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## A Rare Presentation of Rosai-Dorfman Syndrome: First Reported Case in Iran

A case of intracranial Rosai-Dorfman syndrome is presented that was initially diagnosed and treated as meningioma, and was complicated due to a wrong diagnosis of coexistent lung sarcoidosis. Intracranial lesions appeared as dura-based parasellar and anterior fossa enhancing lesions on magnetic resonance images. Excellent result was obtained from whole brain radiotherapy, which can be used as a guideline for treating similar cases.

**Keywords:** skull base, histiocytosis, sinus, Rosai-Dorfman syndrome

### Introduction

Sinus histiocytosis with massive lymphadenopathy (SHML) or more correctly Rosai-Dorfman syndrome (RDD) is a pathological entity first described by Rosai and Dorfman in 1969. Typical clinical features of the disease include massive painless cervical lymphadenopathy, fever and weight loss, leukocytosis, elevated erythrocyte sedimentation rate, and hypergammaglobulinemia. Involvement of an extranodal site is present in approximately 43% of cases, either alone or in association with lymphadenopathy. Every organ system can be affected by RDD, the most common ones being bone, skin and soft tissue, upper respiratory tract, salivary glands, eyes and orbits, digestive system, and breasts.<sup>1</sup> Generally, patients present in their mid-20s with cervical lymphadenopathy (87%) often preceded by a short, non-specific infection.<sup>2</sup> The disease can have a protracted course lasting several months to years, but is commonly accompanied by episodes of exacerbation and remission, with a mortality rate of 7%.<sup>3</sup> Of 423 patients reported in the SHML registry, 36 had some evidence of orbital involvement and there have been 50 reported cases of intracranial involvement.<sup>2</sup>

Herein, we report a first case of intracranial Rosai-Dorfman syndrome with unique clinical and radiological features.

### Case report

The patient was a 42-year-old woman who presented with a chief complaint of left sided loss of vision, which after MR imaging was diagnosed with brain meningioma. The patient underwent brain surgery after which she became completely blind (no light perception in the left eye). The surgical approach was from the right side, since the infiltrating lesion rested on the skull base extending to the right and left, and the patient was right-handed.

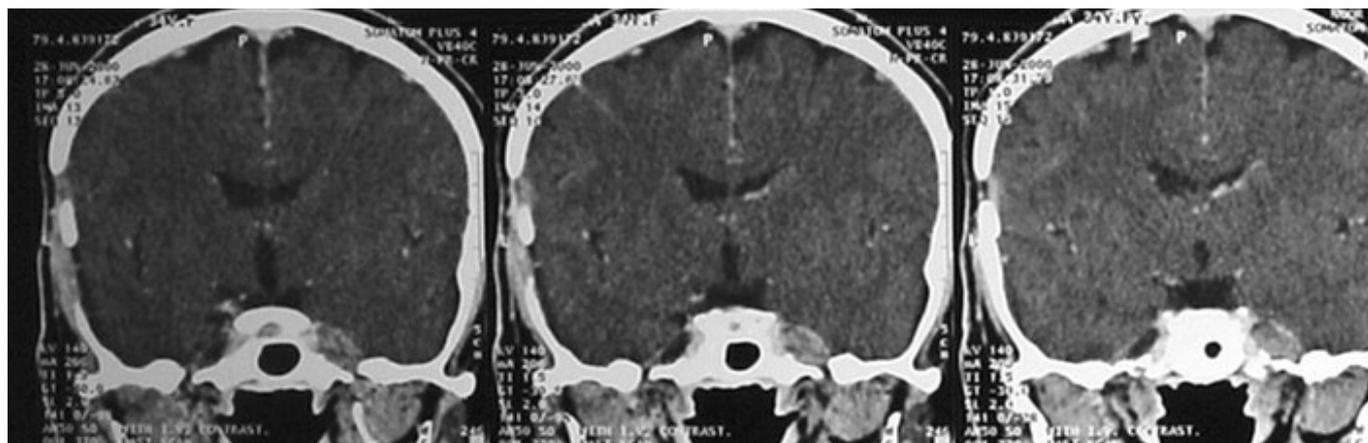
Four years later, the patient began to have right sided visual loss. The patient had cough, generalized weakness and lassitude. She was admitted to hospital and on her chest CT scan multiple adenopathies were evident. Initially, differential

