Case Report

DOI: 10.21276/APALM.2102

Rosai-Dorfman Disease: An Imposter of Plasma Cell Rich Diseases

Priyadarshini Dehuri, Debasis Gochhait*, Debdatta Basu and Neelaiah Siddaraju

Department of Pathology, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India

ABSTRACT

Rosai Dorfman Disease is a histiocytic disorder associated with painless cervical lymphadenopathy. The typical histomorhology includes dilated lymphatic sinuses with a lymphohistiocytic infiltrate with emperipolesis of lymphoid cells and plasma cells as the hallmark feature. We are highlighting a unique case of Rosai Dorfman disease presenting with generalized progressive lymphadenopathy in a 19 year old male, in whom diagnosis of RDD was established by fine needle aspiration cytology.

The case that is discussed here is also worth documenting because of its unusual morphology which is dominated by plasma cells. We have also attempted to determine a possible association of this case of Rosai Dorfman disease with increased IgG4+ plasma cells and IgG4 related disease.

Keywords: *Rosai Dorfmann Disease, Generalised lymphadenopathy, Plasma cell*

Introduction

Rosai-Dorfman disease (RDD) also known as Sinus histiocytosis with massive lymphadenopathy (SHML) was recognised and described for the first time in 1969 by Rosai and Dorfman.[1] It is a histiocytic disorder characterised by bilateral painless cervical lymphadenopathy, which may be associated with fever, leucocytosis. We are highlighting a unique case where the patient presented with progressive generalized lymphadenopathy which is unusual for RDD. It was diagnosed with the help of fine needle aspiration cytology (FNAC)which revealed a morphology dominated by plasma cells. In such an unusual plasma cell rich presentation of RDD case, the pathologists and clinicians should not only consider in differential diagnosis plasma cell rich lesions, but histiocytic lesions as well.

Case Report

A 19 year male presented to the cytology OPD with history of intermittent fever, progressive generalized painless nontender lymphadenopathy (bilateral cervical, axillary and inguinal nodes) (Figure IA and B) for 6 months. Fine needle aspiration cytology smears were very cellular. There was predominance of plasma cells and numerous histiocytes with engulfment (emperipolesis) of the plasma cells(Figure IIA and B). There were only few reactive lymphoid cells and no eosinophils in the smears. Given the above cytomorphological features, the case was diagnosed as Rosai Dorfman disease with a note for haematological and serological work up. A core biopsy was done from the cervical node which confirmed the same disease with the aid of immunohistochemistry. However, emperipolesis was not as strikingly appreciated as in cytology smears(Figure III -A).On immunocytochemistry (IHC), the histiocytes were positive for S 100(Figure III-B) and CD68 and negative for CD1a . We also performed immunostains for IgG (Figure III-C) and IgG4 (Figure III-D) on the biopsy to determine whether RDD in this patient was associated with an increase of IgG4 + plasma cells and presented a spectrum of IgG4 disease, as reported by others.[2,3] IgG stain showed cytoplasmic positivity diffusely in the lymphnode while IgG4 cells were only scattered with a IgG to IgG4 ratio of around 15%. The serology of the patient was proved to be negative for Hepatitis B &C as well as HIV. The haematological work up showed haemoglobin of 9.5 g/dl and WBC count of 4380 /cumm with 5% eosinophils. No atypical cells were seen. Other serum biochemical markers were within normal limits; however, the gamma globulin levels were not available. The patient underwent an ultrasonography of the abdomen and pelvis which showed mild enlargement of retroperitoneal nodes but neither organomegaly nor any other focal lesions were noted.

Discussion

RDD in most cases is associated with significant bilateral enlargement of cervical nodes. There are many hypotheses and postulates regarding the pathogenesis however the etiology is still unknown. Recent evidences based on next generation sequencing suggest that atleast a proportion of cases of RDD are clonal.[4]The authors have suggested presence of mutually exclusive

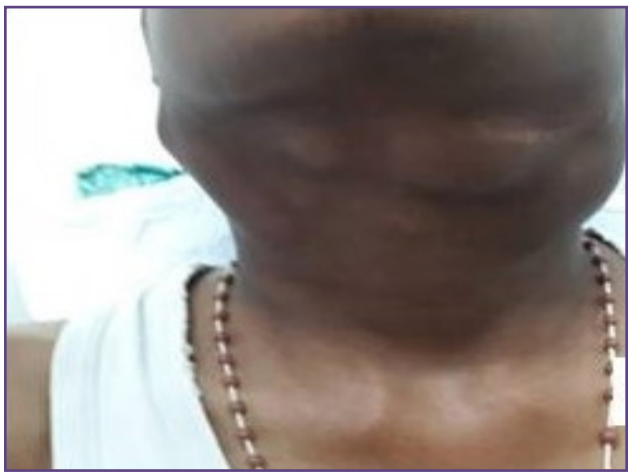

Fig. 1 : Shows the massive multiple cervical and axillary lymphadenopathy.

