CNS Manifestations of Rosai-Dorfman Disease

Zanib Javed[1], Moeez Tariq[2], Muhammad Shahzad Shamim[3]

Abstract

Rosai-Dorfman disease (RDD) is an abnormal proliferation of histiocytes which manifest classically as bilateral cervical lymphadenopathy and B symptoms. Rarely, it also presents with involvement of other systems. CNS RDD is extremely rare and accounts for 5% of reported cases. The clinical picture is dependent on the area of CNS affected. It is mostly diagnosed on MRI, however, it may be confused with a meningioma, dural based metastases, lymphoma, sarcoidosis, etc. Diagnosis is based on typical histopathological features. The recommended treatment for symptomatic CNS manifestations of RDD is complete surgical resection.

Keywords: Rosai-Dorfman disease, Central Nervous System, Histopathology

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Introduction

Rosai-Dorfman disease (RDD) is an abnormal proliferation of histiocytes with variable clinical demonstrations.[1] "Histiocytes" is the term attributed to macrophages residing in connective tissue of various organs.[2] Rosai-Dorfman disease includes familial and sporadic forms, that further include Classical/Nodal RDD, Extranodal RDD, Neoplasia associated RDD, and Immune disease associated RDD.[2] RDD is more common in males and in people of African descent and has a prevalence of 1:200,000, with an approximated 100 new cases diagnosed per year in the United States.[1]

Classical RDD presents as painless bilateral cervical lymphadenopathy with or without B symptoms (fatigue, weight-loss, night sweats).[2,3] Extranodal RDD comprises of over 40% of cases rarely occurs in the absence of nodal involvement.4 Common extranodal sites for RDD are skin, CNS, head and neck, and thorax.[1] CNS involvement is rare and occurs in less than 5% of cases.[1,3] Here we will review the CNS manifestations of RDD, their presentations, diagnostic utilities and treatment strategies.

[1,3]Section of Neurosurgery, Aga Khan University Hospital, Karachi;
[2]Department of Surgery, Dr. Ruth KM Pfau Civil Hospital, Dow University of Health Sciences, Karachi-Pakistan
Correspondence: Muhammad Shahzad Shamim.
e-mail: shahzad.shamim@aku.edu
ORCID ID: 0000-0001-8305-8854

Review of evidence

About 75% of patients who have CNS involvement in RDD present with cranial problems and 25% present with spinal manifestations.[1,4] The mean age of onset is 20.6 years with slight male preponderance.[1] The common sites for stacking of abnormal histiocytes in the cranial cavity are cerebral poles, parasagittal, para-sellar, cavernous sinus, petro-clival, and cerebellar regions, causing symptoms of headaches, visual defects, cranial nerve defects, focal or generalized seizures, gait impairment, focal deficits, raised intracranial pressure, or symptoms due to mass affect.[3,4] The symptoms occur on a period of weeks to months.[3] Familial RDD with CNS involvement presents with impairment in auditory pathway and deafness.[1]

In spine, it usually involves dural and epidural compartments, more common in cervical and thoracic regions.[1,3] Bone and cord parenchyma are also potential sites.[5] It may present with myelopathy, radiculopathy, or symptoms of spinal cord compression, and mean age of presentation is around 33 years.[3,5]

Baseline laboratory panels show increased erythrocyte sedimentation rate with normal complete blood cell count or normocytic/microcytic anaemia, leukocytosis (predominantly neutrophilic), hypoalbuminaemia, hyperferritinaemia, and polyclonal hypergammaglobulinaemia.[1] On MRI intracranial and intraspinal RDD closely mimics tumours such as meningiomas, lymphomas, dural-based metastases, and chronic inflammatory/granulomatous disorders such as sarcoidosis, or tuberculosis.[4-8] The lesions on T1-weighted imaging (T1WI) sequences, generally appear homogeneously isointense with strong and homogeneous enhancement after contrast administration.[7,8] Intracranial lesions of RDD show hypointensity on T2-weighted images (T2WI) giving an impression of lymphoproliferative changes rather than meningeal growth (which appears usually isointense or hyperintense on T2WI).[6,8] There is also no evidence of bone destruction, hyperostosis, calcification, or hypervascularity on angiography which also aids in distinguishing the lesions from meningiomas.[6,9] Lobulation, pseudopodium sign and multiple lesions in different intracranial sites are also important imaging features of RDD.[4] The lobulation and/or pseudopodium sign may be directly linked to the involvement of the cerebral pia mater and possibly lead to postoperative recurrence, while multiple lesions may

indicate the aggressiveness of the lesion and higher risk of recurrence.[4] Purely intraparenchymal RDD lesions are either solid or ring-enhancing without dural attachment, which are often misdiagnosed as primary or metastatic brain tumours.[9]