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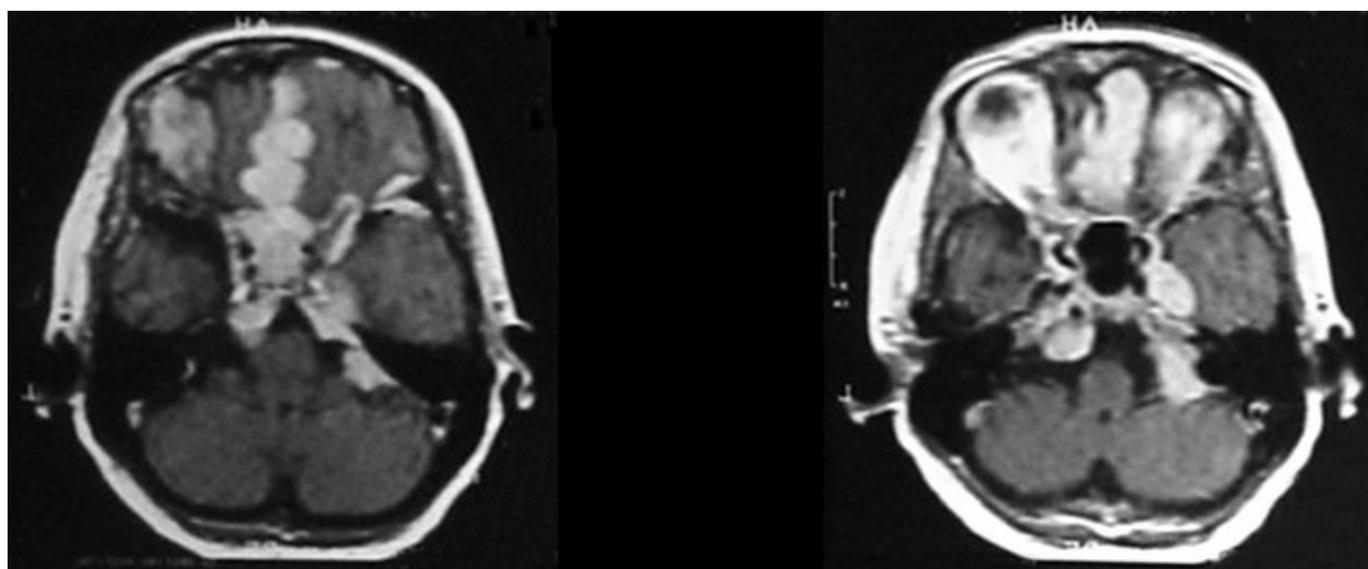
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**Fig 1.** CT with contrast in the early stage of the disease. Parasellar enhancing mass on the left side is seen, Site of the previous craniotomy on the right side is noted. Also remnants of incompletely resected lesion is noted on the right side.



**Fig 2.** CT with contrast (late stage of disease). Enhancing mass in the left parasagittal and suprasellar area.



**Fig 3.** T1 weighted MRI study with contrast material enhancement: Dural based enhancing mass in all portions of the skull base extended from posterior fossae to the olfactory groove in the anterior fossae.

diagnoses of tuberculosis and sarcoidosis were made for the patient; however, she did not respond to treatment. On brain MRI findings, differential diagnoses of sarcoidosis or diffuse meningiomatosis

seemed plausible. Moreover, pathological evaluation of brain biopsy suggested sarcoidosis, tuberculosis and other granulomatous diseases.

