PHOTO ESSAY

Supraorbital Nerve and Cavernous Sinus Invasion with Poorly Differentiated Carcinoma of Unknown Primary

Saagar N. Patel^{a*}, Mohammad Obadah Nakawah^{*b}, Ama Sadaka^c, Shauna Berry^c, Juan Ortiz Gomez^{c,d}, Suzanne Powell^e, and Andrew G. Lee^{c,e,f,g,h}

^aSchool of Medicine, Baylor College of Medicine, Houston, Texas, USA; ^bDepartment of Neurology, Houston Methodist Hospital, Houston, Texas, USA; ^cDepartment of Ophthalmology, Blanton Eye Institute, Houston Methodist Hospital, Houston, Texas, USA; ^dDepartment of Pathology and Genomic Medicine, Houston Methodist Hospital, Houston, Texas, USA; ^eDepartment of Ophthalmology, Baylor College of Medicine, Houston, Texas, USA; ^fDepartments of Ophthalmology, Neurology, and Neurosurgery, Weill Cornell Medicine, New York, New York, USA; ^gSection of Ophthalmology, University of Texas MD Anderson Cancer Center, Houston, Texas, USA; ^hDepartment of Ophthalmology, The University of Iowa Hospitals and Clinics, Iowa City, Iowa, USA

ABSTRACT

A 50-year-old man presented with a 4-month history of right-sided trigeminal neuropathy in the V1 and V2 distribution, right sixth nerve palsy and Horner syndrome. Magnetic resonance imaging (MRI) showed enhancement and thickening along the right ophthalmic nerve and supraorbital nerve and fullness at the right cavernous sinus extending to Meckel's cave. Evaluation for a primary tumour was negative. Cavernous sinus biopsy showed infiltrating poorly differentiated carcinoma; the patient underwent radiation therapy. To our knowledge this is the only case of poorly differentiated carcinoma involving the supraorbital nerve presenting with trigeminal neuropathy and Horner syndrome in the English ophthalmic literature.

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Photo essay

A 50-year-old Caucasian male presented with a 4-month history of intermittent right-sided trigeminal neuralgia in the V1 and V2 distributions followed by rapidly progressive esotropia due to a right sixth nerve palsy and right Horner syndrome 2 months after the onset of his symptoms. The patient initially described his pain as “water dripping on his face” but this progressed to a burning dysesthesia over time.

The trigeminal neuropathic pain was unsuccessfully treated with gabapentin and carbamazepine, while the esotropia worsened from 20 to 60 prism diopter (PD) in less than a month. The review of systems was otherwise unremarkable. Past medical history was remarkable for a right frontal convexity meningioma for which he underwent a surgical biopsy and resection a year prior to presentation. His past ocular history is significant for laser-assisted in situ keratomileusis (LASIK) OU. The family history was significant for an unknown brain tumour in his mother, who died at age 40.

The patient denied cigarette smoking, drinking alcohol, or using any recreational drugs.

At initial examination the visual acuity was 20/50 OD and 20/40 OS. Ishihara colour plates were 14/14 OU. External examination revealed a well-healed right frontal craniotomy scar with no suspicious cutaneous lesions. Pupils measured 3 mm in the dark OU and 2 mm in the light OU; there was no anisocoria or relative afferent pupillary defect (RAPD). Motility examination revealed that the right eye was unable to abduct and locked in the esotropic position; the patient's left eye moved freely. He had a 60 PD esotropia in primary position, which became greater than 100 PD esotropia on right gaze and resolved on left gaze. There was no nystagmus. Slit lamp examination revealed bilateral nuclear sclerosing cataracts consistent with 20/50 vision OU. Visual fields were full to confrontation. Fundus examination did not show disc edema or optic atrophy OU; the macula and vessels appeared normal OU. The patient's intraocular pressure was 12 OD and 10 OS.

CONTACT Saagar N. Patel saagar.patel@bcm.edu 6560 Fannin Street, Scurlock 450, Blanton Eye Institute, Houston Methodist Hospital, Houston, TX 77030, USA.

*Saagar N. Patel, BA, BS and Mohammad Obadah Nakawah, MD contributed equally as co-first authors.

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Repeat examination two weeks later showed pupils measuring 3 mm OD and 4 mm OS in dark and 2 mm OD and 2.5 mm OS in light, no RAPD, consistent with a right Horner syndrome and confirmed with topical apraclonidine. There was no ptosis, proptosis, or conjunctival signs on exam.

