Isolated Horner syndrome as a rare initial presentation of nasopharyngeal carcinoma: a case report

Tanyatuth Padungkiatsagul¹
Anuchit Poonyathalang⁶
Panitha Jindahra²
Piyaphon Cheecharoen³
Kavin Vanikieti¹

¹Department of Ophthalmology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; ²Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; ³Department of Radiology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Background: Horner syndrome refers to a set of clinical presentations resulting from disruption of sympathetic innervation to the eye and adnexa. Classically, the clinical triad consists of ipsilateral blepharoptosis, pupillary miosis, and facial anhidrosis. Ocular sympathetic denervation may signify life-threatening causes. Timely investigation and accurate diagnosis are essential in patients with oculosympathetic denervation.

Case presentation: A 33-year-old Asian man with a heavy smoking habit presented with a 3-week history of left ptosis and no other complaints. His visual acuity was 20/20 bilaterally. An ophthalmic examination was significant for mild ptosis of his left eyelid and anisocoria (smaller left pupil), which was greater in the dark. Both pupils reacted to light briskly without an afferent pupillary defect. Anhidrosis was found on the medial side of the left forehead. A 10% cocaine test was positive. At his first visit, neurologic examination was unremarkable. Comprehensive radiological investigations were scheduled for a left-sided isolated Horner syndrome. Two weeks after his first visit, he experienced a left-sided headache along with ipsilateral Horner syndrome. Neurologic examination revealed hypoesthesia in the left cranial nerve V₁ territories. Emergent computed tomography angiography was suspected for petrous part of the left internal carotid artery (ICA) dissection. Magnetic resonance imaging demonstrated an enhancing infiltrative lesion with its epicenter at the left sphenoid bone. The lesion encased the left ICA and invaded the left Meckel cave. Rhinoscopy with incisional biopsy revealed squamous cell nasopharyngeal carcinoma.

Conclusion: This case involved an unusual initial presentation of nasopharyngeal carcinoma: isolated Horner syndrome with clinical progression to adjacent structures. Infiltration involving the Meckel cave and ICA at the foramen lacerum can present as postganglionic Horner syndrome associated with trigeminal pain and hypoesthesia. These clinical findings may mimic carotid artery dissection on computed tomography angiography. Detailed magnetic resonance imaging with careful attention to the skull base should be performed.

Keywords: Horner syndrome, nasopharyngeal carcinoma, trigeminal

Background

Horner syndrome, or oculosympathoparesis, was first described by Johann Friedrich Horner in 1829. It is characterized by a classic constellation of signs comprising ipsilateral blepharoptosis, pupillary miosis, and facial anhidrosis.¹ The syndrome can result from any disruption of the sympathetic innervation to the eye and ocular adnexa. Differential diagnoses for the pathology responsible for the sympathetic disruption range from benign to life-threatening conditions such as carotid artery dissection and malignancies.² Timely and accurate diagnosis is essential to provide appropriate management.
A definitive diagnosis of Horner syndrome may require pharmacologic confirmation because of the variable clinical findings of sympathetic denervation of the head and eye. Cocaine – a presynaptic norepinephrine reuptake inhibitor – produces mydriasis, lid retraction, and blanching of the conjunctiva in the normal eye, whereas it produces no response in the pathologic eye. Post-cocaine anisocoria of ≥0.8 mm confirms the presence of oculosympathetic denervation.3

The etiologies of Horner syndrome are numerous due to the long and circuitous course of the involved nerves. The three-neuron pathway initiates in the hypothalamus and terminates in the eye. Localization of pathologic site can be inferred by associated clinical findings. Vertigo, ataxia, sensory deficits, dysphagia, or nystagmus suggests a lesion of a central or first-order neuron. Hemifacial anhidrosis, a mass in the anterior neck, hand weakness, or a history of central venous catheterization suggests a lesion of a preganglionic second-order neuron. An ipsilateral headache or neck pain and the absence of anhidrosis (which may present in the medial part of the forehead) suggest damage of a postganglionic third-order neuron.

We herein report a case involving isolated Horner syndrome as an unusual presenting sign of nasopharyngeal carcinoma (NPC). Trigeminal pain and hypoesthesia subsequently developed due to progression of the tumor. Diagnostic procedures and localization of the lesion are discussed in this report.