Final pathological diagnosis of Rosai-Dorfman syn-

drome was made for the patient in the UK. This diagnosis was also confirmed by immunohistochemistry (IHC) for S100 protein. The patient was referred for radiotherapy (13 sessions for a total dose of 30 Gy). Visual problems showed dramatic improvement following the radiotherapy. Six months after radiotherapy, a control MRI revealed a significant reduction in the size of lesion (Figures 1-7).

## Discussion

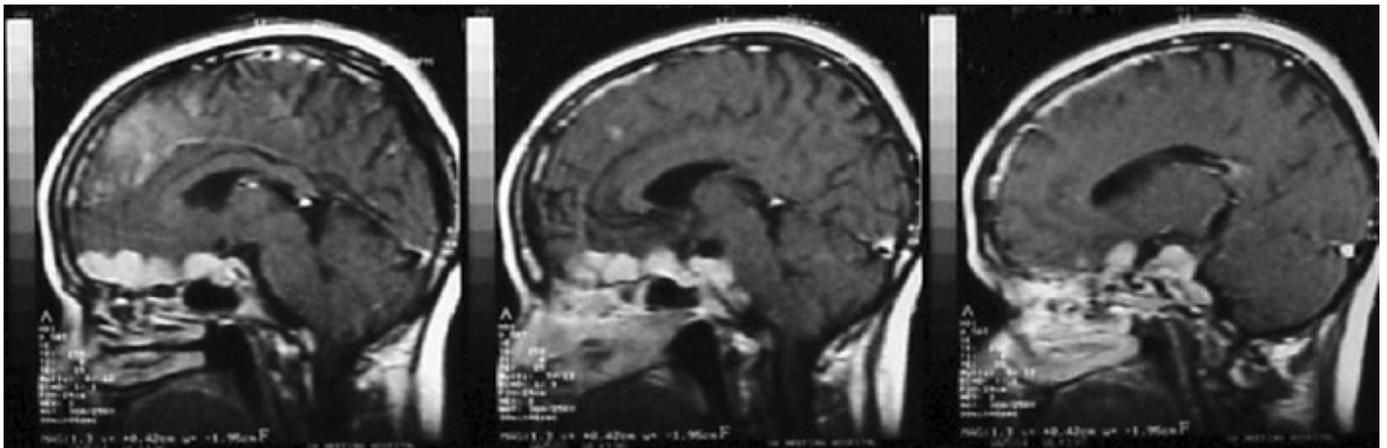
### General presentations of Rosai-Dorfman patients

RDD most commonly affects otherwise healthy individuals in the first two decades of life but no age group is exempt. The etiology still remains obscure, and it is unclear if it is immune-mediated, of infectious origin, or related to some other pathological mechanism yet to be clarified.<sup>3</sup> Patients with intracranial

