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Stereotactic radiotherapy for presumed oculomotor nerve schwannoma masquerading as “ophthalmoplegic migraine”

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Oculomotor schwannomas are a form of nonvestibular schwannoma that may produce a partial or complete third nerve palsy.[1] Although often slowly progressive, oculomotor schwannomas may cause recurrent or painful neurologic deficits. These tumours are distinctly uncommon, with fewer than 107 reported cases across 70 published studies from 1975 to 2017. Contrast-enhanced magnetic resonance imaging (MRI) reveals nodular thickening and enhancement of the oculomotor nerve.[1] Surgical excision or biopsy may cause permanent oculomotor nerve deficit; consequently, many of these tumours are instead treated empirically as "presumed" schwannomas.[1]

"Ophthalmoplegic migraine"—an entity now called "recurrent painful ophthalmoplegic neuropathy" (RPON)—is also considered in the differential diagnosis of painful recurrent third nerve palsies.[2,3] The International Headache Society renamed this entity to reflect that the underlying pathophysiology is an inflammatory cranial neuralgia and not migraine.[3,4] RPON consists of repeated attacks of ocular motor cranial nerve palsy, often presenting in childhood, associated with ipsilateral headache and enhancement and thickening on MRI of the affected cranial nerve during attacks, in the absence of any other causative lesion.[3] Acute attacks of RPON often respond to corticosteroid treatment. Ocular motor nerve schwannomas may closely mimic RPON, as both may produce intermittent cranial nerve palsies and gadolinium enhancement on MRI. Schwannomas, however, are generally slowly progressive and evident on MRI even between attacks.[3,4]

We present a unique case of an oculomotor nerve schwannoma masquerading as RPON. We highlight both the potential consequences of misdiagnosis based on old terminology and the excellent response that can be sometimes achieved with fractionated stereotactic radiation therapy.

A 49-year-old male attended our neuro-ophthalmology clinic for a second opinion regarding a longstanding diagnosis of "ophthalmoplegic migraine." He reported a 20-year history of recurrent, 3–4-day attacks of unilateral right-sided severe head and eye pain accompanied by pupillary mydriasis, ptosis, and inferolateral globe deviation, which had become refractory to treatment with oral prednisone, at doses escalating over 7 years to 60 mg daily with subsequent weight gain, a cushingoid appearance, and hypertension. Three MRI/MRA (magnetic resonance imaging/magnetic resonance angiography) studies over the previous 13 years had all been reported as normal.

Clinical examination, between acute attacks, revealed a best-corrected visual acuity of 20/20 OU. Intraocular pressure was 25 mm Hg in the right eye and 24 mm Hg in the left eye. Ocular motility was full, but he had a 10 prism diopter exophoria. The right pupil was 0.5 mm larger than the left pupil in bright light, and there was no relative afferent pupillary defect. He had a 1 mm right ptosis. He had a posterior subcapsular cataract in the right eye. Fundi were normal.

A critical re-review of his prior MRIs identified a previously unreported nodularity along the course of the right third nerve. A repeat contrast-enhanced MRI orbits with dedicated fine cuts through the cavernous sinuses indeed confirmed the presence of a focal nodular 4 mm enhancing lesion within the right oculomotor nerve at the level of the anterior clinoid process (Fig. 1). Its unchanging and nodular appearance on MRI over many years was consistent with schwannoma; infiltrative inflammatory or neoplastic processes, such as sarcoidosis, tuberculosis, or lymphoma, were thought to be exceedingly unlikely.

The patient was treated with linear accelerator–based hypofractionated stereotactic photon radiotherapy at a dose of 25 Gy in 5 daily fractions (5 Gy/day) using a relocatable Aktina frame for stereotactic immobilization (Figs. 2 and 3), with subsequent taper in steroid therapy. Six months later, the patient reported an 80% reduction of symptoms and a reduction of daily prednisone from 60 to 4 mg; at 18 months, he reported a 90% reduction of symptoms and complete discontinuation of prednisone. Follow-up clinical examinations revealed stability of the anisocoria, reduction of the exophoria to 6 prism diopters, and resolution of the ptosis. MRI 18 months after radiation revealed stability of the lesion.

