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CASE REPORT

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A Case of Isolated Central Nervous System Rosai-Dorfman Disease

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ABSTRACT

Rosai-Dorfman disease (RDD) is a benign histiocytosis with unknown etiology. It generally occurs in cervical lymph nodes. Isolated central nervous system (CNS) RDD is very rare in the literature. We reported a case of no systemic involvement Rosai-Dorfmann which is rarely seen and shows CNS involvement by mimicking meningioma. A 32-year-old man presented with diplopia and a headache he has been experiencing for the past two years. His neurological examination showed left facial paresthesia, consistent with trigeminal nerve trace. Tendon reflexes were increased at the right side and the right plantar reflex was extensor. Brain magnetic resonance imaging demonstrated irregularly shaped, tumor-like lesions in the bilateral cerebellopontin area that were compressing pons. Rosai-Dorfman disease can be differentiated from IgG4 related disease (IgG4-RD) by its characteristic features such as plasma cell density and emperipolesis seen in its histopathology. Rosai-Dorfman disease can be confused with other diseases radiologically and histopathologically, especially the IgG4-RD, so be careful about differential diagnosis.

Keywords: Histiocytosis, IgG4 related disease, meningioma, Rosai-Dorfman disease

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INTRODUCTION

Rosai-Dorfman disease (RDD) is an uncommon benign histioproliferative disorder with systemic symptoms and lymphadenopathy with unknown etiology. It generally occurs in cervical lymph nodes. Central nervous system (CNS) involvement accounts for only 5% with 71–82% of patients having no associated systemic disease (1). The disease affects mostly children and young adults, with a slight predominance in men (2). Although RDD mainly affects lymph nodes, extra nodal sites may also be involved. Central nervous system involvement is rare and usually presents as a dura-based mass, mimicking a meningioma without other systemic manifestations (3). Rosai-Dorfman disease and IgG4 related disease (IgG4-RD) showing isolated CNS involvement are often confused with each other. IgG4-RD is a recently designated benign clinical entity, histopathologically characterized by sclerosing inflammation and infiltration of IgG4+ plasma cells that affects multiple organs. Radiologically isolated CNS IgG4-RD shows affinity of pituitary glands and the skull base dura mater, like RDD. Since both diseases may present as tumor-like lesions, similar clinical presentation may develop due to a compressing effect. Histopathologic diagnosis may be troublesome as plasma cells can accompany RDD and mimic IgG4-RD (4).

We reported a case of no systemic involvement Rosai-Dorfman which is rarely seen and shows CNS involvement by mimicking meningioma.

Highlights

- **Isolated central nervous system RDD requires attention for differentiated diagnosis.**
- **RDD confused with IgG4-RD histopathologically but the disease completely different.**
- **Emperipolesis evaluation with plasma cell density support the correct diagnosis.**
- **It is confused with meningioma radiologically.**
- **In bilateral, dura-based lesions (mass-like), central nervous RDD can be considered.**

CASE

A 32-year-old man presented with diplopia and headache he has been experiencing for the past two years. The patient did not have fever, weight loss or night sweats. There was no history of chronic disease. On physical examination, there was no cervical lymphadenopathy and cutaneous sign. He had neither meningeal signs nor papilledema. Neurological examination revealed left facial paresthesia, consistent with trigeminal nerve trace. There was no paresis in ocular movements. Tendon reflexes were increased at the right side and the right plantar reflex was extensor. His biochemistry and hemogram test results were normal. Anti-nuclear antibody, p-ANCA, complement C3 level and IGG1-G2-G3 levels were normal. Brain magnetic resonance (MR) imaging demonstrated irregularly shaped, tumor-like lesions in the bilateral cerebellopontin area that were compressing pons. An axial T2-weighted and axial, coronal and sagittal T1-weighted MR imaging study showed hypointense mass lesions which were 35×23×17 mm and 22×17×15 mm in size and had homogeneous contrast enhancement (Figures 1–4). Pre-operative serum IgG4 level was not available, post-operative serum IgG4 level was normal.

