Case report

Nasopharyngeal carcinoma presenting as a sixth nerve palsy and Horner's syndrome

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SUMMARY

The combination of a sixth nerve palsy and ipsilateral Horner's syndrome localises the disease process to the posterior cavernous sinus and can be a result of various pathologies in this region. A 74-year-old Chinese woman presented with a 9-month history of binocular horizontal diplopia worse when looking left. She was found to have a left sixth nerve palsy and Horner's syndrome and MRI revealed an enhancing soft tissue mass in the nasopharynx with involvement of the bones of the skull base and invasion of the left cavernous sinus. Endoscopic biopsy of the mass confirmed the diagnosis of non-keratinising squamous cell carcinoma, which was Epstein-Barr virus positive. She was treated with radiation therapy. Patients with a sixth nerve palsy and ipsilateral Horner's syndrome should have urgent neuroimaging with careful attention to the cavernous sinus since sympathetic fibres join the sixth nerve for a short distance in this location.

BACKGROUND

The combination of a sixth nerve palsy and ipsilateral Horner's syndrome localises the disease process to the posterior cavernous sinus.^{1,2} This is because the sympathetic fibres join the sixth nerve for a short distance in this location before joining the ophthalmic division of the trigeminal nerve and has been termed Parkinson's syndrome.¹ A number of disease processes may cause this presentation. Here, we present a case where a sixth nerve palsy and ipsilateral Horner's syndrome were the presenting sign of nasopharyngeal carcinoma.

CASE PRESENTATION

A 74-year-old Chinese woman presented with a 9-month history of horizontal binocular diplopia worse when looking to the left. She had a past medical history of congestive heart failure, mitral valve prolapse, hypertension and dyslipidaemia.

She denied pain or headache. On examination, she had a visual acuity of 20/20 in the right eye and 20/25 in the left eye. There was an incomitant esotropia worse in left gaze corresponding to a complete left eye abduction deficit ([figure 1](#)). She had mild ptosis and anisocoria with the left pupil being smaller. The anisocoria was slightly greater in dim lighting conditions and there was reversal of anisocoria 1 hour after instillation of apraclonidine 0.5% in each eye, confirming a left Horner's syndrome ([figure 2](#)). Dilated fundus examination was normal in both eyes. Cranial nerve function was also normal apart from decreased sensation to light touch in the V2 distribution on the left.

INVESTIGATIONS

The combination of a left sixth nerve palsy and ipsilateral Horner's syndrome, localised the process to the left cavernous sinus. She therefore had an MRI of the brain with intravenous contrast that showed enhancing soft tissue thickening along the left nasopharynx with involvement of the bones of the skull base including the left pterygoid plates, left clivus, sphenoid bone and left petrous apex. There was enhancement of the left cavernous sinus and adjacent dura ([figure 3](#)). There were also enlarged pathological lymph nodes at left level IIA and IIB. This was concerning for nasopharyngeal carcinoma. She underwent endoscopic biopsy of the nasopharyngeal mass and this showed a non-keratinising squamous cell carcinoma, which was Epstein-Barr virus positive.

OUTCOME AND FOLLOW-UP

Given her medical comorbidities, she was not a good candidate for chemotherapy and underwent radiation therapy over the course of 7 weeks. Her neurological examination remained stable at 3 months.

DISCUSSION

The oculosympathetic pathway begins in the hypothalamus and travels down the brainstem to the C8-T2 level of the spinal cord (ciliospinal centre of Budge). After it leaves the spinal cord, it courses over the apex of the lung and synapses in the superior cervical ganglion. It then ascends with the internal carotid artery and in the posterior cavernous sinus it joins with the sixth cranial nerve for a short distance before it joins the ophthalmic division of the trigeminal nerve and enters the orbit. A lesion causing a sixth nerve palsy and ipsilateral

Figure 1 External Photographs demonstrating a complete abduction deficit in the left eye from a left sixth nerve palsy.

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Figure 2 External photographs demonstrating left eye ptosis and miosis (A) that reversed with apraclonidine 0.5% after 1 hour and (B) confirming a left Horner's syndrome.

Horner's syndrome has high localising value and indicates a process in the posterior cavernous sinus.^{1 2} Horner's syndrome can be confirmed with pharmacological testing with cocaine or apraclonidine eye drops. Apraclonidine is a pharmacological agent with strong alpha-2 and weak alpha-1 agonist activity and when sympathetic nerve stimulation is interrupted in Horner's syndrome, denervation supersensitivity results in upregulation of alpha-1 receptors in the iris.³ The Horner's pupil therefore dilates with apraclonidine whereas there is little to no effect in the normal pupil.

Any disease process in the posterior cavernous sinus could theoretically cause a sixth nerve palsy and ipsilateral Horner's syndrome. The cavernous sinus contains cranial nerves III, IV, V1, V2 and VI. This patient also had involvement of V2 due to perineural spread of the tumour in the cavernous sinus. The largest case series on the topic of combined sixth nerve palsy and Horner's syndrome was by Ebner *et al*⁴ who included five cases due to cavernous sinus meningiomas (n=2), carotid-cavernous aneurysm, metallic foreign body and squamous cell carcinoma. Additional case reports have documented additional causes such as a cavernous-carotid aneurysms,^{5 6} petrous internal carotid artery aneurysm,⁷ carotid cavernous-sinus fistula,^{8 9} facial abscess,¹⁰ herpes zoster ophthalmicus arteritis¹¹ and metastatic carcinomas.^{12 13} Nasopharyngeal carcinoma may also cause a sixth nerve palsy and ipsilateral Horner's syndrome. Top Karti *et al*¹⁴ reported a case of a 62-year-old man who was diagnosed with nasopharyngeal carcinoma 10 years prior to onset of horizontal binocular diplopia which was the first sign of a recurrence of the disease. Kang *et al*¹⁵ described a 68-year-old man who had a known diagnosis of nasopharyngeal carcinoma and presented with a sixth nerve palsy and a sequential ipsilateral Horner's syndrome. The patient died 15 months later. We were unable

Figure 3 Coronal T1 MRI of the head and neck demonstrating an enhancing mass in the left nasopharynx (red arrows) with enhancement of the left cavernous sinus and adjacent dura (yellow arrow).

to retrieve a case in the English-language literature where nasopharyngeal carcinoma was initially diagnosed after a sixth nerve palsy and ipsilateral Horner's syndrome.

Learning points

- The combination of a sixth nerve palsy and ipsilateral Horner's syndrome localises the disease process to the posterior cavernous sinus and MRI should be performed with close attention to this area.
- The disease processes that have been reported to cause a sixth nerve palsy and ipsilateral Horner's syndrome include nasopharyngeal carcinoma, meningiomas, cavernous-carotid aneurysms or carotid-cavernous fistulas and metastatic disease.
- Horner's syndrome can be confirmed with pharmacological testing with apraclonidine 0.5% and a positive test is reversal of anisocoria.

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