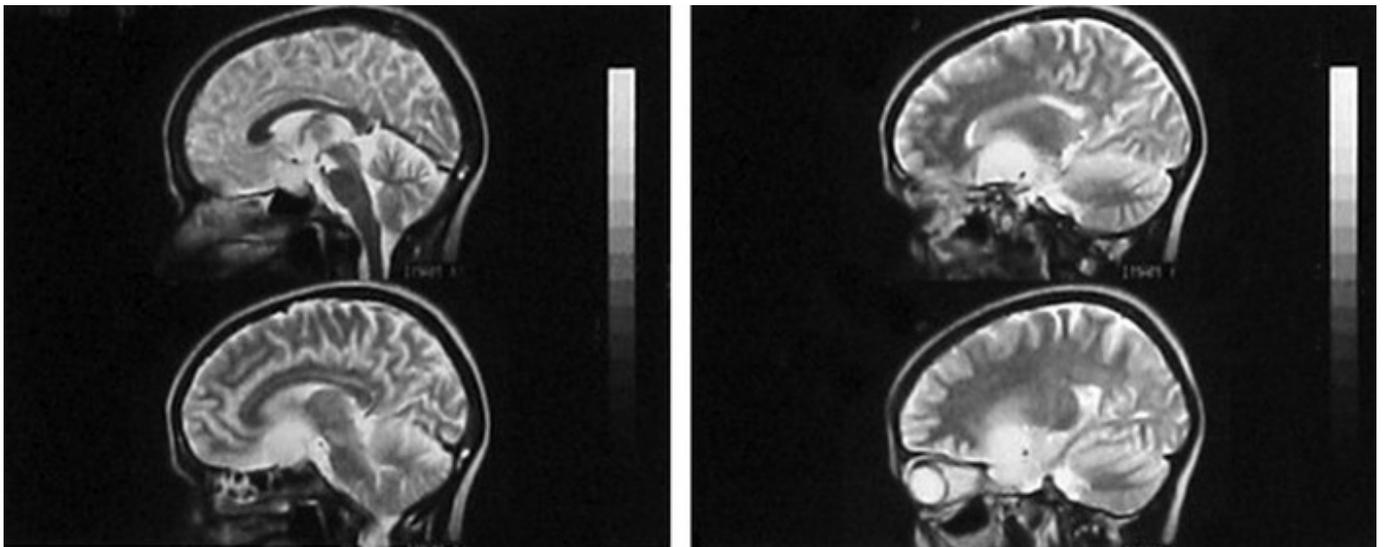
involvement usually present at higher ages than those with classic manifestations of the disease.<sup>4</sup> There is a slight male predominance. Our patient had thoracic lymphadenopathies that led to a misdiagnosis of sarcoidosis. To our knowledge this is the first case of intracranial RDD associated with sarcoidosis-like lesions in the thoracic cavity

### Radiological findings

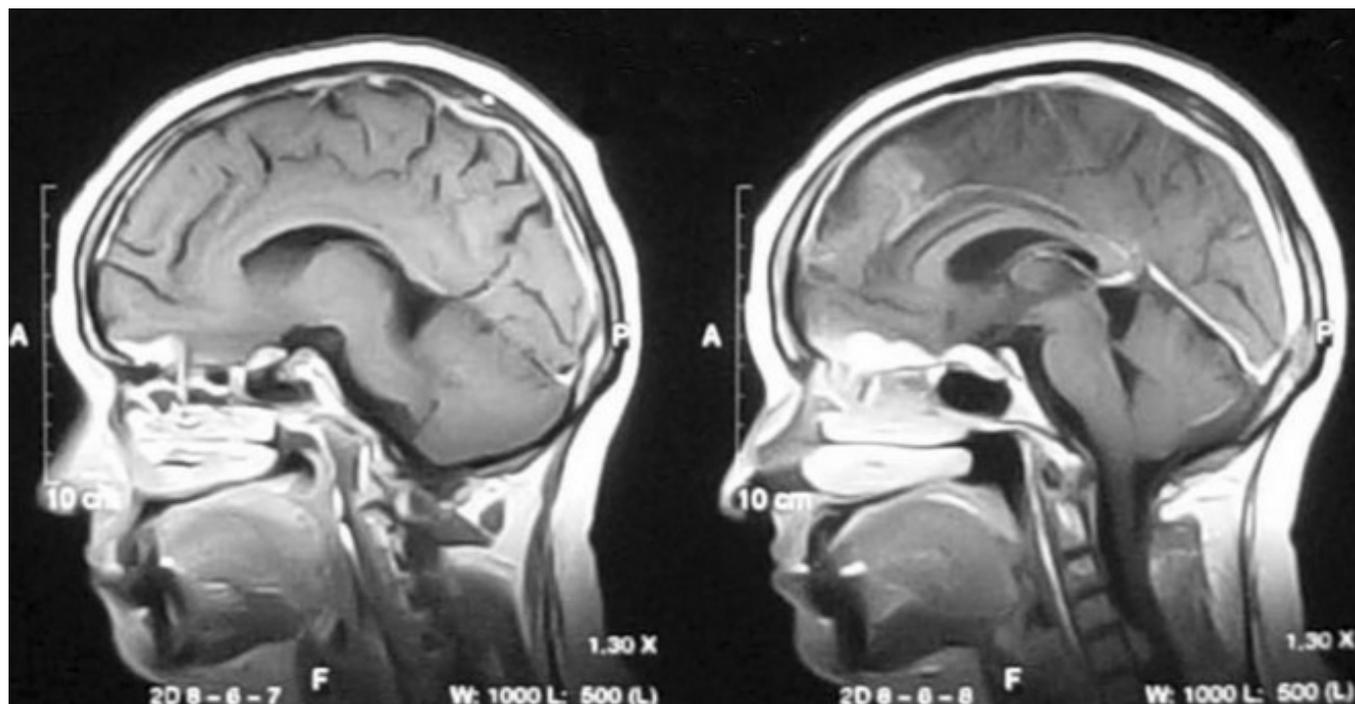
Intracranial lesions of Rosai-Dorfman disease, are usually dura-based, and clinically mimic meningiomas. On T2 weighted MR images, meningiomas show low to high signal intensity, the variation being a reflection of histological subtype. In contrast, Rosai-Dorfman syndrome shows a rather low signal intensity, although hypersignal patterns on T2 images is also reported.<sup>4,5</sup> The brain lesion in our case had also a hypersignal intensity on T2 MR image.