Case presentation
A 33-year-old Thai man with a heavy smoking habit presented with a 3-week history of ptosis in his left eye without any other complaints. His visual acuity was 20/20 bilaterally. His intraocular pressure and ocular motility were unremarkable. Ophthalmic examination was significant for mild ptosis of the left eyelid with anisocoria (smaller pupil in the left eye) as shown in Figure 1. The difference in the pupillary diameter between the right and left sides was greater in dark than in bright conditions. In bright light, the right and left pupils were 3 and 2 mm, respectively (Figure 2A). Under dim light, however, the right pupil dilated to 4 mm, whereas the left pupil was almost unchanged (2.5 mm), as shown in Figure 2B. This finding was the result of iris dilator impairment in the left eye. Both pupils reacted to light briskly without an afferent pupillary defect. Anhidrosis was noted on the medial side of the left forehead. A Horner syndrome confirmatory test (the 10% cocaine test) was positive; the difference in pupillary diameter increased to 2.5 mm (6.0 mm on the right and 3.5 mm on the left) after the instillation of 10% cocaine bilaterally (Figure 2C). This was accompanied by right upper eyelid retraction (Figure 2C). At his first visit, physical examination (including a neurologic examination) was unremarkable. Thus, a provisional diagnosis of left-sided painless isolated Horner syndrome was made. Comprehensive radiological investigations including magnetic resonance imaging (MRI) and magnetic resonance angiography of his neck and brain combined with computed tomography of the chest were scheduled. Two weeks after his first visit, he developed a left-sided headache along with ipsilateral Horner syndrome. Neurologic examination revealed hypoesthesia in the left cranial nerve V1,3 territories. Emergent computerized tomography angiography (CTA) of the neck, including the
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Discussion and conclusion
Horner syndrome is characterized by ipsilateral blepharoptosis, pupillary miosis with anisocoria that is greater in the dark, and facial anhidrosis on the affected side. Establishing the diagnosis and localizing the disruption of the oculosympathetic pathway are essential. Disruption of the three-neuron pathway can be divided into three types: central, preganglionic, and postganglionic.2,5,6

The first-order neuron originates from the hypothalamus and travels from the brain stem through the ciliospinal center of Budge–Waller, located at the spinal cord levels C8–T2.6 Central causes of Horner syndrome are commonly accompanied by neurologic signs and symptoms. Ataxia, sensory loss, vertigo, vestibular nystagmus, and dysphagia are usually present in patients with Horner syndrome caused by a brain stem lesion. Brain stem infarcts are the most common cause

Figure 3 Emergent computed tomography angiography of the neck, including the base of the skull.
Notes: Contrast-enhanced (A) axial and (B) coronal studies show long segmental luminal narrowing of the petrous part of the left ICA (arrows) compared with the normal luminal size of the right ICA (arrowheads). Left ICA dissection is suspected.
Abbreviation: ICA, internal carotid artery.

Figure 4 Magnetic resonance imaging of the brain, orbit, and neck.
Notes: (A) Axial T1-weighted imaging with gadolinium injection shows a large infiltrative lesion with strong enhancement encasing the left ICA (arrowhead) and causing segmental luminal narrowing with invasion to the left Meckel cave and left sphenoid wing (arrow). (B) Coronal T1-weighted imaging with gadolinium injection shows that the epicenter of the enhancing infiltrative lesion involves the central skull, and the lesion extends to the medial left middle cranial fossa and left Meckel cave (arrowheads) with extensions to the pterygopalatine fossa and lateral wall of the nasopharynx (not shown).
Abbreviation: ICA, internal carotid artery.
of central Horner syndrome.7 Our patient had no associated 
brain stem neurologic signs or symptoms, except ipsilateral 
loss of facial sensation in the cranial nerve V1–3 territories. 
Therefore, a central lesion was considered unlikely.

After the preganglionic neuron exits the ciliovisceral 
center of Budge–Waller, it travels down through the pul-
monary apex and turns upward within the carotid sheath to 
superior cervical ganglion. Horner syndrome accompanied 
by ipsilateral shoulder pain should raise the suspicion for 
neoplastic involvement of the pulmonary apex, pleura, and 
brachial plexus. Various neck and cardiothoracic surgical 
procedures that can reportedly cause preganglionic Horner 
syndrome include coronary artery bypass surgery, carotid 
derarterectomy, intracostal chest tube insertion, and internal 
jugular catheterization.2 Our patient had neither a history 
of prior surgical procedures nor clinical manifestations of 
thoracic abnormalities, including chest pain or hemoptysis. 
Moreover, anhidrosis was reported only in the medial part of 
his forehead; other areas of his face were normal. Pregangli-
onic Horner syndrome was, therefore, unlikely in this patient.