Treatment for cranial nerve schwannomas is aimed at reducing or eliminating symptoms caused by the tumour without inflicting iatrogenic damage.[5] Surgical excision has been the historical approach but is associated with morbidity. Stereotactic radiotherapy, alternatively, distributes a targeted dose of radiation in 3 dimensions with submillimeter precision. After radiotherapy, schwannomas may transiently enlarge, with subsequent stabilization; delayed tumour shrinkage may occur.[6] In our patient, the excellent response of symptoms

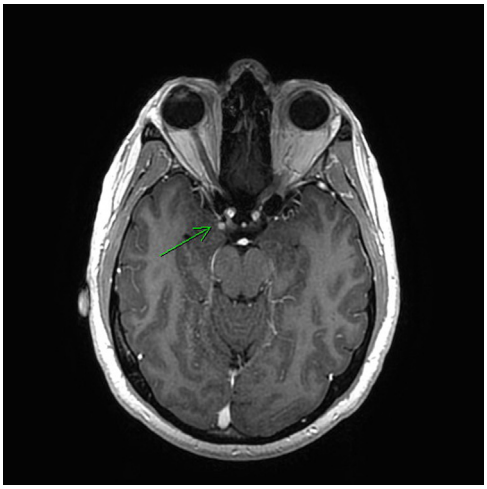

Fig. 1—Axial T1-weighted contrast-enhanced magnetic resonance imaging of the head, demonstrating nodular thickening and enhancement of the right oculomotor nerve (arrow) at the level of the anterior clinoid process.

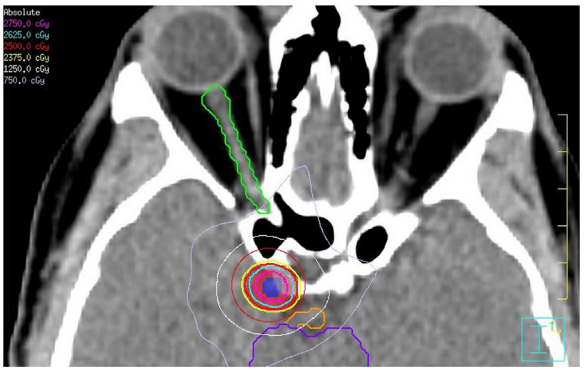

Fig. 2—Dose distribution of stereotactic radiation delivery to the right third nerve schwannoma. Prescribed dose was 2500 cGy in 5 daily fractions.

without significant post-treatment radiologic change in tumour appearance was likely due to a radiation-related reduction in focal oculomotor nerve inflammation. This theory is supported by the fact that the patient was able to completely discontinue prednisone therapy. Similar disconnects between early postradiation clinical improvement and negligible radiologic change have been noted with other benign tumours.[7]

Our case highlights 4 key points. First, oculomotor schwannomas can closely mimic RPON in many respects. They may both have periods of clinical quiescence punctuated by acute exacerbations. Both conditions demonstrate cranial nerve enhancement on MRI; however, enhancement in RPON is diffuse rather than nodular and is only seen during acute exacerbations of the disease. A careful radiologic search (or critical re-review) for an oculomotor nerve schwannoma is therefore paramount to avoid chronic, potentially indefinite, corticosteroid therapy and its associated side effects. Second, our case highlights the potential for improvement in symptoms with fractionated stereotactic radiotherapy: our patient reported a 90% reduction of symptoms 1.5 years after radiation with complete discontinuation of steroid therapy; moreover, risk of iatrogenic palsy associated with surgical excision was avoided. The outcome reflected similar favourable rates of control (80%–90%) in vestibular schwannoma treated with hypofractionated radiotherapy.[8,9] Third, our case suggests that control of inflammation within an oculomotor nerve schwannoma may be more important than reduction of tumour size. Finally, our case highlights that inaccurate medical terminology can have adverse and long-term affects on patient care. RPON was initially named "ophthalmoplegic migraine," and this misnomer encouraged physicians to think of this entity as a primary headache syndrome and not look more deeply for an underlying structural mimic. Although the official terminology has been appropriately changed, the old terminology still persists and can result in delayed diagnosis, harm in the form of prolonged corticosteroid use, and significant frustration for patients.

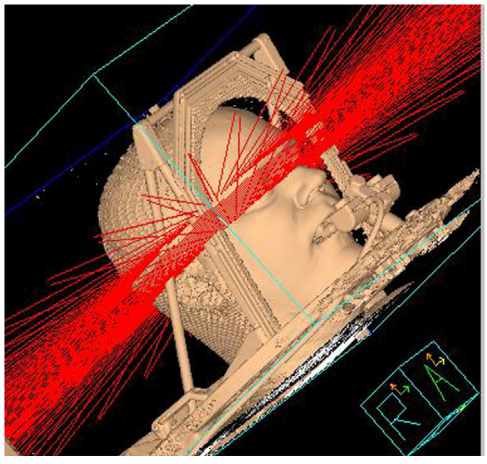

Fig. 3—Illustration of the radiation delivery by a single 360-degree intensity-modulated arc beam. The immobilization frame is visible, including the stereotactic bite block.

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