Indian Journal of Medical Case Reports ISSN: 2319–3832
Online, International Journal, Available at http://www.cibtech.org/jcr.htm
2021 Vol.10, pp. 56-59/Bhargavi et al.
Case Report (Open Access)

CNS ROSAI DORFMAN DISEASE WITH IgG4 POSITIVE PLASMA CELLS

***Bhargavi Ilangovan[1] , Nikita Mulchandani[2] , Janarthinakani[1] and Jegan Niwas Kannan[3]**
[1]Department of Radiation Oncology (Madras Cancer Care foundation)
[2]Department of Pathology
[3]Department of Medical Oncology (Madras Cancer Care foundation)
**Author for Correspondence: bhargavi.ilangovan@gmail.com*

ABSTRACT
Rosai Dorfman Disease (RDD) is a rare form of non-Langerhans cell histiocytosis. The common age group is between 22 and 63 years with a median age of 23 years at presentation. Presentation in the elderly is rare and the most common presentation is nodal, which is also called the classic type. Central Nervous system (CNS) presentation is also a rarity. We are presenting this case where an octogenarian presented with a CNS RDD to display its rarity and to also discuss about the presentation, pathology and management of the disease.

Keywords*: Rosai Dorfman Disease, CNS, IgG4 Positive Plasma Cells*

INTRODUCTION
Rosai-Dorfman Disease (RDD) is a non-Langerhans cell histiocytosis, characterised by an uncontrolled proliferation of non-clonal S100 positive histiocytes. It was first described in 1969 by Rosai and Dorfman(J and RF, 1969). It has a male preponderance and the age at presentation is between 22 and 63 years, with the median age being 23 years. They are classic (nodal) and extra nodal in presentation. The most common presentation is as large cervical lymphadenopathy. Extra nodal RDD occurs in about 75% of the people. The common sites being skin, nasal cavity, soft tissue, CNS, bone and parotid glands.

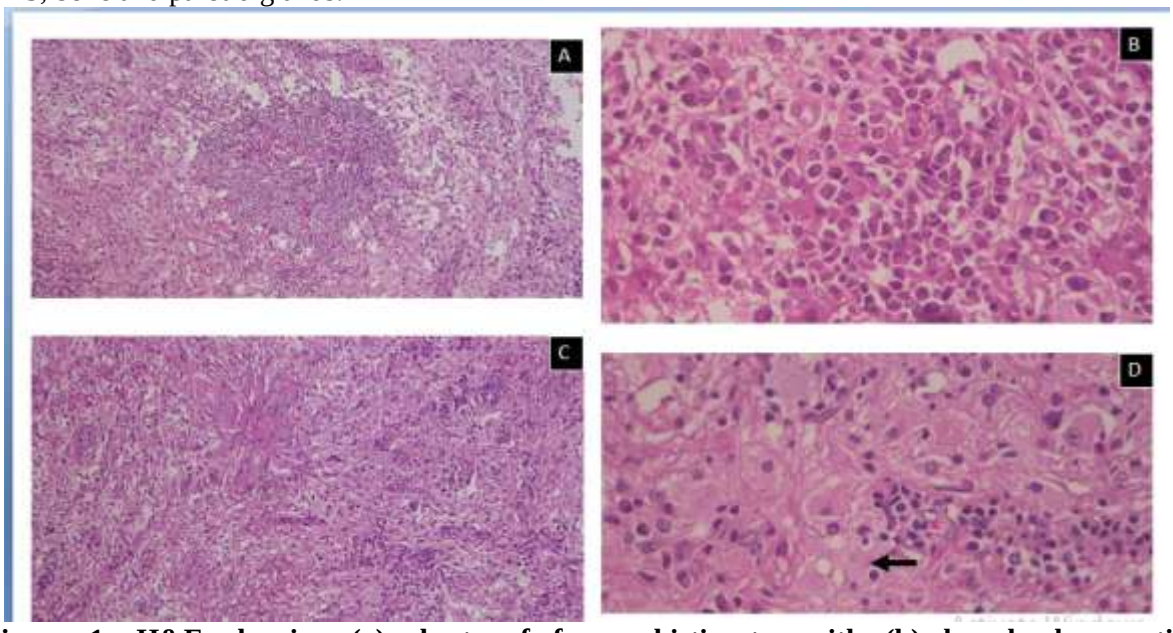

Figure 1: H&E showing (a) sheets of foamy histiocytes with (b) lymphoplasmacytic inflammatory infiltrate, (c) storiform fibrosis. (d) Emperipolesis in a large foamy histiocyte (arrow)

CASE

An 84 year old fit gentleman was evaluated for unsteadiness of gait. He has had previous sub dural hematomas and hence was evaluated with an MRI of brain. The MRI scan showed 3 dural based soft tissue lesions in the left parieto occipital region (2.2 x 1 cm), left frontal region(3.5 x 1.5 cm) and in the right parietal region (1.8 x 1.3 cm). The image also showed adjacent dural thickening related to all the lesions. The left parieto occipital region was associated with marked oedema. The lesions showed a low signal rim on gradient sequence and the right sided lesion showed restriction diffusion. The differentials included metastatic lesions and atypical meningiomas as these were not noted in the previous MRI done in January 2020.