MRI of brain and orbits with contrast showed an enhancing right cavernous sinus mass extending into the right Meckel's cave. The ophthalmic nerve and its supraorbital branch demonstrated smooth thickening and abnormal enhancement consistent with perineural tumour spread (Figure 1).^{1,2} A sinus CT scan with contrast confirmed the MRI findings. An extensive workup in search for a primary tumour, including PET-CT scan, dermatology, and otolaryngology evaluation, was subsequently performed but was unrevealing. A cavernous sinus biopsy revealed fibrocollagenous tissue with scattered nests of poorly differentiated carcinoma cells with multifocal intraneural and perineural invasion. The tumour cells stained strongly positive for pancytokeratin and p63 with moderate staining for p40. Immunohistochemistry was negative for cytokeratin 7, cytokeratin 20, TTF-1, S100 protein, adipophilin, and monoclonal CEA. Therefore, the patient was diagnosed with an infiltrating poorly differentiated carcinoma showing squamous differentiation based on the positive p63 and p40 immunohistochemistry (Figure 2). He subsequently underwent uneventful radiation therapy to his cavernous sinus mass leading to improvement in his pain.

Perineural tumour invasion (PNI) is a well-recognised complication of head and neck malignancies and is generally viewed as an adverse prognostic factor.²⁻⁴ It is defined as the presence of cancer cells within or around the nerve sheath. Interestingly, tumour spread through the nerves can occur in an anterograde or retrograde fashion.^{1,2} The most commonly involved nerves in these malignancies are the facial nerve, and the maxillary (V₂) and mandibular (V₃) divisions of the trigeminal nerve.^{2,3} Invasion of the ophthalmic nerve is less commonly seen, but frequently involves its supraorbital branch.^{2,4} Clinical PNI initially manifests as dysesthesia in the distribution of the affected sensory nerve and may progress to pain, numbness, and/or weakness over a period of months.^{4,5} Squamous cell carcinoma (SCC) is the most common head and neck cancer, and thus accounts for the largest number of reported cases of PNI. Primary SCC of the cavernous sinus is exceedingly rare, and most reported cases of cavernous sinus SCC are metastatic in origin.

Multiple cranial nerves (III, IV, V1, V2, and VI) and sympathetic fibers (Horner syndrome) from the internal carotid plexus travel through the cavernous sinus as they make their way anteriorly towards the orbit. The abducens nerve (VI) is the only cranial nerve that does not lie on the lateral wall of the cavernous sinus and is positioned inferolateral to the cavernous internal carotid artery. Sympathetic fibers from the internal carotid plexus travel with the abducens nerve at the level of the posterior carotid knee (the transition point of the

Figure 1. A. Fat-suppressed, contrast-enhanced T1-weighted coronal MR image reveals enhancement and smooth thickening of the right supraorbital nerve (arrow), B. Fat-suppressed, contrast-enhanced T1-weighted axial MR image reveals fullness on the right causing asymmetry of the cavernous sinus (arrow).

Figure 2. A. Hematoxylin & eosin, 200x. Nests of atypical cells with pleomorphic nuclei consistent with poorly differentiated malignancy are present (arrow), B. Pancytokeratin immunohistochemistry, 400x. Nests of tumour cells demonstrate strong cytoplasmic positivity for pancytokeratin stain consistent with poorly differentiated carcinoma, C. p63 immunohistochemistry, 40x. The majority of tumour cells show nuclear positivity for p63 consistent with squamous differentiation. Tumour cells surround and infiltrate nerve structures (arrows), D. S100 immunohistochemistry 200x. S100 immunohistochemistry highlights nerve bundles (arrow) surrounded and infiltrated by S100 negative malignant cells.

vertical to horizontal course of the internal carotid artery) before dissociating and meeting the ophthalmic nerve (V1) anterior into the cavernous sinus.⁶ Our patient demonstrated signs and symptoms of PNI along the supraorbital, ophthalmic, and presumed abducens and sympathetic pupillary nerve fibers at the cavernous sinus. We speculate that the primary carcinoma originated as a carcinoma involving the forehead or adnexal structures with retrograde extension into the cavernous sinus via the supraorbital nerve; however extensive dermatologic and ophthalmic examinations have been unrevealing. Nasopharyngeal carcinoma with superior extension was considered to be less likely as there was no definitive involvement of the pterygopalatine fossa on imaging and otolaryngology examinations were unrevealing. The presence of cavernous sinus syndrome or an intractable trigeminal neuralgia should alert the physician to the possibility of an underlying primary or metastatic cavernous sinus malignancy. To our knowledge this is the only case demonstrating clinical and radiographic involvement of the supraorbital

nerve from a poorly differentiated carcinoma presenting with trigeminal pain and a Horner syndrome in the English language ophthalmic literature.^{4,7,8}

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Declaration of interest

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

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