The postganglionic third-order neuron starts from the 
superior cervical ganglion as a sympathetic plexus traveling 
along the ICA. The fibers responsible for sweating of the 
face (submotor fibers) exit the superior cervical ganglion 
with the external carotid artery. The remaining sympathetic 
plexus joins the ICA and enters the skull base through the 
carotid canal and foramen lacerum and then travels up into 
the cavernous sinus. At the posterior part of the cavernous 
sinus, the sympathetic fibers briefly travel with the abducens 
nerve before joining the ophthalmic division of the trigeminal 
nerve and entering the orbit. A lesion at the posterior part of 
the cavernous sinus can produce postganglionic Horner 
syndrome with abducens paresis,8 the so-called Parkinson sign. 
Differential diagnoses of painful postganglionic Horner 
syndrome always include life-threatening carotid artery 
dissection, cluster headache, a cavernous sinus lesion, and 
Raeder paratrigeminal neuralgia.2,6

Our patient initially presented with painless, left-sided, 
isolated Horner syndrome, comprising miosis with anisocoria 
that was greater in the dark (Figure 2A and B), mild ipsilateral

ptosis (Figure 1), and anhidrosis in the medial part of the ipsi-
lateral forehead. The patient’s blepharoptosis was subtle and 
could be explained by paralysis of Müller’s muscle, which is 
responsible for only 2 mm of eyelid elevation.5,7 The diagnosis 
of Horner syndrome (oculosympathetic denervation) is usu-
ally based on clinical characteristics. Nonetheless, the cocaine 
test is still a reliable gold standard test with which to confirm 
the diagnosis. The 10% cocaine test confirmed the diagnosis 
of left-sided Horner syndrome in our patient (Figure 2C).

After confirmation with the topical cocaine test, the lesion 
can be localized with the hydroxyamphetamine test. This 
test can be used to distinguish a postganglionic lesion from 
preganglionic and central lesions by hydroxyamphetamine’s 
action of releasing norepinephrine from the presynaptic 
terminal. Only an intact postganglionic neuron can produce 
mydriasis. The hydroxyamphetamine test is unavailable in 
our center. This test is now rarely performed because of its 
high false-positive and false-negative rates.8 Therefore, the 
clinician must localize the lesion causing Horner syndrome 
based upon clues from the patient’s history and examina-
tion.2 At our patient’s first visit, the physical examination, 
including a neurologic examination, was unremarkable. A 
provisional diagnosis of painless, left-sided, and isolated 
Horner syndrome was made. Based solely on the patient’s 
clinical signs, it was difficult to clearly distinguish between 
a preganglionic and postganglionic lesion. Retrospectively, 
only the patient’s heavy smoking history raised suspicion for 
NPC. Two weeks after his first visit, he developed a dull, left-
sided headache and ipsilateral hypoesthesia in the left cranial 
nerve V1–3 territories, leading to localization of a third-order 
nervon lesion (specifically at the left skull base). However, 
life-threatening carotid artery dissection must be ruled out 
in patients with postganglionic Horner syndrome with an 
ipsilateral headache or facial pain. Our patient underwent 
emergent CTA of the neck, including the skull base. CTA 
revealed long segmental luminal narrowing of the petrous 
part of the left ICA, and left ICA dissection was suspected 
(Figure 3). Further MRI of the brain and neck demonstrated 
a large enhancing infiltrative lesion encasing the left ICA, 
causing segmental luminal narrowing with invasion to the 
central skull, and extending to the left Meckel cave, left 
sphenoid wing, pterygopalatine fossa, and the lateral wall of 
nasopharynx (Figure 4). NPC along with other head and neck 
malignancies were suspected. Rhinoscopy with incisional 
biopsy was performed, and pathologic examination showed 
undifferentiated, non-keratinizing, squamous cell NPC.

The age at onset of NPC is usually 40–60 years.10 Men 
are affected twice as often as women.10 The lack of specific
initial symptoms and slow growth are responsible for the delay in diagnosis of NPC. Otorhinologic symptoms and signs are present in about half of the patients.11–13 The tumor typically arises from the roof or lateral wall of the nasopharynx. NPC can disrupt the oculosympathetic pathway at either the preganglionic level through the cervical lymph node and sympathetic plexus involvement12 or the postganglionic level. The third-order neuron can be damaged by infiltration of NPC in the skull base and cavernous sinus area, including involvement of various branches of the trigeminal nerve.13–16 NPC rarely presents initially as isolated Horner syndrome, as shown in the present case.15,16 NPC should also be strongly suspected in any patient who presents with unilateral facial pain associated with ipsilateral trigeminal neuropathy and postganglionic Horner syndrome.12 Detailed MRI with careful attention to the skull base should be performed in such cases.

Ethics approval and consent
This study was approved by the Institutional Review Board of Faculty of Medicine Ramathibodi Hospital. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Data sharing statement
Data for this case report were collected by chart review of the patient’s electronic medical record, which is not publicly available because of privacy considerations.

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Author contributions
All authors made substantial contributions to the conception and design of the study. TP, PC, and KV contributed to the acquisition of data. All authors contributed to data analysis and interpretation of data. All authors took part in drafting the work and TP and KV revised it critically. All authors gave final approval for submission; and are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Disclosure
The authors report no conflicts of interest in this work.

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