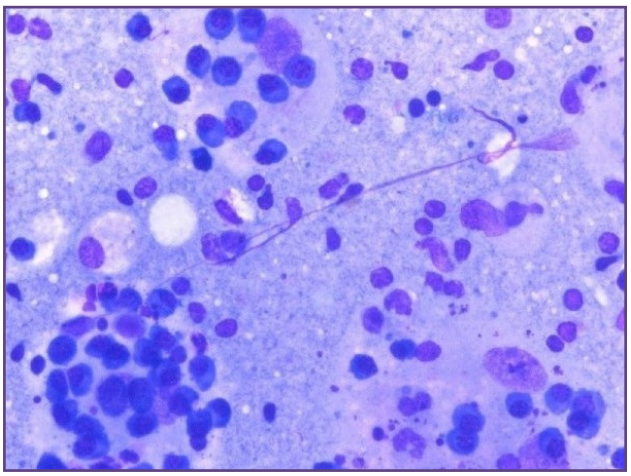

Fig. 2: (May Grunwald Giemsa stain - 200X) Cytology smears showing histiocytes with pale stained nuclei showing emperipolesis of plasma cells.

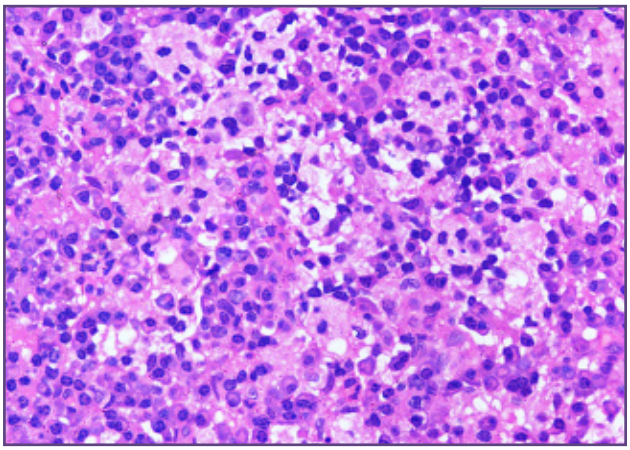

Fig. 3: (Hematoxylin and Eosin stain – 200X) Biopsy showed the dominance of plasma cells in most part of the core. The emperipolesis is appreciable in occasional macrophage.

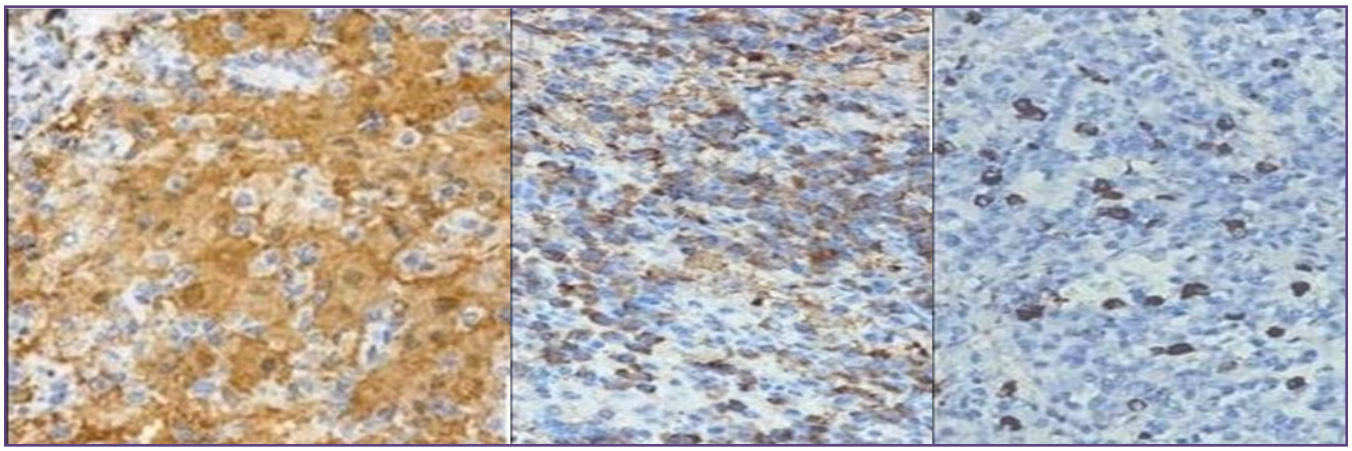

Fig. 4 (A,B,C) : (Immunohistochemical stain for S100,IgG and IgG4- 200X) : A -shows diffuse positivity for S100 in the histiocytes.B- More than 90% of the non histiocytic cells in most areas staining for the Immunoglobulin G marker .C- Image highlights the scattered IgG4 positive cells. the ratio of the IgG:IgG4 positive cells being less than 30%.

recurrent somatic KRAS and MAP2K1 mutations in 33% of RDD cases.

