

# ROSAI-DORFMAN DISEASE (RDD) WITH ISOLATED COMPROMISE OF THE CENTRAL NERVOUS SYSTEM. CASE REPORT AND LITERATURE REVIEW



## Key words (MeSH)

Histiocytosis, sinus  
Central nervous system  
Tomography X-ray  
computed

## Palabras clave (DeCS)

Histiocitosis sinusal  
Sistema nervioso central  
Tomografía  
computarizada por  
rayos X

Enfermedad de Rosai-Dorfman (ERD) con compromiso exclusivo del sistema nervioso central. Presentación de caso y revisión de literatura

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## Summary

Rosai-Dorfman Disease (RDD) or Sinus Histiocytosis with Massive Lymphadenopathy (SHML) is a rare benign histiocytic disorder, usually affecting the lymph nodes. Intracranial involvement is an uncommon variant of the disease; however, intracranial lesions without concomitant nodular involvement is exceptional. The lack of typical brain imaging patterns can lead to surgery due to misdiagnosis, with causes attributed to a probable malignant origin. Histopathological diagnosis is usually made after the surgical procedure. There is no consensus related to diagnosis, clinical course and treatment of this disease. A case report is presented on isolated intracranial RDD, with a retrospective reading of the imaging studies.

## Resumen

La enfermedad de Rosai-Dorfman (ERD) o histiocitosis sinusal con linfadenopatía masiva (HSLM) es una entidad histiocítica benigna rara, que usualmente afecta los ganglios linfáticos. Se han descrito algunos casos en el sistema nervioso central, y son excepcionales los que aparecen sin afección nodular concomitante. La falta de patrones imaginológicos cerebrales típicos puede llevar a una cirugía por un diagnóstico erróneo, con causas atribuidas a un probable origen maligno.

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Usualmente, el diagnóstico histopatológico se realiza después del procedimiento quirúrgico. Esta entidad clínico-patológica carece de consenso en diagnóstico, curso clínico y tratamiento. Se presenta un caso de ERD con extensión intracraneal, con la lectura retrospectiva de los estudios imaginológicos.

## Introduction

Rosai-Dorfman disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy (SHML), is a rare disease, described in 1969, that primarily affects male adults and adolescents (1). It is histologically characterized by distortion of normal lymph node architecture secondary to histiocyte emperipolesis, resulting in dilation of lymphatic sinusoids (1). Although it is a benign disease, progressive in nature, its presentation simulates a malignant pathology, leading to equivocal treatment (2).

The most common clinical manifestation is related to painful bilateral cervical lymphadenopathies, fever and weight loss (1). Extranodal extension has also been documented, mainly in skin, genitourinary tract, lower respiratory tract, oral cavity and soft tissues, in 43% of cases. Additionally, documented cases of SHML with extension to the central nervous system (CNS) are rare and represent < 5% of reported cases (3,4).

Likewise, documented cases of isolated SHML, i.e. without nodal injury, represent 23% and are more frequent in the gastrointestinal and pulmonary systems. Isolated cases of RDD in the CNS are very rare, approximately 0.5% of them (5). Magnetic resonance imaging (MRI) and computed tomography (CT) are important tools for diagnosis and treatment (4,5).

A case of extranodal extension of RDD with extension to the central nervous system is presented, along with a review of histopathology.

## Case report

Male patient of 37 years of age, with no history of cigarette smoking or abuse of psychoactive substances, with neurosurgical intervention of skull base fifteen years ago, without pathology report or clear information about the procedure. He goes to the emergency department after a car accident. The CT images (figure 1) and MRI with contrast medium (figure 2), show an extraaxial lesion in the anterior region of the interhemispheric fissure, with associated vasogenic edema, which was interpreted as a plaque meningioma. The histopathological study, after surgical resection, showed a dense fibrous tissue with lymphoplasmocytic content and histiocyte infiltration known as emperipolesis, without cellular evidence of meningioma, with secondary astrocytic reaction (figure 3). The previously described findings are compatible with Rosai-Dorfman disease.

## Discussion

Rosai-Dorfman disease is a reactive proliferative histiocytic disorder, of benign and progressive clinical course, of unclear aetiology, with an estimated incidence of 100 cases per year in the United States (6), most frequently in young adults and male adolescents, documented between the ages of 1 and 78, with a ratio of

4:1 with respect to the female population, without any distinction between races (7,8).