He underwent excision of the left frontal lesion. The Histopathological examination was consistent with Rosai-Dorfman disease with increased IgG4-positive plasma cells (Fig 1).

On immunohistochemistry (IHC), the biopsy showed a diffuse proliferation of S100 positive histiocytes against a background showing mixed population of CD3 and CD20 positive T- and B-lymphocytes respectively with a substantial number of CD138 positive plasma cells (Fig 2).

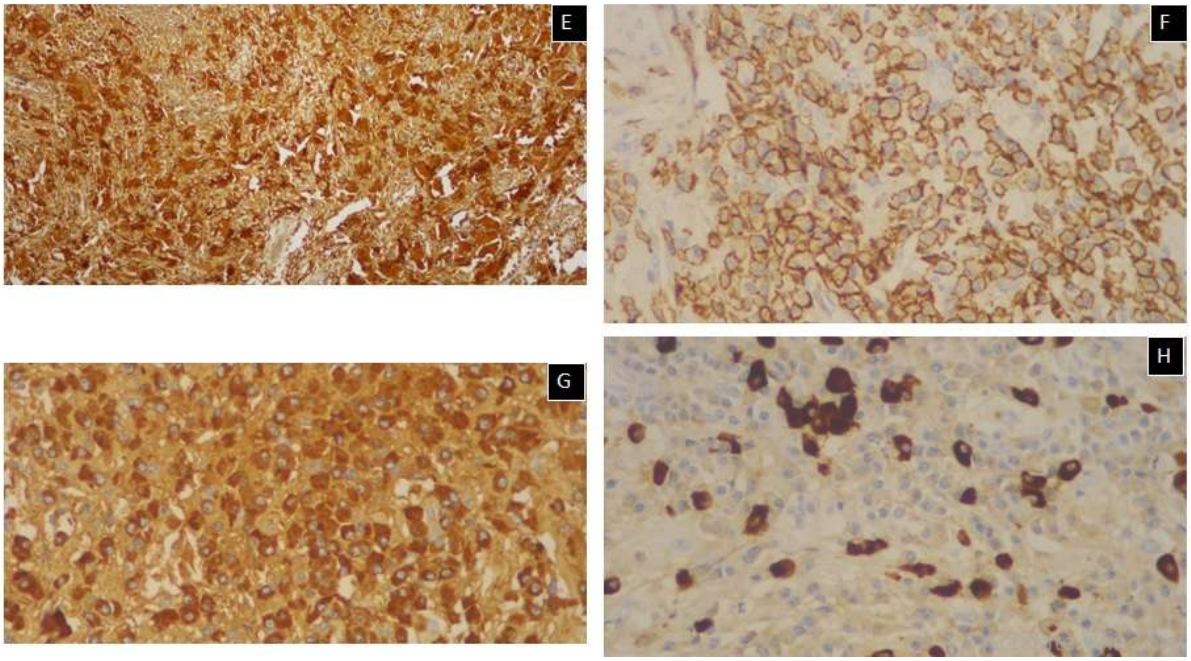

Figure 2: IHC showing (d) sheets of S100 positive foamy histiocytes with (e) CD138 positive plasma cells. (f) These plasma cells express IgG with (g) IgG4 positivity seen in a subset of these plasma cells.

The plasma cells were polyclonal with reactivity for both kappa and lambda. The IgG4/IgG ratio was 12.5%.

DISCUSSION

CNS RDD has been reported in about 7% of the people with RDD. They commonly present as extra axial, dural based lesions mimicking meningiomas (Andriko *et al.*, 2001) (Zhang *et al.*, 2010). Intra parenchymal lesions are rare. The common location is cerebello pontine. Radiologically, they mimic meningiomas. However, the classic arteriovenous shunting and hypervascularity in digital subtraction angiography, seen in meningioma is absent in RDD (Wang *et al.*, 2020).

Histopathological examination of RDD, regardless of the site, characteristically shows proliferation of histiocytes with pale cytoplasm and a dark nucleus. Emperipolesis (plasma cells, lymphocytes and erythrocytes engulfed within a large foamy histiocyte) is seen, but is not necessary for diagnosis (Oussama *et al.*, 2018). Immunohistochemical diagnosis is based on the histiocytes showing S100 positivity.

