H&E,1000X)

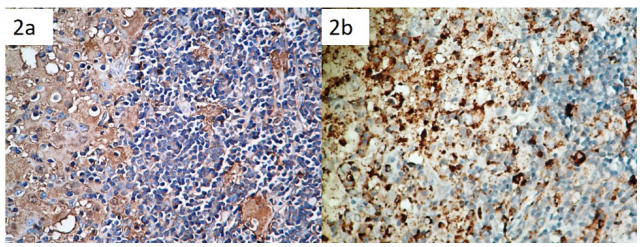

Fig. 2: a: CD68 positivity in histiocytes; **b:** S100 positivity in histiocytes (DAB, 400X)

3. Discussion

RDD is a rare, idiopathic, non-neoplastic histiocytic proliferation of unknown etiology typically presenting with bilateral massive cervical lymphadenopathy with or without systemic involvement. RDD is a heterogeneous entity that can occur as an isolated disorder or in association with autoimmune, hereditary, and malignant diseases.[2] The presence of lymphadenopathy is often significant with nodes as large as it can lead to respiratory compromise in some cases. RDD presenting with isolated unilateral cervical lymphadenopathy is a rare presentation and only few reports are available. Kaltman et al reported a case of unilateral cervical lymphadenopathy in a 11 year old boy.[9] Baden et al reported a case of RDD presenting with unilateral submandibular lymphadenopathy in a four year old girl.[10]

RDD occurring in a pregnant woman is very rare and very few cases have been documented so far as follows: Raychaudhuri et al reported a case of intracranial rosai-dorfman disease in pregnancy.[5] Abdulkader et al presented a case of metachronous Rosai-Dorfman disease arising in multifocal bone sites in a 25-year-old pregnant woman.[6] Bing et al documented RDD in an 8-month pregnant woman that occurred in the left parietal-occipital bone in the ventricular and periventricular area.[7] Alawi et al reported a pregnant patient with RDD involving the mandible.[8] Butler et al. reported a patient with clinical relapses of her RDD lesions during two separate pregnancies with complete disease remission in between.[11] Pagel et al reported another nodal RDD where the patient developed relapses in between pregnancies.[12]

FNAC smears and touch imprints are typically highly cellular with many histiocytes and phagocytosed lymphocytes in a reactive background of lymphocytes and plasma cells. The phagocytosed lymphocytes do not appear surrounded by a “halo,” as they often do in tissue sections because of a fixation artifact. This can lead to difficulty in distinguishing emperipolesis from overlapping lymphocytes. Otherwise FNAC has proved to be a reliable tool in diagnosis. This case also showed all cytological features of RDD but there were significant increase in plasma cell which was also observed to be emperipolosed by the histiocytes. Also there were few large mononuclear and binucleate cells which could raise the suspicion of lymphoma which was one of the differentiatial diagnosis from outside report. Early RDD lesions shows prominent germinal centers and yield many lymphocytes and occasional immunoblasts. In later stages, numerous plasma cells and Russell bodies can predominate.[13] This particular case showed increase in both large cells probably immunoblasts and plasma cells which raised the suspicion of an associated immune disorder in the patient.

The etiology of RDD remains unclear, although it has been regarded as a reactive inflammatory process, immune deficiency and viral infection (eg, Epstein-Barr virus, parvovirus B19, and human herpesvirus 6) have also been postulated to play a role in the pathogenesis.[2,14,15] Emerging evidence suggests that RDD may be associated with an abnormal autoimmune response as most cases of RDD demonstrate abundant plasma cells

and sclerosis mimicking IgG4 related disease, especially in extranodal sites.[4] Kuo et al reported IgG4-positive plasma cells in cutaneous RDD.[4] Although there is a close relationship between RDD and IgG4 sclerosing inflammation, a definitive link between RDD and IgG4 positivity has yet to be established. However, recent studies identified NRAS, KRAS, MAP2K1, and ARAF mutations in patients with features of RDD.[16,17] RDD have been observed in patients with malignancies like Hodgkin and non-Hodgkin lymphomas, cutaneous clear cell sarcoma, where RDD can either precede or follow each other.[2]

RDD is usually positive for IHC markers S100, macrophage markers like CD68 but negative for CD1a which could differentiate it from other differential diagnosis which includes nonspecific sinus hyperplasia, Langerhans cell histiocytosis, malignant histiocytosis, granulomatous lesions, Hodgkin lymphoma and metastatic malignant melanoma. This case showed histiocytes positive for CD 68, S100 and negative for CD1a confirming the diagnosis.

4. Conclusion

RDD though usually presents as bilateral massive cervical lymphadenopathy there can be rare clinical presentations and unsual morphologies. This is one such rare case of pregnant female presenting with unilateral cervical lymphadenopathy with increase in plasma cells and sclerosis. Though RDD can be diagnosed by FNAC, sometimes it causes diagnostic dilemmas as seen in this case, and needs histopathology and IHC for definitive diagnosis.

5. Conflict of Interest

There are no conflicts of interest in this article.

6. Source of Funding

None.

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Cite this article: Kalaivani S, Siddaraju N. Rosai-dorfman disease in pregnancy with rare presentations – A case report. *IP J Diagn Pathol Oncol* 2023;8(2):105-107.