Regression of intracranial Rosai–Dorfman disease following corticosteroid therapy

Case report

CHRISTOPHER M. MCPHERSON, M.D., JUSTIN BROWN, M.D., ANGELA W. KIM, M.D., AND FRANCO DEMONTE, M.D.

Departments of Neurosurgery and Ophthalmology, The University of Texas M. D. Anderson Cancer Center, Houston, Texas

Rosai–Dorfman disease (RDD) is an idiopathic histioproliferative disorder usually presenting with massive, painless lymphadenopathy. Extranodal involvement has been reported including at least 50 cases affecting the central nervous system (CNS). The treatment of CNS RDD as reported in the literature has primarily involved a surgical technique. The authors report on the case of a 53-year-old man presenting with multiple skull base lesions mimicking meningiomas. The patient suffered visual deterioration and underwent a right orbitopterional craniotomy as well as optic nerve decompression. Histopathological analysis revealed histiocytic cells and emperipolesis consistent with RDD. Following surgery, corticosteroid agents were administered, leading to marked resolution of both the remaining surgically untreated lesions and the balance of the patient’s symptoms. This report represents the first case of the resolution of intracranial RDD following corticosteroid therapy. Corticosteroid agents should be considered an effective option in the treatment of CNS RDD.

KEY WORDS • Rosai–Dorfman disease • sinus histiocytosis • corticosteroid therapy • multiple meningiomas

OASAI–DORFMAN disease was first described in 1969 as a systemic histioproliferative disorder with massive lymphadenopathy. Since then this pathological entity has been well described, including many cases with extranodal involvement. Central nervous system involvement of RDD is rare and occurs as enhancing dural-based lesions mimicking meningiomas. Although options such as radiotherapy and chemotherapy have been reported, the primary form of treatment for CNS RDD according to the literature remains surgical. We report on the first case of CNS RDD with regression of nonsurgically treated lesions following the administration of corticosteroid agents.

Case Report

History. This 53-year-old right-handed man was referred to The University of Texas M. D. Anderson Cancer Center neurosurgery clinic because of headaches and visual loss. His headaches began in February 2004 and gradually worsened. By May 2004, he began to notice decreased vision in his right eye and diminished hearing in his right ear. Furthermore, he had problems swallowing (especially solid foods), maintaining balance, and ambulating. He had no significant medical history, although he was a smoker with a 40 pack-year history; there was no significant family history other than ischemic cardiac disease in his father. The patient had no other constitutional symptoms such as fevers, weight loss, night sweats, or notably swollen lymph nodes on a review of his systems.

Examination. On physical examination the patient was found to have dysmetria on the right side, with a slight wide-based gait and difficulty in tandem walking. He also demonstrated a decreased gag reflex on the left side. On formal neuroophthalmological examination his best-corrected visual acuities were 20/60 in the right eye and 20/40 in the left eye. Additionally, he had bitemporal visual field defects, which were worse inferiorly. Extraocular movements were intact. There was no evidence of lymphadenopathy on general examination.

Results of MR imaging revealed multiple dural-based enhancing lesions of the skull base including a lesion at the planum sphenoidale and tuberculum sella compressing the optic nerves, bilateral lesions from the cerebellopontine angle to the foramen magnum compressing the brainstem, and a lesion at C-2 (Fig. 1). These lesions were believed to be most consistent with multiple meningiomas.
Operation. Based on the patient’s worsening optic neuropathy caused by optic nerve compression, it was decided to proceed first with a resection of the planum sphenoidale/tuberculum sella lesion. A right orbitopterional craniotomy and optic nerve decompression were performed, and the tumor was maximally debulked. Tumor adherent to both the left optic nerve and the dorsum sella was intentionally left behind. The optic apparatus was maximally decompressed. An intraoperative frozen section examination was performed, and the lesion was believed to be most consistent with an inflammatory process.

Pathological Analysis. Results of a final pathological examination showed a lesion composed of mostly histiocytic cells positive for S100 protein and CD68. In addition, emperipolesis was demonstrated; that is, histiocytes engulfed lymphocytes and plasma cells. Therefore, the final diagnosis was consistent with RDD (Fig. 2).