The classic presentation is composed of painful bilateral cervical lymphadenopathies, fever, weight loss and anemia (1). Additionally, extension to extranodal organs has been described in 43% of cases, most frequently in skin, genitourinary tract and lower respiratory tract (3). There have also been documented cases of histiocyte emperipolesis without nodular affection, known as isolated SHML, with greater involvement in the gastrointestinal and respiratory systems. Extension to the CNS is rare, so the isolated presentation is less than 0.5% (7).

As for the presentation of SHML cases in the CNS, intracranial lesions and spinal lesions have been described, of which the most frequent, in 70%, are intracranial lesions (8).

The aetiology of SHML/RDD is not known with certainty. However, the immunophenotypic profile and studies related to the expression of monoamines derived from activated macrophages have shown expression of interleukin  $1\beta$  and tumor necrosis factor  $\alpha$ , which are related to histiocyte migration known as emperipolesis (9). Infectious diseases, herpes viruses, Epstein-Barr and parvovirus B19 (3,10,11) have been described as possible causes. Likewise, molecular studies using polymorphic regions for human androgen receptors have demonstrated that RDD is a polyclonal disease (12).

Clinical manifestations are mainly determined by location. The main reasons for consultation associated with RDD/SHML with or without lymphoid nodule involvement in CNS are headache, convulsions, weakness and motor and/or sensory deficit (8,13,14).

The imaging characteristics of isolated intracranial RDD are not pathognomonic, they frequently share imaging manifestations with other pathologies, such as: meningioma, melanoma, granulomatous inflammatory diseases (tuberculosis and sarcoidosis) and subdural hemorrhages. As for its intracranial presentation, it usually manifests as extraaxial masses with dural base, supratentorial, the most frequent being convexity, sellar region, parasellar, clivus and cavernous sinuses. However, cases of intraparenchymal lesions have been described. To date, only 76 cases have been isolated in the CNS since 1969 (1,7,8,15-18).

However, in CT scans they are described as low and medium density extra-axial masses, without erosive bone lesions or associated calcifications, which can sometimes share characteristics with chronic subdural hematoma (19,20-23). In MRI images, RDD lesions are usually of intermediate signal in the gray substance in T1 and T2 weighted images, with homogeneous enhancement after administration of intravenous contrast medium.

Treatment of Rosai-Dorfman disease is generally recommended when lesions are symptomatic, taking into account that it is a non-neoplastic lymphoproliferative disorder (18).

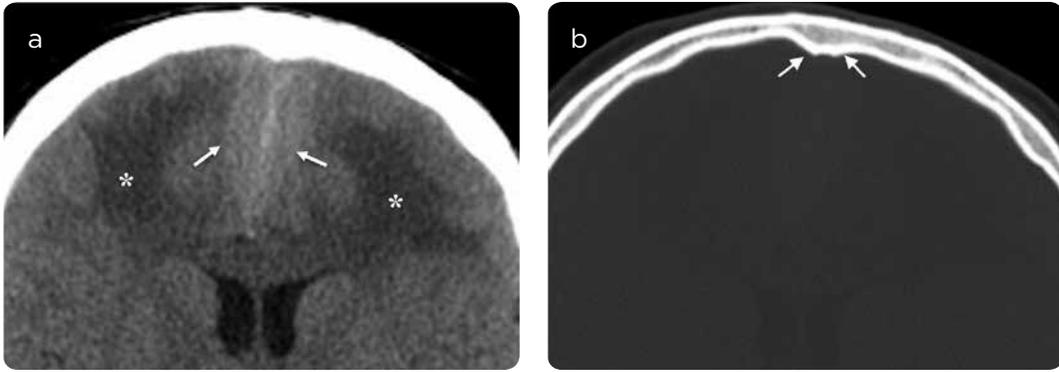


Figure 1. Single CT scan of the skull, axial, a) in the cerebral parenchyma window and b) bone window. Slightly hyperdense mass is identified, with poorly defined contours, which occupies the anterior region of the interhemispheric fissure (arrows in a), associated with low density of the white substance of the frontal lobes due to vasogenic edema (\*). No calcifications or hyperostosis adjacent to the lesion are identified (arrows in b).