This disease is predominantly confined to the cervical nodes however upto 40% of cases may show extranodal involvement. [5] Among extranodal sites, head and neck is the commonest with cases reported in orbit, eye, oral cavity, salivary gland, central nervous system, upper respiratory tract and rarely in thyroid. In addition it is also described at other sites like skin, soft tissue, breast, bone and genitourinary tract.[6-10] Majority of the cases (around 80%) are seen in the second decade with slight dominance of male over females.[11]

Our case presented with generalized lymphadenopathy which is extremely unusual in RDD, described only in occasional case reports.[12] Moreover the morphological features were also unique in this case. The prominent cell population in the cytologic smears was constituted by plasma cells which were seen both within histiocytes(emperipolesis) as well as in the background population. Mature lymphocytes and reactive lymphoid cells have been known to constitute the major population of cells besides histiocytes with admixed plasma cells and rarely polymorphonuclear cells. In the present case however, plasma cells outnumbered the lymphoid cells which were very sparse. Some of the histiocytes had multiple vacuolations . The predominance of plasma cells in the cytologic smears as well as biopsy brought in all the plasma cell rich lesions (Plasma cell rich variant of Castleman's disease, HIV lymphadenopathy, Plasmacytoma) in the differential diagnosis. Emperipolesis, the hallmark characteristic of RDD may not be prominent at extranodal sites which may cause diagnostic problems with these plasma cell rich lesions. Plasmacytoma which is also common in head and neck region (both nodal and extranodal) shows exclusive population of plasma cells and is commonly seen in the 4th and 5th decade. Lack of significant emperipolesis may also bring the histiocytic disorders (Hemophagocytic lymphohistiocytosis, Sinus hyperplasia and Langerhan cell histiocytosis) in to the differential diagnosis. Lymphophagocytosis can also be seen in hemophagocytic lymphohistiocytosis (HLH) syndrome however it is dominated by phagocytosis of red cells apart from lymphoid cells. In addition the patients with this syndrome have some history of viral infections/ malignancy along with pancytopenia, hepatosplenomegaly which is unusual in RDD. Sinus hyperplasia is unusual in cervical nodes and does not show significant emperipolesis/ phagocytosis. In eosinophilic granuloma (LCH) the histiocytes have grooved and twisted nuclei and many multinucleated cells in addition to the varying proportion of eosinophils, lymphocytes, plasma cells and polymorphs. Immunohistochemistry has an important role in the diagnosis of RDD as is evident from the proposed latest diagnostic criteria for RDD which classifies RDD under R group of histiocytoses.[13] It requires the presence of large histiocytic cells displaying hypochromatic nuclei and pale cytoplasm, often with abundant emperipolesis with S100^{+}, fascin^{+}, CD68^{++}, CD14^{+}, HLA-DR^{+}, CD163^{+} macrophages without CD1a or CD207 staining. In RDD, the histiocytes are positive for S 100 and CD68 while in sinus hyperplasia and HLH only CD 68 is positive. All the three entities are negative for CD1a which is strongly positive in the histiocytes of LCH.[14]

Another fact that also needs to be emphasized is that although core biopsies are being increasingly performed for diagnosis of various lymphadenopathies, there are few limitations. First is the difficulty in appreciating emperipolesis. Another challenging situation is what we encountered in the present case ,that is predominance of plasma cells. There were sheets of plasma cells in the biopsy with occasional histiocytes showing emperipolesis which prompted the exclusion of plasma cell rich lesions for diagnosis. In addition, the ratio of IgG to IgG4 positive plasma cells cannot be determined by the existing criteria as it needs an inspection of the fields with maximum plasma cells.