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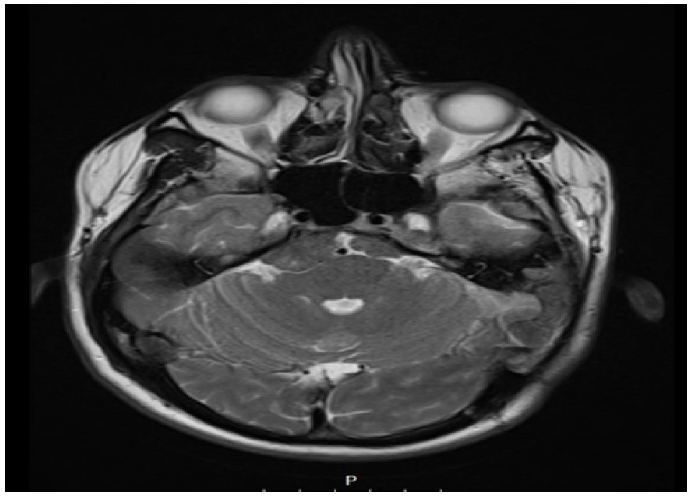


Figure 1. Cranial T2-weighted axial MR.

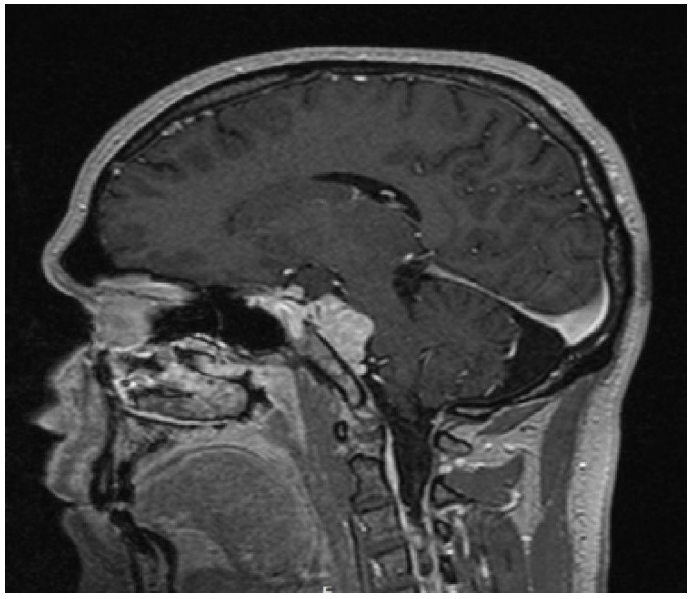


Figure 2. Cranial T1-weighted sagittal MR with contrast.

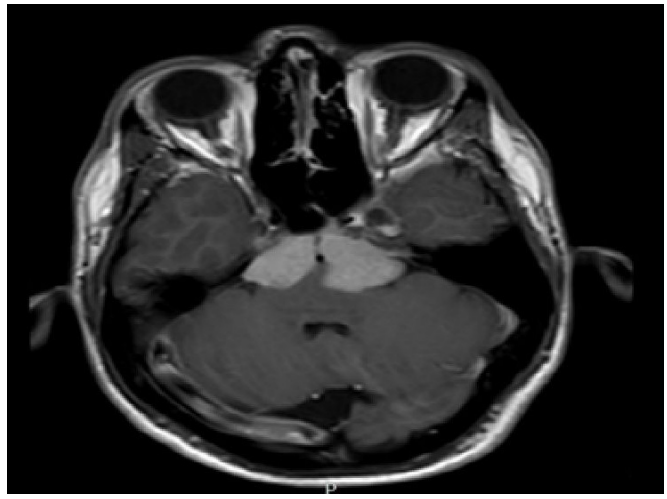


Figure 3. Cranial T1-weighted MR with contrast.

