

Horner Syndrome in Children: A Clinical Condition with Serious Underlying Disease

Christophe Barrea¹ Tiphaine Vigouroux¹ Joe Karam¹ Ariane Milet² Sandrine Vaessen¹
Jean-Paul Misson¹

¹ Division of Child Neurology, Department of Pediatrics, Centre Hospitalier Régional, Liège, Belgium

² Department of Ophthalmology, Centre Hospitalier Régional, Liège, Belgium

Address for correspondence Dr. Christophe Barrea, MD, Division of Child Neurology, Department of Pediatrics, CHR Citadelle de Liège, Boulevard du Douzième de Ligne, 1, 4000 Liège, Belgium (e-mail: chbarrea@gmail.com).

Neuropediatrics

Abstract

Aim Horner syndrome corresponds to the clinical triad of miosis, ptosis, and facial anhidrosis. These symptoms are related to injury of the oculosympathetic chain. In children, Horner syndrome is classified as congenital or acquired. While the diagnosis is made through clinical examination, there is some debate regarding the use of imaging modalities and the extent of anatomical coverage required.

Methods Here, we describe two cases of children with acute Horner syndrome. We then review the literature about the different etiology and discuss the interest of some investigations.

Results *Case 1:* An 8-month-old girl without personal or familial history, has presented a right acquired Horner syndrome without additional signs. Frontal chest radiography and ultrasonography of the neck and the abdomen was first achieved and returned normal. The cerebral and cervical magnetic resonance imaging (MRI) with angiographic sequences performed in a second time was also normal. Finally, an enhanced thoracic computed tomography (CT)-scan demonstrated a mass at the right pulmonary apex. *Case 2:* A 9-year-old boy without personal or familial history has presented an acute headache with loss of consciousness during a basketball competition. Upon waking up, the child has right hemiplegia, aphasia, and left Horner syndrome. The cerebral CT scan realized in the first line was normal. The MRI with angiographic sequences demonstrated M1 left carotid dissection with homolateral white matter infarction.

Conclusion Imaging studies seem critical in delineating the nature and extent of any underlying pathology along the oculosympathetic pathway in children presenting a Horner syndrome. In these patients, a history of trauma or surgery may reduce the need for extensive systemic evaluation. Without such anamnesis, a decision to proceed with further evaluation is made with consideration of the relative incidence of tumor, especially neuroblastoma, or other treatable lesions. In this condition, MRI is the more sensitive and recommended investigation.

Keywords

- Horner syndrome
- oncology
- vascular disease

received
February 3, 2016
accepted after revision
April 3, 2016

© Georg Thieme Verlag KG
Stuttgart · New York

DOI <http://dx.doi.org/10.1055/s-0036-1584085>.
ISSN 0174-304X.

Introduction

Epidemiology

Horner syndrome in children is a set of signs and symptoms corresponding to the clinical triad of miosis, mild upper eyelid ptosis, facial anhidrosis, and/or hyperemia. This relatively rare disease, with an incidence estimated at 1.42 per 100,000 patients under the age of 19 years,¹ is related to injury of the oculosympathetic chain.

Anatomic Consideration

The oculosympathetic pathway provides sympathetic innervation to the eye through three orders of neurons in specific anatomical locations.

The first order neurons (central) arise in the posterolateral hypothalamus, descend through the brainstem and travel in the intermediolateral cell column of the spinal cord, synapsing at the ciliospinal center (of Budge) located approximately at the C-8 to T-2 level in the spinal cord.

Second order neurons (preganglionic) exit the ciliospinal center of the thoracic cord, enter the chest cavity, arches over the apex of the lung, and ascend through the stellate and middle cervical ganglia to synapse in the superior cervical ganglion located at the level of the carotid bifurcation and angle of the jaw.

Third order neurons (postganglionic) leave the superior cervical ganglion and ascend within the adventitia of the internal carotid artery to enter the skull and then the cavernous sinus. Sympathetic fibers then enter the orbit through the superior orbital fissure with the nasociliary branch of the ophthalmic division of the trigeminal nerve, the long ciliary nerves. Another branch passes through the ciliary ganglion and joins the postganglionic ciliary nerves, the short ciliary nerves. These two fibers penetrate the sclera, travel in the suprachoroidal space to innervate the dilator pupillae muscle, the inferior, and the superior (Müller) tarsal muscles.

Other third order axons travel from the superior cervical ganglion and follow the external carotid to supply vasomotor and sudomotor innervation of the hemiface.

The clinical implications of the long circuitous route of the oculosympathetic chain should be evident: diseases that affect brainstem, spinal cord, chest, or neck, can present with Horner syndrome. As there is no decussation, all the symptoms will be homolateral to the lesion. Following the level of injury, the clinical presentation will be pure, with the characteristic triad, or only with the ocular signs.

