Clinical Reasoning:

Compressive optic neuropathy secondary to intracranial Rosai-Dorfman disease

Ronald C.H. Siu, MBBS,
BMedSc, FRACP
Ik Lin Tan, MBBS,
MPH, MRCP, FRACP
Andrew S. Davidson,
MBBS, MS, PhD,
FRACS
Alasdair Robertson,
MBBS, FRANZCR,
CCST
Clare L. Fraser, MBBS,
MMed, FRANZCO

Correspondence to
Dr. Siu:
ronaldsiu@alumni.unimelb.edu.au

SECTION 1

A 60-year-old man presented to our clinic with a 6-month history of progressive visual loss in the left eye. Twelve months prior, he experienced an acute left hemianopia secondary to a stroke. He was anticoagulated and fully recovered. Six months following the stroke, he began to notice blurred vision in his left eye. There was no formal ophthalmic examination performed at that time, but a plastic surgeon believed that a left medial upper eyelid mass lesion was causing distortion of his vision, and proceeded to excision biopsy. Histopathology revealed Rosai-Dorfman disease (RDD). Postoperatively, the patient's visual loss continued to worsen and he was referred to our clinic.

On examination, visual acuity was 6/6 on the right and 6/12 on the left. The patient correctly identified all

Ishihara color plates with the right eye, and only the test plate and one other plate with the left eye. There was also a left relative afferent pupillary defect. Funduscopy revealed subtle left optic disc pallor. Orbital examination was normal. Humphrey visual field of the left eye showed superior and inferior arcuate defects and a normal right visual field (figure, A). Neuroimaging revealed a dural-based, intensely enhancing mass in the left anterior cranial fossa, which had been documented as a small incidental meningioma 6 months earlier (figure, B and C).

Questions for consideration:

1. What is the differential diagnosis?
2. What is the appropriate next step in diagnostic evaluation?

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From Macquarie Neurology (R.C.H.S., I.L.T.) and Macquarie Neurosurgery (A.S.D.), Macquarie University Hospital, Macquarie University; Edgecliff Castlereagh Imaging (A.R.), NSW; and Macquarie Ophthalmology (C.L.F.), Australia.

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(A) Humphrey visual field of the left eye shows superior and inferior arcuate defects and a normal right visual field on the first visit. (B, C) Brain MRI shows a dural-based, intensely enhancing mass in the left anterior cranial fossa, diagnosed as incidental meningioma. (D) Histopathology of the lesion shows emperipolesis consistent with Rosai-Dorfman disease.

SECTION 2

The differential diagnoses for a growing intracranial lesion that may mimic meningioma include lymphoma, metastatic carcinoma, Langerhans cell histiocytosis, neurosarcoidosis, granulomatous diseases, and neurofibromatosis type 1.¹ Since the patient's vision was threatened and a tissue diagnosis was required for definitive diagnosis, he was referred to a neurosurgeon for urgent debulking surgery via endoscopic transsphenoidal approach. Given the patient's history of RDD and the expanding lesion, intracranial RDD was suspected.

Intraoperatively, the surgeon noted severe distortion of the left optic nerve with inferomedial compression from the tumor. Macroscopic resection of the tumor was achieved. Histopathology revealed positive CD 68/S100 staining and emperipolesis (histiocytes with intracytoplasmic lymphocytes), consistent with RDD (figure, D).

Questions for consideration:

1. How would you further manage the patient?
2. What is the prognosis and long-term management of CNS RDD?

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SECTION 3

Approximately half of all reported cases of RDD resolved spontaneously,² and treatment should be reserved for symptomatic RDD.³ However, to our knowledge, there has been no literature on the outcome of untreated asymptomatic CNS RDD. Neurosurgical intervention was indicated in our patient with an enlarging lesion threatening vision. In general, surgical debulking is the primary treatment for CNS RDD. Despite variable outcomes in the literature, corticosteroid, adjuvant radiotherapy, or chemotherapy may be considered where complete resection is not possible,³ and methotrexate may be beneficial in those unresponsive to corticosteroid or radiotherapy.³ Rituximab, 2-chlorodeoxyadenosine, imatinib, and interferon- α have been used with some success in systemic disease.³

Postoperatively, the patient was discharged with tapering dexamethasone over 2 weeks. Within a week of corticosteroid discontinuation, he represented with increasing headaches. An MRI scan identified a nodular enhancement at the surgical site, concerning for disease recurrence. He was treated with pulsed IV methylprednisolone. A diagnostic whole-body FDG-PET-CT revealed no uptake in the CNS, suggesting that the MRI changes were unlikely to be disease recurrence, and probably only postsurgical change. However, there was avid disease extracranially in the lymphoid tissues. Hematology opinion was obtained for the systemic disease, and close surveillance was recommended. Prednisolone was weaned over 4 weeks.

The intracranial disease has not recurred in our patient. There have been several orbital recurrences with a subsequent right medial canthus lesion, bilateral conjunctival lesions, and further lesions in the left upper lid, which were biopsy proven to be RDD. Local skin lesions on the arms have also been amenable to excision biopsy.

DISCUSSION RDD was named after Juan Rosai and Ronald Dorfman⁴ when it was recognized as a nonmalignant and unique histiocytic lymphoproliferative disorder in 1969. RDD is also known as sinus histiocytosis with massive lymphadenopathy, and it usually presents as painless lymphadenopathy associated with fever and leukocytosis. RDD is considered a chronic, relapsing disease and usually affects young adults or children.^{5,6} Isolated intracranial RDD is rare, and fewer than 80 cases have been reported in the literature.^{3,7} Clinical manifestation of intracranial RDD depends on the location of the lesion, ranging from asymptomatic to headaches and seizures due to mass effect and edema. Intracranial RDD is typically a meningeal process, with involvement of the sellar and pituitary regions

being most common, which may cause pituitary dysfunction. CNS RDD may mimic meningioma on neuroimaging.^{8,9} The lesion in our patient was initially diagnosed as meningioma, but due to its rapid expansion, RDD was suspected. Bone destruction and hyperostosis may be associated with meningioma but has not been reported in RDD.¹ Due to its rarity, CNS RDD is often not considered until tissue diagnosis is made. A definite diagnosis of RDD is made histopathologically with characteristic features of S100 protein-positive histiocytes and emperipolesis described.⁸

In the absence of systematic studies, clinical care can only be based on anecdotal reports and case series. The recurrence rate of surgically resected RDD was reported at 14% in a case series of 29 patients.¹⁰ Surveillance for relapse has been recommended for at least 5 years,¹⁰ with serial MRI scan and PET FDG/CT being the most useful investigations.¹

AUTHOR CONTRIBUTIONS

Dr. Siu collected patient information and all relevant investigations including imaging and Humphrey visual field charts from medical records, performed all literature searches, drafted the article, and formatted the figures. Dr. Tan was the treating neurologist, provided patient histories, information on the diagnosis, and follow-up, and provided comments on the manuscript draft. Dr. Davidson was the treating neurosurgeon, provided information on the neurosurgical interventions and patient histories, and provided comments on the manuscript draft. Dr. Robertson provided comments on the MRI. Dr. Fraser was the treating ophthalmologist, provided patient history, information on the diagnosis, and follow-up, and provided comments on the manuscript draft.

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DISCLOSURE

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