Many authors have tried to look into the relationship between Rosai Dorfman disease and the spectrum of IgG4 related disease by comparing the clinical and histopathological features along with the IgG4 staining of plasma cell.[3] However, in our case we did not find an increase in IgG4+ plasma cells and thus this case may represent RDD with no increase in IgG4+ plasma cells. Till date there is no consensus regarding the possibility that cases with increased IgG4 positive cells lie within the spectrum of IgG4 related disease and merely demonstrate morphologic RDD disease- like features or presence of increased IgG4 positive cells in these cases is coincidental and does not necessarily typify IgG4 related disease. There have been speculations that the IgG4 positive subset represents a more steroid responsive group akin to IgG4 related disease.[2]

Rosai Dorfman disease is usually self-limiting though a remitting relapsing course is also known. Patients with non-selflimited histiocytoses with specific genetic abnormalities could potentially benefit from targeted therapy, although large scale studies are required to sustain this idea.[4] In the present case the patient improved with prednisolone and has been relapse free in a 1 year follow up period.

Conclusion

A patient presenting with generalised lymphadenopathy also needs to evaluated for excluding benign conditions like

Rosai Dorfman disease. Fine needle aspiration cytology undoubtedly plays a pivotal role in the initial diagnostic grouping of lymphadenopathies as well as categorisation of histiocytic disorders .Plasma cell rich morphology of lymphadenopathies also needs consideration of histiocytic disorders in the differential diagnosis. Some cases of RDD may be associated with increased IgG4+ plasma cells and those patients can benefit from corticosteroid therapy. However, further research is required to better understand the mechanism and clinical significance of this association.

Reference

1. Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy. A newly recognized benign clinicopathological entity. Arch Pathol. 1969 Jan;87(1):63–70.
2. Menon MP, Evbuomwan MO, Rosai J, Jaffe ES, Pittaluga S. A subset of Rosai-Dorfman disease cases show increased IgG4-positive plasma cells: another red herring or a true association with IgG4-related disease? Histopathology. 2014 Feb;64(3):455–9.
3. Zhang X, Hyjek E, Vardiman J. A subset of Rosai-Dorfman disease exhibits features of IgG4-related disease. Am J Clin Pathol. 2013 May;139(5):622–32.
4. Garces S, Medeiros LJ, Patel KP, Li S, Pina-Oviedo S, Li J, et al. Mutually exclusive recurrent KRAS and MAP2K1 mutations in Rosai-Dorfman disease. Mod Pathol Off J U S Can Acad Pathol Inc. 2017 Oct;30(10):1367–77.
5. Sennes L, Koishi H, Cahali R, Sperandio F, Butugan O. Rosai-Dorfman disease with extranodal manifestation in the head. Ear Nose Throat J. 2004 Dec;83(12):844–7.
6. Ju J, Kwon YS, Jo KJ, Chae DR, Lim JH, Ban HJ, et al. Sinus Histiocytosis with Massive Lymphadenopathy: A Case Report with Pleural Effusion and Cervical Lymphadenopathy. J Korean Med Sci. 2009 Aug;24(4):760–2.
7. Kumar B, Karki S, Paudyal P. Diagnosis of sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease) by fine needle aspiration cytology. Diagn Cytopathol. 2008 Oct;36(10):691–5.
8. Vemuganti GK, Naik MN, Honavar SG. Rosai dorfman disease of the orbit. J Hematol OncolJ Hematol Oncol. 2008 Jun 28;1:7.
9. Kala C, Agarwal A, Kala S. Extranodal manifestation of Rosai-Dorfman disease with bilateral ocular involvement. J Cytol. 2011 Jul;28(3):131–3.
10. Sandoval-Sus JD, Sandoval-Leon AC, Chapman JR, Velazquez-Vega J, Borja MJ, Rosenberg S, et al. Rosai-Dorfman disease of the central nervous system: report of 6 cases and review of the literature. Medicine (Baltimore). 2014 May;93(3):165–75.
11. Bist SS, Bisht M, Varshney S, Pathak VP. Rosai Dorfman syndrome with extranodal manifestation. J Assoc Physicians India. 2007 Jun;55:445–7.
12. Khalilzadeh S, Karimi S, Fakharian A, Hakimi SS. Generalized lymphadenopathy: A case report of Rosai-Dorfman disease. Tanaffos. 2007;6(3):65–7.
13. Emile J-F, Abla O, Fraitag S, Horne A, Haroche J, Donadieu J, et al. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. Blood. 2016 02;127(22):2672–81.
14. Garza-Guajardo R, García-Labastida LE, Rodríguez-Sánchez IP, Gómez-Macías GS, Delgado-Enciso I, Chaparro MMS, et al. Cytological diagnosis of Rosai-Dorfman disease: A case report and revision of the literature. Biomed Rep. 2017 Jan;6(1):27-31.

***Corresponding author:**
Dr. Debasis Gochhait, Assistant. Professor, .Dept of Pathology, Room no 2023, Institute block, JIPMER.
Phone: +91 8489334333
Email: debasis.go@gmail.com

Financial or other Competing Interests: None.