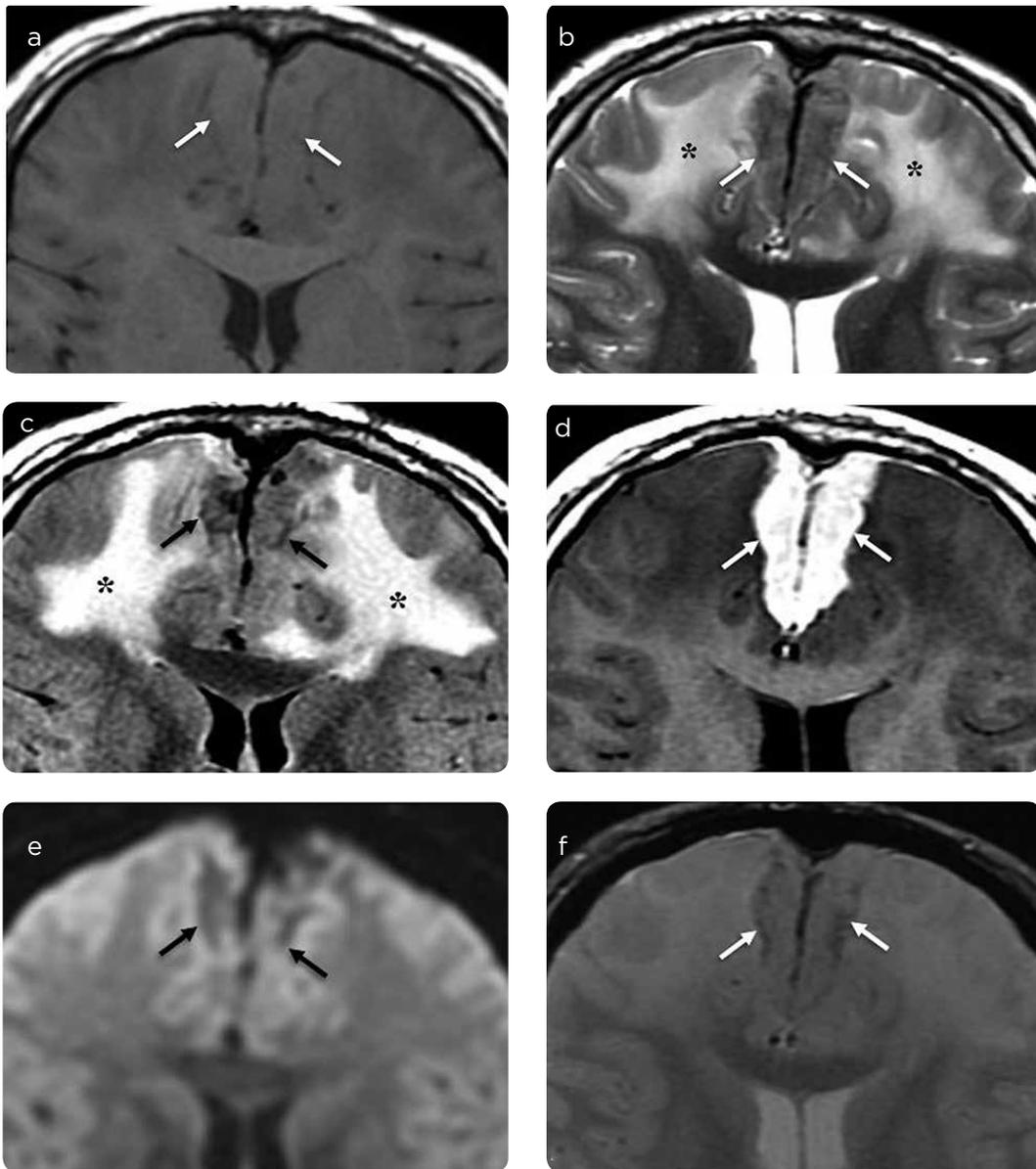


Figure 2. Brain MRI with contrast medium, axial cuts. a) T1 weighted images, b) T2, c) T2-FLAIR, d) T1 after intravenous administration of contrast medium (e), diffusion and (f) echo gradient sequence. Extraaxial mass that occupies and widens the interhemispheric fissure, with well-defined lobed contours, with signal intensity similar to the grey substance in T1 (arrows in a) and in fluid-sensitive sequences (arrows in b and c). The described lesion generates vasogenic edema of the frontal lobes (\*) and enhances avidly after the administration of contrast medium (arrows in d). No restriction on water movement is identified in the diffusion images (arrows in e) indicative of hypercellularity, nor calcifications or haemorrhage foci in the echo gradient images (arrows in f).

