CASE REPORT

Metastatic Melanoma of the Optic Nerve Sheath

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ABSTRACT

A 23-year-old man with a history of metastatic melanoma developed painful vision loss to counting fingers with enhancement of optic nerve on contrast-enhanced magnetic resonance imaging (MRI) and received a diagnosis of optic neuritis from an outside hospital. Despite empiric corticosteroid therapy, the patient worsened and developed secondary central retinal vein occlusion with further deterioration of vision. Repeat MRI demonstrated optic nerve sheath (ONS) involvement suggestive of optic perineuritis (OPN) and an ONS biopsy confirmed a rare case of isolated metastatic melanoma. Our case highlights the clinical and radiographic features that can mimic OPN and delay diagnosis and treatment.

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Introduction

Cutaneous melanoma constitutes the third most common source of intracranial metastases but rarely demonstrates ocular or orbital metastases, accounting for less than 5% of all such cases.¹ Isolated cases involving the optic nerve or the optic nerve sheath (ONS) are especially rare.^{2–4} Loss of vision can occur due to infiltrative metastatic optic neuropathy, papilledema, melanomatous leptomeningeal disease, compressive optic neuropathy, or cortical visual loss. Therapeutic options in orbital metastatic disease include radiotherapy, surgical resection, chemotherapy, or multimodality treatment. Barash et al. reported a case of painless vision loss due to metastatic melanoma to the ONS presenting as a central retinal vein occlusion (CRVO), but to our knowledge this is the first case of optic perineuritis (OPN) as a presentation of metastatic melanoma in the English language ophthalmic literature.⁵

Case report

A 23-year-old Caucasian man was diagnosed with a BRAF V600E-positive non-ulcerated primary

cutaneous melanoma of the right occipital skin, with 4 mm Breslow thickness and Clark level IV.⁶ He was treated for cervical lymph node metastases 38 months later, lung metastases 51 months later, and a 1.8-cm left cerebellar enhancing mass and three other smaller lesions found on brain magnetic resonance imaging (MRI) 71 months later.

Seventy-six months later, the patient presented at an outside hospital with painful progressive loss of vision, proptosis, lid oedema, and injection of the right eye (OD). The left eye (OS) was normal. Visual acuity was counting fingers (CFs) OD and 20/20 OS. The pupil exam showed a right relative afferent pupillary defect. Extraocular motility, intraocular pressure, and slit-lamp examinations were normal. Dilated fundus examination showed marked optic disc oedema OD. Post-contrast T1 orbital MRI showed enhancement of the right optic nerve and sheath with adjacent fat enhancement (Figure 1IA/IB). He was diagnosed with possible “optic neuritis” (ON) and prescribed oral prednisone 100 mg. The patient's vision worsened to no light perception (NLP) OD and did not respond to IV dexamethasone. A lumbar puncture

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Figure 1. T1-weighted post-contrast magnetic resonance imaging. Enhancement of optic nerve complex on axial (IA) and coronal (IB) views in September 2015. Similar enhancement of optic nerve sheath (IIA, IIB) reflecting optic perineuritis in October 2015 and (IIIA, IIIB) post-treatment progression of disease to involve optic nerve parenchyma and right lateral rectus muscle in January 2016.

was normal. Repeat MRIs of the brain 77 months later showed worsening enhancement of the ONS OD (Figure 1IIA/IIB). No meningeal enhancement or parenchymal intracranial metastatic disease was noted.

He was subsequently referred to the neuroophthalmology service at the Blanton Eye Institute, Houston Methodist Hospital. Visual acuity was NLP OD and 20/15 acuity OS. External examination showed 2 mm of proptosis OD. The pupils were 5 mm bilaterally (OU), with an amaurotic pupil OD. The fundus exam showed marked optic disc oedema with four-quadrant intraretinal haemorrhages, scattered cotton-wool patches, and retinal venous dilation consistent with a concomitant CRVO OD. There was also localized retinal whitening and oedema in the macula suggestive of an adjacent retinal or cilioretinal artery occlusion OD (Figure 2).

A right ONS biopsy confirmed metastatic melanoma involving the fibroconnective tissue, with infiltrating tumour cells, along with chronic

inflammatory infiltrate composed of lymphocytes and foamy histiocytes. Immunohistochemistry for melanocytic cocktail (HMB-45, anti-MART-1, and anti-tyrosinase) and SOX-10 highlighted the atypical cells, supporting the diagnosis (Figure 3). The patient was started on a combination regimen of dabrafenib and trametinib, but treatment was discontinued due to poor tolerance. Repeat MRI 80 months later revealed progression of disease in the ONS and parenchyma including a new intraconal lesion inseparable from the right lateral rectus muscle (Figure 1IIIA/IIIB). Chemotherapy was reinitiated. However, follow-up exam at 82 months later continued to show visual acuity at NLP OD. The patient subsequently underwent right orbital exenteration with intracanalicular optic nerve resection, with plans for post-operative radiation therapy. Unfortunately, shortly thereafter, the patient experienced rapid progressive neurological deterioration secondary to suspected meningeal disease and died.

Figure 2. Fundus photography at composite view (left) and magnified (right) at 50-degree field of view. Marked optic disc oedema with four-quadrant retinal haemorrhages, scattered cotton-wool patches, and retinal venous dilation consistent with central retinal vein occlusion (CRVO) secondary to metastatic melanoma in October 2015.

Figure 3. Histopathology left optic nerve sheath biopsy. (A) Haematoxylin and eosin-stained sections reveal hyperchromatic cells with barely discernible cytoplasm, high nuclear to cytoplasmic ratio (lower right, delineated by dashed white line; magnification: 200×). (B) Higher magnification of melanoma cells (magnification: 400×). The cells are diffusely positive for (C) pan-melanocytic cocktail (HMB-45, anti-MART-1 and anti-tyrosinase) and (D) SOX-10 (magnification: 400×).

Discussion

Rosenberg and Finger examined 93 cases of ocular metastasis in malignant cutaneous melanoma and found that two-thirds of cases involved intraocular structures, few were in the optic disc and nerve (4%), and none were in the ONS.⁴

Our patient initially presented to an outside hospital with radiographic and clinical features

that overlap with OPN including enhancement of the ONS and corresponding ipsilateral optic disc oedema with severe, painful visual loss that is distinct from a similar report from Barash et al.⁵ Signs of cilioretinal artery occlusion seen on our patient's fundus exam can mimic cases of OPN.⁷ However, OPN is typically inflammatory and may occur as idiopathic OPN or secondary

to inflammatory or granulomatous disease. The typical appearance on MRI of OPN in the acute phase is the “tram-track” sign with circumferential ONS enhancement, but may also be seen in ONS meningioma, sarcoidosis, leukaemia, lymphoma, perioptic haemorrhage, orbital pseudotumor, and metastases, as in our case.^{8,9} Additional signs distinct from OPN include lid oedema and proptosis in our patient. ONS biopsy may be required to make the diagnosis of metastatic disease so that appropriate treatment regimens may be planned and initiated. Our patient experienced disease progression on combination chemotherapy and then underwent orbital exenteration and neural resection with poor outcome. Prior series indicate that less than half of patients with unilateral ocular metastases respond to chemotherapy in comparison with a 70% response to radiotherapy. A fourth of all patients eventually require enucleation or exenteration.⁴ Perineural fenestration may also be a therapeutic option to significantly reduce optic disc oedema and may lead to some recovery of vision.¹⁰ Clinicians should be aware of the possibility of metastatic disease in the differential diagnosis of OPN clinically and/or radiographically.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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