Postoperative Course. The patient tolerated the craniotomy procedure well and was discharged home on postoperative Day 4. He had marked improvement in his vision: 20/25 in the right eye and 20/25 in the left, without corrective lenses. Postoperative MR images showed decompression of both optic nerves as well as the expected amount of residual disease (Fig. 3). The patient was discharged home and initially placed on a regimen of Decadron (4 mg twice daily for 2 weeks) and then switched to prednisone (16 mg twice daily). He was seen at a follow-up evaluation 6 weeks later; an MR image obtained at that time demonstrated marked resolution of the patient’s multiple skull base lesions (Fig. 4). Visual acuities returned to 20/20 in each eye, with full

Fig. 1. Coronal MR images obtained after Gd administration, showing enhancing skull base lesions at the level of the tuberculum sella (left) and bilaterally surrounding the brainstem and involving the cranial nerves (right).

Fig. 2. Photomicrograph showing a mixture of lymphocytes and large histiocytes; some histiocytes have engulfed other lymphocytes (that is, emperipolesis has occurred; center of image). H & E, original magnification × 400.

Fig. 3. Coronal Gd-enhanced MR image obtained immediately postoperatively, demonstrating partial resection of the tuberculum sella lesion as well as decompression of optic nerves.
visual fields. In addition, his swallowing and gait disturbances had substantially improved. He returned to full-time work and resumed normal levels of activity. The prednisone was gradually tapered.

At the 10-month postoperative follow up, the patient reported the return of some visual symptoms and difficulty swallowing. Repeated MR imaging results showed interval progression of enhancing lesions especially in the posterior fossa (Fig. 5). Prednisone (10 mg twice daily) was again administered, with subsequent complete resolution of symptoms. A follow-up MR image obtained 1 month later (11 months postoperatively; Fig. 6) demonstrated resolution of the enhancing lesions again. The patient maintains full functional abilities and will remain on prednisone therapy.

Discussion

This case report is the first to demonstrate resolution of a nonsurgically treated lesion associated with RDD following corticosteroid therapy. In 1969 Rosai and Dorfman described the first case of sinus histiocytosis accompanied by massive lymphadenopathy. Rosai–Dorfman disease has since become a well-described entity, with at least 1000 cases reported since its first description. Patients most often present with massive, painless lymphadenopathy affecting the cervical region more than other areas. Symptoms of fever and weight loss are common. Laboratory results are nonspecific. Diagnosis relies on histological and immunohistochemical analysis of pathological specimens. Microscopic examination shows a diffuse heterogeneous infiltrate of histiocytes, lymphocytes, and plasma cells. The key finding is emperipolesis characterized by the engulfment of lymphocytes or plasma cells by large histiocytes, which are typically positive for S100 protein.

As demonstrated in the present case, RDD does not occur solely in the lymph nodes. In 25 to 40% of cases, RDD presents in extranodal locations including the skin, orbits, respiratory tract, bones, and CNS. Involvement of the CNS

Fig. 4. Coronal Gd-enhanced MR images obtained at the 6-week follow-up evaluation, demonstrating resolution of the tuberculum sella lesion (left) as well as the posterior fossa lesions (right).

Fig. 5. Coronal Gd-enhanced MR images obtained at the 10-month follow up, showing slight progression of the tuberculum sella lesion (left) and definite progression into the posterior fossa (right).
Regression of Rosai–Dorfman disease