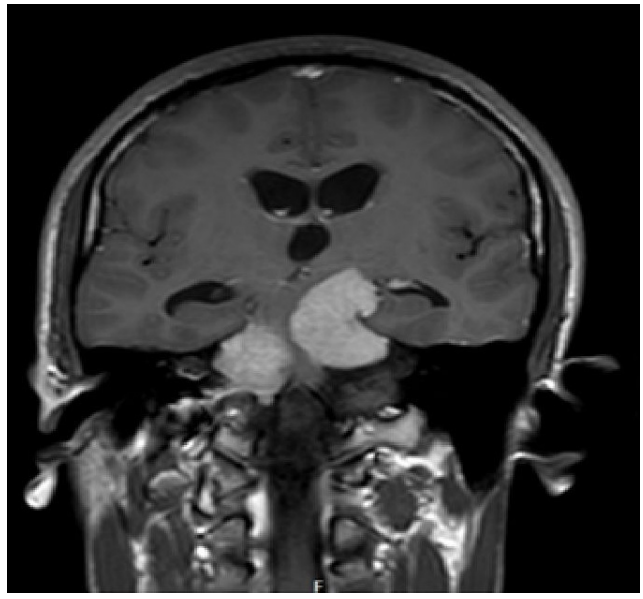


Figure 4. Cranial T1-weighted coronal MR with contrast.

An emergency operation was performed. The compressing lesions were removed and the material was sent for pathological analysis.

Pathological findings

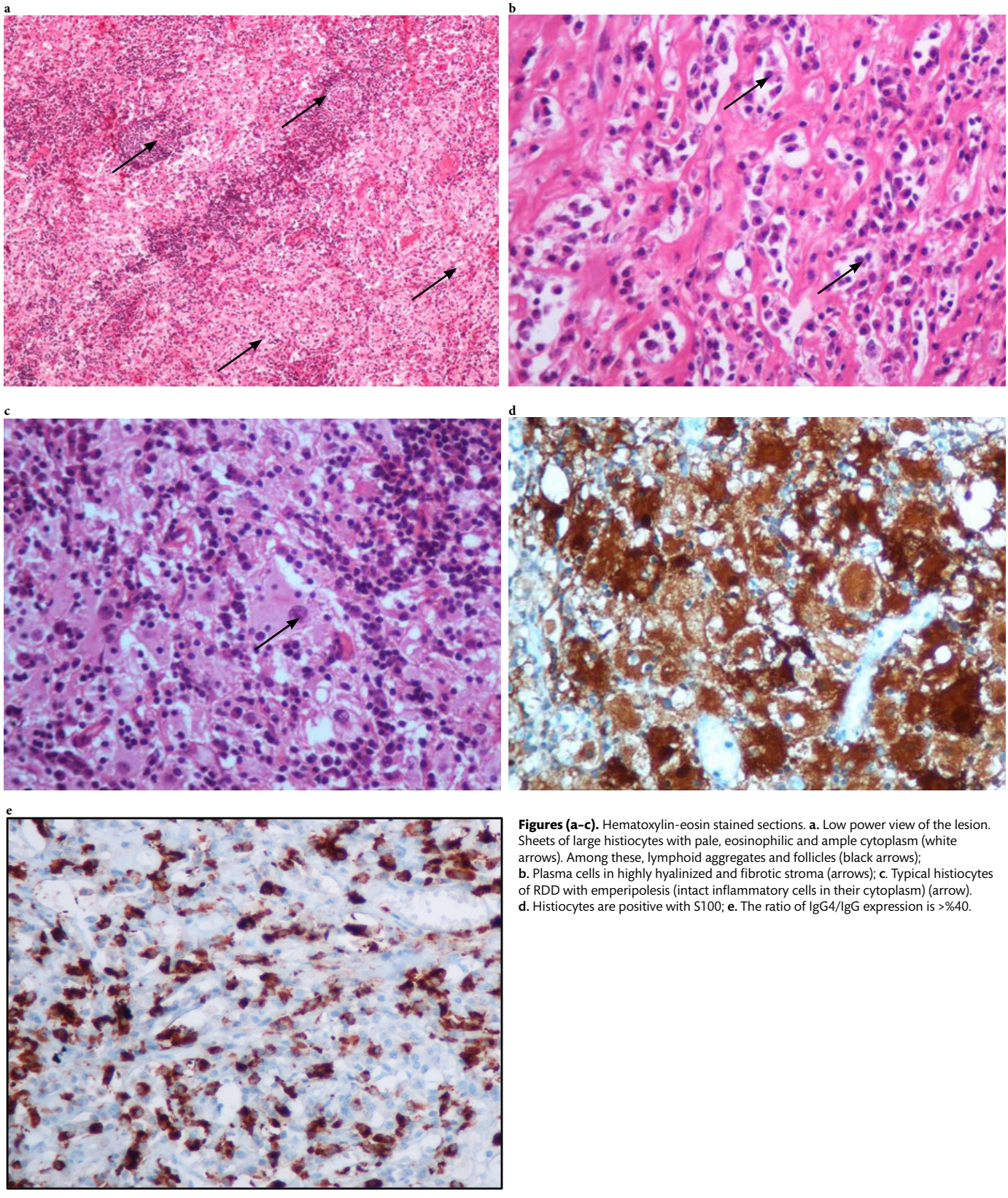
Histopathologic examination showed similar findings on both biopsies. Stroma was highly collagenized with hypo- and hypercellular areas. The cellular component was a mixture of lymphocytes, plasmacytes and histiocytes. Amongst these, reactive lymphoid follicles and aggregates were seen (Figure a). Plasma cells were buried in a hyalinized stroma (Figure b). The most remarkable finding was the presence of large sheets of histiocytes with emperipolesis (Figure c). These cells contained preserved inflammatory cells in their ample, pale eosinophilic cytoplasm. Differential diagnoses included IgG4-related disease and histiocytosis. Histiocytes lacked groove and lobulation, which are characteristic findings of Langerhans cell histiocytosis (LCH). Immunohistochemical staining for CD1a and Factor XIII was negative (not shown) for LCH and Erdheim-Chester disease. No other system involvement was observed in the patient either. We found the histiocytes to be CD68 (not shown) and S100 positive (Figure d), which is exclusive to Rosai-Dorfman disease. Along with these findings, plasma cells contained an overall IgG4/IgG ratio of more than 40% (Figure e). Therefore, our diagnosis was Rosai-Dorfman disease with an increase of IgG4 in the plasma cells.