Symptoms

Miosis

Interruption of the oculosympathetic pathway causes a paresis of the dilator pupillae muscle. It results in an anisocoria with a smaller but reactive pupil on the affected side, most evident by observing the pupils as they are in the process of dilating in darkness. After 10 to 15 seconds in the dark,

anisocoria will be less apparent. This dilation lag is very characteristic, but may not always be evident clinically.

Ptosis

The upper eyelid elevation is supplied by the levator palpebrae, innervated by the third cranial nerve, and, to a lesser extent, by the Müller muscle, which is innervated by the sympathetic network. A defect of the latter results in a ptosis of the upper lid—typically 1 to 2 mm. In some cases, the lower lid also may be slightly elevated from paresis of a rudimentary sympathetically innervated lower lid analog of Müller muscle.

Sudomotor and Vasomotor Deficiency

Patients who have interruption of the sympathetic pathway may also interrupt vasomotor and sudomotor innervation. The distribution of this anhidrosis varies from the entire half face to a small patch on the forehead, depending on the lesion location. Occasionally, a lack of facial flushing on the affected side is noted as a consequence of the interruption of unilateral sympathetic vasomotor innervation to the face.

Other Symptoms

Iris heterochromia develops due to the absence of the sympathetic trophic effect on iris melanocytes. Heterochromia is typical of the congenital Horner syndrome, but may also develop in Horner syndrome acquired before 2 years of age.

Narrowing of the palpebral fissure will cause apparent enophthalmos, so called pseudoenophthalmos, present in the majority of patients.

It has been suggested that, as the cervical sympathetic nerves have a trophic influence on the orbitalis muscle, some cases with long standing could present a real enophthalmos due to the shrinking of the tissues in this orbit.²

Finally, acute features of sympathetic disruption can also include ipsilateral conjunctival injection, nasal stuffiness, and increased near point of accommodation.

Clinical Cases

Case 1

An 8-month-old girl without personal or familial history, has suddenly presented an acquired Horner syndrome without additional signs. An ophthalmologist has been consulted and the child was referred to emergency for more investigation. Frontal chest radiography with cervical and abdominal ultrasonography was first achieved and returned normal. The cerebral and cervical magnetic resonance imaging (MRI) with angiographic sequences performed in a second time was also normal. Finally, the thoracic computed tomography (CT)-scan demonstrated a mass at the pulmonary apex (→Fig. 1), suggestive of neuroblastoma. Urinary concentrations of homovanillic acid and vanillylmandelic were normal. No ocular pharmacological testing was performed. Thoracic MRI was finally realized to clarify tumor extension before surgery. Sympathetic nerve had to be sacrificed. Analysis of the tumor confirmed the diagnosis of neuroblastoma.

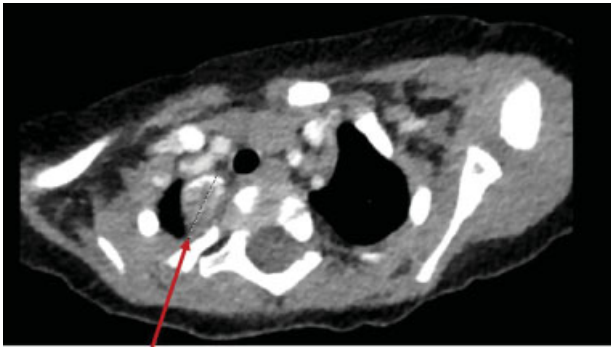


Fig. 1 Thoracic CT-scan with contrast demonstrates a mass of 1.67 cm of diameter at the apex of the right lung (arrow). Calcifications are presents on the periphery of this lesion. CT, computed tomography.

Case 2

A 9-year-old boy without personal or familial history has presented an acute headache with loss of consciousness during a basketball competition. On waking, the child has right hemiplegia, aphasia, and a left Horner syndrome. The cerebral CT-scan realized in the first line was normal. The MRI with angiographic sequences demonstrated M1 left carotid dissection with homolateral white matter infarction (► **Fig. 2**). Anticoagulant and antithrombotic treatments were introduced. One year after the incident, the child keeps a mild paresis with a residual ptosis and miosis.