is rare, with only approximately 50 cases having been reported in the literature to date. The majority of these lesions mimic meningiomas presenting as dural-based lesions that enhance strongly following Gd administration on T₁-weighted MR imaging. Lesions can be solitary or occur in multiples. Given that these lesions mimic the appearance of meningiomas on MR imaging, diagnosis relies on histological and immunochemical analyses of pathological specimens. Several entities mimicking meningiomas have been described and should be considered in the differential diagnosis, including Langerhans cell histiocytosis, sarcomatoid, infectious processes (tuberculoma), lymphoproliferative disorders, plasma cell granuloma, and inflammatory pseudotumor. The key features in RDD are S100 protein–positive histiocytes that are polyclonal in nature, separating the disorder from plasma cell granulomas, sarcomatoid, and infectious origins for which histiocytes are S100 protein–negative, and distinguishing it from lymphoproliferative disorders for which there is a monoclonal, homogeneous immunophenotype. Inflammatory pseudotumor can be differentiated on the basis of its histological appearance, that is, hyperplastic follicles of mature B and T lymphocytes, which are similar to changes seen in reactive lymph nodes. Langerhans cell histiocytosis can appear similar to RDD, but eosinophils are more prominent in Langerhans cell histiocytosis and emperipolesis is not seen in the former disease. In fact, emperipolesis is the hallmark diagnostic feature of RDD.

In the past, the treatment of CNS RDD has been primarily surgical. Pathological evaluation is required for diagnosis. Most cases in the literature have been regarded and treated as though they were meningiomas, based on neuroimaging. Despite surgical treatment, relapse of CNS RDD has been reported in as many as 14% of cases. In some instances, adjuvant treatment with radiotherapy and/or chemotherapy has been instituted with some success. Several combinations of adjuvant chemotherapy have been used as well, including cyclophosphamide, vinblastine, mercaptopurine, etoposide, and methotrexate, with mixed results. Stereotactic radiosurgery has also been used. Specifically, Hadjipanayis and colleagues reported on the stereotactic radiosurgical treatment of a case of residual petroclival RDD. Follow-up images obtained 13 months postsurgery showed near-complete resolution of the lesion.

Corticosteroid agents have been used successfully in systemic forms of RDD, including two cases with dramatic responses. In addition, corticosteroid administration has been combined with cytotoxic chemotherapy in orbital disease, with successful results. Contrast, the use of corticosteroids has only been described in two cases with intracranial involvement, neither of which demonstrated definitive resolution of the nonsurgically treated lesion. Franco-Paredes and Martin described a patient with leptomeningeal enhancement, proven to be RDD on biopsy sampling. The patient was treated using corticosteroids postoperatively without additional symptoms, but no follow-up images were available to indicate whether resolution had occurred. Shaver and associates reported on the case of a 5-year-old boy with a cavernous sinus lesion who had undergone subtotal resection; histopathological analysis demonstrated RDD. Postoperatively, the patient was maintained on dexamethasone and follow-up MR images showed resolution of the mass. Nonetheless, it remains unclear whether this resolution was due to the effect of the corticosteroids or the surgery. In the present case, the patient had multiple intracranial skull base lesions including one spinal lesion at C-2. Surgical treatment was directed at the tuberculum sella lesion given the significant further decline in visual function, which was attributed to optic nerve compression. Postoperatively, the patient was maintained on prednisone, and follow-up images showed resolution of all lesions including those not surgically treated.

There is pathophysiological data supporting the use of corticosteroid or immunomodulatory agents in this disease. Although the origin of RDD is unclear, there is evidence that the disease is an expression of immune system dysfunction or possibly even an autoimmune process. The inflammatory infiltrate seen has been shown to be polyclonal and is therefore regarded as a reactive process rather than a neoplastic one. In addition, Epstein–Barr virus and human

**Fig. 6.** Coronal Gd-enhanced MR images obtained at the 11-month follow up, revealing lesion resolution once again both at the tuberculum sella (left) and in the posterior fossa (right).
herpesvirus Type 6 have been detected by in situ hybridization in some specimens. In the final analysis, whether RDD represents an overactive immune response to one of these agents remains unanswered. Nonetheless, data demonstrating regression of multiple lesions with the administration of corticosteroids in our case lends support to the hypothesis that RDD is an immunological disease process.

Conclusions

We reported on a case involving multiple skull base lesions found to be consistent with RDD and successfully treated with corticosteroid agents. This case represents the first to demonstrate definitive resolution of nonsurgically treated intracranial RDD lesions following corticosteroid therapy. Corticosteroid agents should be considered as a viable treatment option in patients with intracranial RDD.

References


C. M. McPherson, et al.