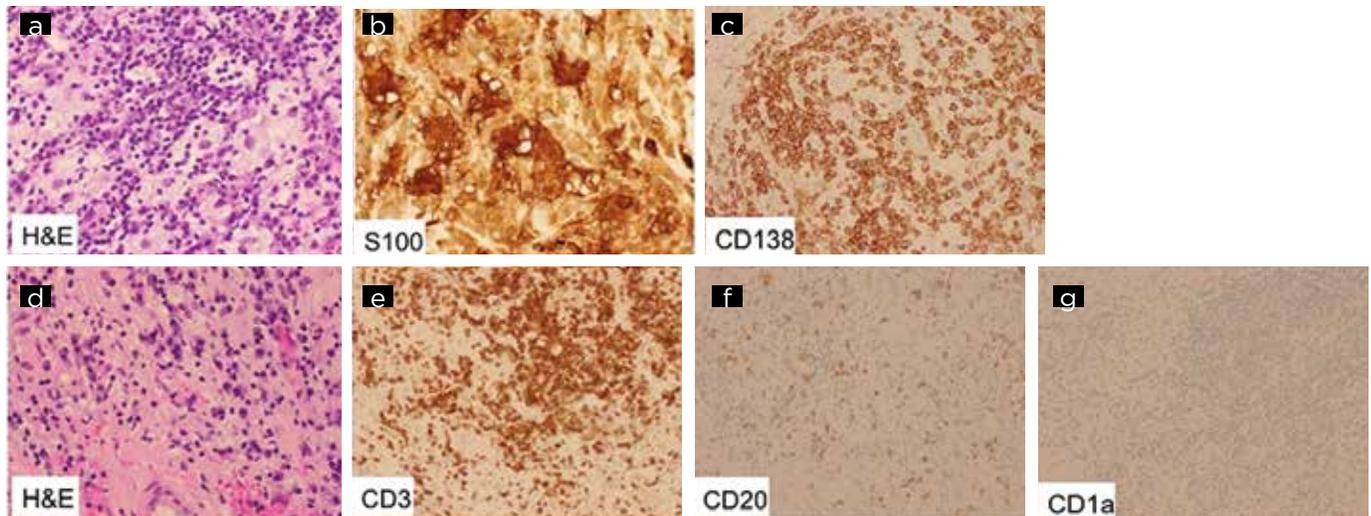


Figure 3. Microscopic examination: fibrous tissue with a lymphoplasmocytic infiltrate with macrophages (H&E upper panel). Macrophages with intact lymphocytes in the cytoplasm, indicating emperipolesis. Stain for S100: histiocytes are positive and confirm emperipolesis. Lymphocytic infiltrate mainly T cells (CD3+) with few B cells (CD20+) and numerous plasma cells (CD138). Some of the plasma cells demonstrated Russell bodies (H&E central panel). Staining for CD1a was negative.

Likewise, it has also been shown that in 20 % of the cases it has self-limited remission, a situation not described in cases of isolated intracranial SHML (19,20). Given these circumstances and the low incidence of this pathology, there is no clear consensus established to date for the treatment of cases of intracranial isolated RDD. However, surgical intervention is proposed as the first choice due to the evident symptomatic improvement. Total or subtotal resection of intracranial lesions is subject to parenchymal extension (21). Radiotherapy, chemotherapy and corticosteroid therapy are recommended in situations where symptoms persist after surgical treatment (22).

## Conclusion

Isolated central nervous system involvement in Rosai-Dorfman disease occurs in less than 0.5% of reported cases to date, about 76 since 1969. The imaging characteristics of this disease are not pathognomonic, as it shares diagnostic criteria with many other diseases. This pathology should always be considered within the differential diagnosis of extraaxial intracranial masses in the clinical context.

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