Discussion

Etiology

Horner syndrome can be classified as congenital or acquired in children. Congenital Horner is mostly due to birth trauma and congenital abnormalities of internal carotid arteries such as hypoplasia or agenesis. Also, ectopic thymus in the neck, congenital neuroblastoma, and congenital varicella have been reported. Rarely, the congenital Horner syndrome may be of autosomal dominant inheritance.³⁻⁵

An acquired Horner syndrome in children can be of neoplastic or nonneoplastic etiology. The most common childhood tumor causing the acquired Horner syndrome is neuroblastoma,¹ with an incidence, risk estimated around 1 per 10 cases. If we take in consideration the other mass lesions including paraganglioma, ganglioneuroma, childhood thyroid cancer, schwannoma, rhabdoid tumor, astrocytoma of the hypothalamus, leukemia, and reactionary lymphadenopathy, this risk increase at 1/7.³⁻⁷

Vascular etiology is the most common cause in adult, but also manifest in children, and not just among teenagers as seen in case 2. It implicates arterial dissection⁸ and aneurysm.⁹ Horner syndrome can be caused by internal (thoracic or neck surgery, jugular vein cannulation) and external trauma (lower brachial plexus palsy [Klumpke]). Other intrathoracic etiologies are pneumothorax⁷ and thoracic empyema.¹⁰ Finally, cases of the Arnold Chiari syndrome, syringomyelia,³ and middle ear infection¹¹ have been described as another cause of the acquired Horner syndrome.

Current Imaging

There is some debate regarding the use of imaging modalities and the extent of anatomical coverage required for the radiological workup of Horner syndrome in children.

Since many Horner syndromes suggest malignant process or treatable causes, imaging seems important in delineating the nature and extent of any underlying disease. Some etiology, such as (birth) trauma and recent surgery, would obviously require less investigation.

Clinical signs and symptoms can sometimes provide some information about the level of the lesion and orient the investigation, as seen in case 2. On the other side, as demonstrated in the first case, the entire oculosympathetic pathway should be imaged in patients in whom the clinical examination does not provide enough information to localize the lesion with certainty.

MRI of the head, neck, and upper chest, with the field of view extending from the cavernous sinuses to the midthoracic spine,



Fig. 2 Cerebral MRI demonstrate an acute ischemic stroke in the left lenticulostriatal region on FLAIR sequences (circle) and a decreased vascular flow in the left internal carotid artery secondary to dissection on angiographic sequences (arrow). FLAIR, fluid-attenuated inversion recovery; MRI, magnetic resonance imaging.

including T2–T3 vertebrae, seems to be the more sensitive examination. If a postganglionic origin is suspected or if there is no other clinical etiology, an angiogram of the neck vessels should be added. Compared with previous imaging recommendations, this proposed protocol is simpler for clinicians to use and seems more cost-effective.¹²

As MRI is not easily available, other tests can be made to orient the diagnosis. However, their sensibility and specificity are lower, and MRI exploration is often necessary to clarify the nature and extension of a lesion.

Chest radiography with frontal and lateral projections is advisable to look for any mediastinal or apical chest mass lesion. Nevertheless, opacity at the apex of the lung seems not always obvious, as seen in our patient.

Enhanced CT could represent an alternative, but limitations are due to radiation dose delivered, beam hardening artifacts known to compromise the quality of images at the posterior fossa and thoracic inlet levels, and its less sensibility to highlight (vascular) lesion as seen in case 2. Nevertheless, CT is mostly indicated if a traumatic injury of the skull base is suspected to be the cause of Horner syndrome.

The role of ultrasound of the neck is very limited because of its less sensibility and its operator-dependency. It may be useful for demonstrating a neck mass or an abnormal flow in the carotid. Regardless, its result, further cross-section imaging will be needed to cover the US-blinded regions as well as to better define the extent of the anomaly.

As different authors report Horner syndrome in patients suffering from abdominal neuroblastoma without other etiology highlighted,¹³ abdominal ultrasound can be useful to detect this mass. Possible explanations of this phenomenon could be that of a paraneoplastic effect or of a missed small focus of neuroblastoma in the cervical sympathetic chain.

Other Investigations

Pharmacological testing includes cocaine, apraclonidine, and hydroxyamphetamine drops. Cocaine, an inhibitor of the reuptake of norepinephrine, dilates the normal pupil, but has no effect on the pathological one. Apraclonidine, an α_2 -adrenergic agonist, has no effect on normal pupil, but dilates the affected eye. Hydroxyamphetamine eye drops, by releasing stored norepinephrine from healthy postganglionic adrenergic nerve endings, can help distinguish a third-order Horner syndrome from either a first- or second-order syndrome.

Evaluation traditionally has been handled with cocaine testing to confirm the presence of Horner syndrome, followed by hydroxyamphetamine testing to localize the lesion. This evaluation is now limited because of poor availability of the reagents.