**Fig 4.** Sagittal T1 with contrast , showing a lobulated enhancing mass involving all portions of the anterior and middle cranial fossae, resembling a dural based meningioma .

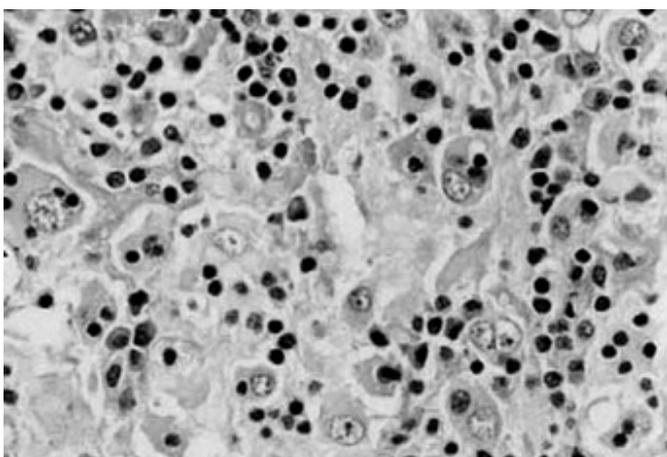


**Fig 5.** T2 weighted image: hypersignal mass in the planum-sphenoidal and parasellar regions.



**Fig 6.** Postradiotherapy contrast enhanced T1 weighted MR image showing shrunk lesion volume.

On angiograms, meningiomas are commonly seen as hypervascular lesions. In contrast, the results are variable for Rosai-Dorfman syndrome.<sup>4</sup> Various amounts of edema might also be present surrounding the lesion.<sup>6</sup> Clinically, as it is true for meningiomas, intracranial Rosai-Dorfman syndrome causes a variety of clinical symptoms depending on the location of the lesion. Thus, headache, seizure, cranial nerve deficits, and various other symptoms may be seen or become evident as the disease progresses.<sup>4</sup> In our pa-



**Fig 7.** Pathology slide showing characteristic lesion of the Rosai-Dorfman syndrome. Numerous distinctive histiocyte with round or oval vesicular nuclei are seen. The cytoplasm of many of the histiocytes contains well-preserved lymphocytes, a phenomenon known as emperipolesis.

tient, visual disturbances resulted from her tumoral mass.