It has been found to be associated with certain inherited conditions such as the familial histiocytosis, H syndrome and pigmented hypertrichotic dermatosis with insulin dependent diabetes. All these are

described ad histiocytosis- lymphadenopathy plus syndrome. These syndromes show germline mutations in the SLC29A3 gene. Also heterozygous germline mutations in the FAS gene, TNFSF, leading to auto immune lymphoproliferative syndrome type 1 has also been associated with RDD.
In patients with lymphoma, Hodgkin's or non-Hodgkin's, RDD pattern has also been observed. It has also been found after myelodysplatic syndrome or bone marrow transplantation for leukaemia. Presence of RDD-like pathology in >10 % of the specimen isneeded to classify them as neoplasia associated RDD. Immune related RDD has been found with SLE, juvenile arthritis, auto immune haemolytic anaemia and also in a case of RAS-associated autoimmune leuko proliferative disease.
A subset of RDD cases show increased IgG4 positive plasma cellsand need to be distinguished from IgG4-related disease(IgG4-RD) (Menon *et al.*, 2014). While the cut-off for the number of $IgG4^+$ plasma cells varies from organ to organ, a $IgG4^+/IgG^+$ positive plasma cell ratio more than 40 % is indicative of IgG4-RD (Deshpande *et al.*, 2012).
The etiopathogenesis of the disease is unknown. NGS(next generation sequencing) on some of the tumor tissue has shown BRAF mutations, suggesting the involvement of MAP Kinase pathway in their formation (Richardson *et al.*, 2018).
The management options are wide and varied. Surgery seems to be the mainstay in CNS RDD. Systemic treatment options include steroids, immunomodulators and chemotherapy. Rituximab has also been used. Immune related RDD respond well to immunomodulators and steroids, whereas the non-immune related respond to chemotherapy(Goyal *et al.*, 2020). Radiotherapy has been found to be useful in refractory cases, localised disease or for palliation of pressure symptoms.

CONCLUSION

We are discussing this case in view of his age and site of presentation. CNS manifestation itself is a rare presentation, especially at this age. He is being managed with steroids and is doing well.

REFERENCES

Andriko J A, A Morrison, C H Colegial, B J Davis, R V Jones (2001). Rosai-Dorfman disease isolated to the central nervous system: a report of 11 cases', *Modern pathology*, **14**(3), 172–178. doi: 10.1038/MODPATHOL.3880278.

Deshpande V *et al.* (2012). Consensus statement on the pathology of IgG4-related disease. *Modern Pathology,* **25**(9), pp. 1181–1192. doi: 10.1038/MODPATHOL.2012.72.

Goyal G *et al.* (2020). Clinicopathological features, treatment approaches, and outcomes in Rosai-Dorfman disease', *Haematologica*. *Ferrata Storti Foundation*, **105**(2), 348–357. doi: 10.3324/HAEMATOL.2019.219626.

Menon Madhu P, Moses O Evbuomwan, Juan Rosai, Elaine S Jaffe, Stefania Pittaluga (2014). 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*, **64**(3), 455–459. doi: 10.1111/HIS.12274.

Oussama Abla, Eric Jacobsen, Jennifer Picarsic, Zdenka Krenova, Ronald Jaffe, Jean-Francois Emile, Benjamin H Durham, Jorge Braier, Frédéric Charlotte, Jean Donadieu, Fleur Cohen-Aubart, Carlos Rodriguez-Galindo, Carl Allen, James A Whitlock, Sheila Weitzman, Kenneth L McClain, Julien Haroche, Eli L Diamond (2018). Consensus recommendations for the diagnosis and clinical management of Rosai-Dorfman-Destombes disease, *Blood*, **131**(26), 2877–2890. doi: 10.1182/BLOOD-2018-03-839753.

Richardson TE *et al.* (2018). BRAF mutation leading to central nervous system rosai-dorfman disease', *Annals of neurology*. *Annals of Neurology*, **84**(1), 147–152. doi: 10.1002/ANA.25281.

Rosai J and RF Dorfman (1969). Sinus histiocytosis with massive lymphadenopathy. A newly recognized benign clinicopathological entity. *Archives of Pathology*, **87**(1), 63–70. *Available at: https://pubmed.ncbi.nlm.nih.gov/5782438* (Accessed: 28 September 2021).

Wang Y *et al.* (2020). Neuroimaging features of CNS histiocytosis syndromes', *Clinical Imaging*.

Elsevier Inc, **60**(1), 131–140. doi: 10.1016/j.clinimag.2019.10.001.

Zhang JT *et al.* (2010). Primary intracerebral Rosai-Dorfman disease, *Journal of Clinical Neuroscience*. Elsevier Ltd, **17**(10), 1286–1288. doi: 10.1016/j.jocn.2010.01.048.