Spinal RDD lesions mostly present as homogeneous, isointense to hypointense masses on T2WI with or without peri-lesional oedema, closely mimicking meningiomas, the differentiation from which can be achieved via histopathology.[6] PET/CT is helpful to screen whole-body lymph nodes and discover some uncommon and small lesions.[5]

On histopathological analysis, there are histiocytes mixed with lymphocytes and plasma cells and avid fibrosis.[1,4,8] The immunohistochemical stains show positivity in expression of CD4, CD11c, CD14, CD68 (KP-1), CD163 and S-100 proteins, but not CD1a, CD207, CD21, CD23, CD35, langerin, and clusterin.[1,4,8,9] The RDD histiocytes are usually large with round-to-oval nuclei, dispersed chromatin, prominent nucleoli, and abundant clear-to-foamy or vacuolated cytoplasm.[1] These cells also exhibit "emperipolesis" i.e. engulfing intact cells and sometimes nuclear debris and lipids.[1,8] The engulfed cells remain viable and can exit histiocytes in contrast to the process of phagocytosis (Figure 1).[1]

Hu et al., strongly recommend the strategy of "wait and watch" for patients without signs and symptoms of neurological impairment and spinal instability.[5] Treatment modalities of symptomatic CNS RDD include surgical resection, corticosteroids, chemotherapy, interferon, and radiation, all with variable responses.[8,10] Surgical resection is curative, and recommended choice for both intracranial and intraspinal disease.[1,3,5,8,11] Radical resection is the recommended method, since residual lesions tend to relapse.[8] Crush cytology combined with frozen sections is useful for intraoperative diagnosis.[8] In case of multifocal disease, surgical resection of single focus should be reserved for bulky disease with neurologic dysfunction.3 Adjuvant therapies including steroids, chemotherapy, and radiotherapy are indicated for progressive lesions and patients with systemic involvement.[5]

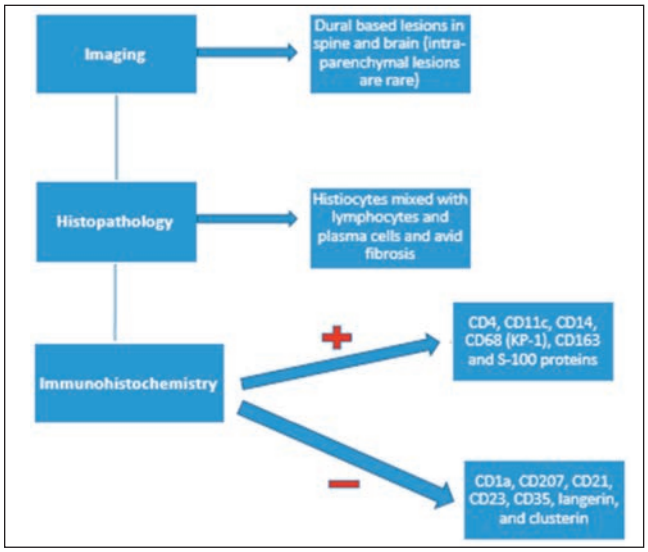

Figure: Algorithm for diagnosis of CNS Rosai Dorfman Disease.

Residual lesions may regress without requiring further treatment, but non-regressing lesions may require radiotherapy.[8] External-beam radiotherapy can be used in patients with localized unresectable symptomatic steroid-refractory masses.[1,3] Steroids have an effective role in RDD with nodal and intracranial lesions.[3] Chemotherapy is mainly used to treat extensive symptomatic RDD or in patients that are refractory to other therapies.[8]

Conclusion

Rosai Dorfman disease is a histiocytic proliferation that usually affects lymphoid tissue but can be found at extranodal sites. CNS RDD is very rare and mimics CNS tumours and granulomatous conditions in clinical and radiologic presentations. Treatment of symptomatic RDD at CNS is complete surgical resection, while steroids, radiotherapy, chemotherapy, etc. are used for severe, unresectable, or recurrent lesions.

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