Most frequent locations of the intracranial lesions might include the convexity, the parasagittal region, and the cavernous sinus. The petroclival region and intraparenchymal or intraventricular locations have been also reported.<sup>4</sup>

A vast number of previously reported intracranial cases of RDD displayed dural attachment while some of them were associated with erosion of the adjacent bone.<sup>4</sup> A wider differential diagnosis in such lesions includes meningioma, germinoma, granulomatous disease, other histiocytoses, and metastases. Our case was a unique presentation in the literature regarding the nature of mass progression (parasellar mass extending into the anterior fossa).

#### General laboratory findings

This type of histiocytosis may show no specific abnormalities on laboratory examination of both blood and CSF; only high erythrocyte sedimentation rate, hypergammaglobulinemia or other immunologic manifestations may be seen.<sup>7</sup> Furthermore, although Rosai-Dorfman syndrome may include a history of fever, malaise, night sweats, and weight loss in patients with systemic involvement, isolated intracra-

nial Rosai-Dorfman disease usually causes only neurological symptoms.

### Pathologic differential diagnosis

The histological differential diagnosis of dural-based intracranial Rosai-Dorfman syndrome includes Langerhans cell histiocytosis (LCH), infectious processes and lymphoproliferative disorders. LCH and Rosai-Dorfman disease both have polymorphous infiltrates of histiocytes. However, they can be distinguished histologically because in LCH eosinophils are usually prominent, the histiocytes' nuclei are folded, and on Birbeck granules are demonstrated on electron microscopy.

Due to the polymorphous infiltrates and occasional abscess formation in Rosai-Dorfman syndrome, infectious processes like CNS tuberculosis and fungal infections are also in the differential diagnosis. Emperipolesis and S100-positive histiocytes along with specific stains and culture studies help with distinguishing Rosai-Dorfman syndrome from infections. The immunohistochemical phenotype (KP-1 and S100 positivity) of the histiocytes has features of both mononuclear phagocytic systems and interdigitating reticulum cell histiocytic lineages.<sup>2,8</sup> The tumor cells are assumed to be activated macrophages derived from circulating monocytes.

In our case, besides the general histologic features of RDD, histiocytes were CD68 and S100 positive but were CD1a negative. Sarcoidosis or malignancy has not been a reported possible diagnosis.

### Treatment options and outcome

Intracranial Rosai-Dorfman syndrome has been treated with conventional surgery, pharmaceutical treatment involving steroids and chemotherapeutic agents, conventional radiotherapy, and radiosurgery.<sup>9</sup> Among these treatments, surgical resection seems to be the most effective and when the intracranial lesion is totally excised, the disease will not recur.<sup>10</sup> Total resection was not possible in our case due to both the location of the lesion and the obscure early diagnosis. Our case however, fairly responded to the radiation therapy and symptoms were largely improved after extracranial radiation therapy.

The prognosis of RDD is variable. Most patients experience an indolent course that is characterized by

exacerbations and remissions. In 50% of systemic cases, the signs will resolve spontaneously as in our case in whom lung lesions disappeared.<sup>6</sup>

Seventeen percent of patients will have asymptomatic persistent adenopathy, and 17% will have residual symptoms for 5 to 10 years after onset. Relapsing patients tend to be slightly older (mean age 42 years) without remarkable gender predominance. Mortality has been reported to be approximately 7%, possibly due to immune system dysfunction.<sup>1</sup>

The prognosis of Rosai-Dorfman syndrome with CNS involvement has not been reported as poor. In a review of follow-up data of 43 such patients, most patients (58%) were still alive. Only two patients (4.7%) had died. Moreover, no death was reported to have occurred as a result of isolated intracranial Rosai-Dorfman syndrome.<sup>11</sup>

### Conclusion

In conclusion, we presented the diagnostic dilemmas and management of a case of intracranial Rosai-Dorfman syndrome that can be applicable to diagnosis and management of similar cases.

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