Apraclonidine testing offers an alternative, but there are several issues with its use, including the possible safety issues in using the drug to test young children and the possibility of false-negative results. These rates are higher in the very acute stages of the Horner syndrome as the test relies on denervation hypersensitivity or transmitter depletion, which may not have occurred.¹⁴

Spot urine testing homovanillic acid and vanillylmandelic acid is of interest to exclude neuroblastoma. However,

because urine catecholamine studies have been normal in a few children with neuroblastoma, as in our patient, further investigations are often needed to exclude tumoral lesion.¹⁵

Finally, metaiodobenzylguanidine scintigraphy is out of the initial radiological approach. Nevertheless, it is an interesting technique to characterize the nature of a neck or chest mass in pediatric population when neuroblastoma is suspected.

Conclusion

Horner syndrome is caused by a lesion in the oculosympathetic pathway and is characterized by homolateral ptosis, miosis, and anhidrosis or hyperemia.

Here, we describe two cases with serious underlying diseases. Case 1 has neuroblastoma, the most common childhood tumor causing the acquired Horner syndrome, with an incidence risk estimated around 1 per 10 cases. Case 2 has carotid dissection, a common etiology in adults, which can also manifest in young children.

There is some debate regarding the use of imaging modalities and the extent of anatomical coverage required. In absence of history of birth trauma or cervicothoracic surgery, Horner syndrome in a child should be evaluated with complete neuroimaging to rule out life-threatening diseases. As demonstrated in this article, the use of radiography, ultrasonography, biology, and CT is limited. MRI–MR angiography of the head, neck, and upper chest, covering at least the regions extending from the orbital apices to the T3 vertebrae, seems to be the more sensitive, simple, cost-effective, and so recommended investigation.

References

- Smith SJ, Diehl N, Leavitt JA, Mohny BG. Incidence of pediatric Horner syndrome and the risk of neuroblastoma: a population-based study. *Arch Ophthalmol* 2010;128(3):324–329
- Wagener HP. Enophthalmos in Horner's syndrome. *Trans Am Ophthalmol Soc* 1933;31:166–175
- Kadom N, Rosman NP, Jubouri S, Trofimova A, Egloff AM, Zein WM. Neuroimaging experience in pediatric Horner syndrome. *Pediatr Radiol* 2015;45(10):1535–1543
- Zafeiriou DI, Economou M, Kolioukas D, Triantafyllou P, Kardaras P, Gombakis N. Congenital Horner's syndrome associated with cervical neuroblastoma. *Eur J Paediatr Neurol* 2006;10(2):90–92
- Lambert SR, Taylor D, Kriss A, Holzel H, Heard S. Ocular manifestations of the congenital varicella syndrome. *Arch Ophthalmol* 1989;107(1):52–56
- Ruiz E, Resende LS, Gaiolla RD, Niéro-Melo L, Custódio Domingues MA, de Lima Resende LA. Post-ganglionic Horner's syndrome: an unusual presentation of non-Hodgkin lymphoma. *Case Rep Neurol* 2012;4(1):43–46
- Nashila H, Genevieve S, Nadeem A. The risk of neuroblastoma in paediatric Horner syndrome – a systematic reappraisal of the literature. *Neuro-ophthalmology* 2012;36(6):227–231
- Chan CC, Paine M, O'Day J. Carotid dissection: a common cause of Horner's syndrome. *Clin Experiment Ophthalmol* 2001;29(6):411–415
- Mangat SS, Nayak H, Chandna A. Horner's syndrome and sixth nerve paresis secondary to a petrous internal carotid artery aneurysm. *Semin Ophthalmol* 2011;26(1):23–24

- 10 Bhaskar G, Lodha R, Kabra SK. Unusual complications of empyema thoracis: diaphragmatic palsy and Horner's syndrome. *Indian J Pediatr* 2006;73(10):941–943
- 11 Spector RH. Postganglionic horner syndrome in three patients with coincident middle ear infection. *J Neuroophthalmol* 2008; 28(3):182–185
- 12 Chen Y, Morgan ML, Barros Palau AE, Yalamanchili S, Lee AG. Evaluation and neuroimaging of the Horner syndrome. *Can J Ophthalmol* 2015;50(2):107–111
- 13 George NDL, Gonzalez G, Hoyt CS. Does Horner's syndrome in infancy require investigation? *Br J Ophthalmol* 1998;82(1): 51–54
- 14 Mughal M, Longmuir R. Current pharmacologic testing for Horner syndrome. *Curr Neurol Neurosci Rep* 2009;9(5):384–389
- 15 Smith SJ, Diehl NN, Smith BD, Mohny BG. Urine catecholamine levels as diagnostic markers for neuroblastoma in a defined population: implications for ophthalmic practice. *Eye (Lond)* 2010;24(12):1792–1796



THIEME