In the postoperative follow-up, the patient had two generalized tonic-clonic seizures. Levetiracetam 1000 mg/day, azathioprine 100 mg/day and deltacortril 40 mg/day was started. Control cranial MR and routine tests were performed after one month, and there was no progression of the disease. No other involvement was observed in any part of the body in the FDG-PET examination.

A written informed consent form was obtained from the patient.

DISCUSSION

Rosai-Dorfman disease (RDD) is considered a benign self-limiting histiocytic disorder of presumed non-neoplastic nature. However, patients with RDD have been reported to undergo malignant transformation to histiocytic sarcoma and high-grade lymphoma (1). Central nervous system involvement in RDD is the first case of multiple intracranial RDD lesions reported by Song et al. in 1989 (5). In CNS, it usually appears as a solitary lesion; multifocality is extraordinary. It is primarily dura-based, mimicking meningioma and cerebellopontine angle is not an expected localization (6). Our case is unique by being isolated in CNS and bilaterally at the cerebellopontine angle. Intracranial RDD usually affects adult males between 22 and 63 years of age (1). Demographic features of our case were consistent with literature.



Figures (a–c). Hematoxylin-eosin stained sections. **a.** Low power view of the lesion. Sheets of large histiocytes with pale, eosinophilic and ample cytoplasm (white arrows). Among these, lymphoid aggregates and follicles (black arrows); **b.** Plasma cells in highly hyalinized and fibrotic stroma (arrows); **c**. Typical histiocytes of RDD with emperipolesis (intact inflammatory cells in their cytoplasm) (arrow). **d.** Histiocytes are positive with S100; **e.** The ratio of IgG4/IgG expression is >%40.

The pathogenesis is unknown but immunological studies suggest that dysfunction of the immune system or an autoimmune process might be the causative factor. Although the possible role of Epstein-Barr Virus (EBV), cytomegalovirus (CMV), human herpes virus 6 (HHV-6) and brucella in the etiology has been emphasized, a significant relationship has still not been determined (7). Histopathologic diagnosis is a challenge as it can be confused with IgG4-RD. Fibrosis is a prominent finding in extra nodal RDD. Nevertheless, it is not storiform as seen in IgG4-RD. Plasma cell increase and intracytoplasmic eosinophilic inclusions (Russel bodies) can be expected in both lesions. Obliterative phlebitis, which is characteristic of IgG4-RD, is not expected in RDD (4). Instead, blood vessels are frequently outlined by cuffs of plasma cells and lymphocytes.

Moreover, histiocytes with emperipolesis (lymphophagocytosis) are the hallmark of RDD. Single case reports in the literature report RDD with IgG4 increase. However, only a few series are documented. IgG4 increase is observed in approximately 30% of patients with RDD (8). However, where they belong to the same spectrum or if this finding is coincidental is not well understood. Studies did not incorporate IgG4 levels in the blood since most were retrospective (9). Our case had an IgG4/IgG ratio of more than 40% immunohistochemically, but IgG4 levels in his blood were low. IgG4 levels should be documented in the pathology reports in cases with plasma cell increase since IgG4-RD respond well to steroids; it may be promising for patients with RDD who cannot recover.

RDD is a systemic heterogeneous entity. In CNS-RDD, systemic signs are usually absent and clinical manifestations depend on the localization, size and number of the lesions. RDD patients were usually asymptomatic before lesions became large enough to be detected. Usually, symptoms may include seizures, headaches, endocrine abnormalities or focal neurological deficits due to mass effects and oedema. Visual changes, weakness, loss of sensation, gait impairment, pituitary dysfunction also have been described (10). In our case, the first complaint was diplopia due to mass effect. Cases with cerebral involvement usually have dural involvement and are mistakenly diagnosed as meningioma clinically and radiologically before surgical and histopathological diagnosis (11), like our case. This is because both of the disorders are usually dura-based. However, meningiomas can be hypo-hyperintense on T2-weighted sequences, while RDD lesions are generally hypointense. At subtraction angiography, meningiomas are generally hypervascular, while RDD lesions are hypovascular. Meningiomas often present bony changes, such as hyperostosis, bone destruction and calcifications; these findings are generally absent in RDD (12). Primary CNS-RDD is most commonly located in the skull base, suprasellar region, petroclival region, parasagittal region and cavernous sinus (13).

Therapeutic approach differs from case to case. Currently, the first therapeutic option in cerebral RDD is performing surgical resection, which is usually performed to remove the compressing lesion and to make a histopathological diagnosis. 90% of cases resolve spontaneously or remain asymptomatic. Complete resection is usually not performed because the lesion has multiple foci, extends to the neuronal parenchyma and invades other structures (14). Corticosteroid administration has been shown to be beneficial in systemic RDD, but there is a possibility of recurrence. Radiotherapy can be used for local control of inoperable cases. Imatinib, a tyrosine kinase inhibitor and anti-cd20 monoclonal antibody are new treatments used in the treatment of systemic RDD (15).

Isolated CNS-RDD is a very rare condition. It appeared with a lesion that has a mass-like effect in the brain stem. In this case, steroid and immunosuppressive therapy were administered after relaxing surgery. Early diagnosis and treatment is very important. Its radiological appearance may be confused with meningioma and its histopathological features may be confused with IgG4-RD. Since the follow-up and treatment approaches are different, it is necessary to be sensitive in distinguishing these entities.

Informed Consent: A written informed consent form was obtained from the patient.

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