Atypical Acquired Pediatric Horner Syndrome

Horner syndrome poses a challenge for the physician. Confusion in the diagnostic process may arise because some patients with Horner syndrome do not exhibit the classic findings of simultaneously occurring miosis and mild ptosis. When that is the case, the diagnosis may be missed and essential lifesaving treatment not rendered.

In classic Horner syndrome findings, the physician observes mild ptosis and miosis. The less common secondary symptoms of anhidrosis and inverse ptosis of the ipsilateral lower eyelid may also be present. In Horner syndrome that is congenital or has occurred very early in life, one may see heterochromia of the iris with the lighter colored iris on the side of the Horner syndrome. The physician must not eliminate the possibility of Horner syndrome when only miosis or only mild ptosis is seen. Subsequently, both symptoms may occur at the same time, elucidating the diagnosis of Horner syndrome.

Anatomically, Horner syndrome is produced when there is an interruption of the oculosympathetic pathway in 1 of 3 sites. The first site of Horner syndrome is the central neuron, which originates in the hypothalamus. The fibers leaving the hypothalamus descend ipsilaterally in the reticular formation of the brain stem. They continue in the anterolateral columns of the spinal cord in the lower cervical and upper thoracic area. They synapse in the intermediolateral column, which is also known as the ciliary center of Budge. From here, the second neuron, also called the preganglionic neuron, leaves the intermediolateral column via the ventral roots and joins the white rami communicantes to enter the paravertebral sympathetic chain. These fibers synapse in the superior cervical ganglion located just below the base of the skull. From this third neuronal site emerges the postganglionic neuron, which forms a plexus around the external and internal carotid arteries. The plexus around the internal carotid artery follows the artery through the foramen lacerum into the cavernous sinus. Most of the sympathetic fibers to the eye join the ophthalmic division of the trigeminal nerve, while some travel with the oculomotor nerve and the ophthalmic artery. The fibers to the eye innervate the dilator muscle of the iris and Muller muscle in the upper and lower eyelids.

Horner syndrome in children is differentiated from adult Horner syndrome by the location of the involved neuron. The most frequent anatomical location of childhood Horner syndrome is the preganglionic or second-order neuron. At this site, the most common cause of acquired Horner syndrome is a neuroblastoma of the paravertebral sympathetic chain. Damage to this neuron can be caused by either birth trauma to the brachial plexus or mediastinal tumors. Often, with congenital Horner syndrome, the iris on the involved side can be hypopigmented. Central, or neuron 1, lesions are primarily seen in adults and encompass tumors or hemorrhages of the brain stem. Pancoast tumor, with involvement of the apex of the lung, is one of the best-known causes of a preganglionic lesion in an adult. The third-order neuron lesion is seen mainly in adults. This lesion is often associated with a dissection of the internal carotid artery or nasopharyngeal carcinoma spreading along the internal carotid artery.

Years ago, in the workup of a child with Horner syndrome, we scanned the brain, the neck, and the chest. Now, we do not routinely scan the brain because we know that neuron 1 and neuron 3 lesions occur almost exclusively in adults. In children, we currently routinely scan the neck and chest as Horner syndrome is almost always associated with neuron 2 (preganglionic) lesions.

In this study, we discuss several unusual manifestations of Horner syndrome in infants. Two cases were associated with preganglionic lesions and 1 occurred with a postganglionic lesion. These manifestations were uncharacteristic in mode of appearance for several reasons. At times, miosis was present without ptosis; in other instances, ptosis appeared without miosis. Adding to the perplexity of diagnosis, we also observed a child with intermittent Horner syndrome whom we diagnosed as having a neuroblastoma.

Report of Cases. Case 1. A 6-month-old boy had a 2-week history of anisocoria. When examined, he had a small pupil on the left side but no ptosis. The mother reported that the pupil was sometimes normal in size. Initially, no tests were ordered. However, the child returned 1 week later because the mother had observed the occurrence of ptosis for the first time. The ptosis was on the same side as the miosis (Figure 1). The mother noted that there were times when there was no ptosis or pupillary involvement (Figure 2). At times during the office examination, only anisocoria without ptosis was observed. Occasionally, we saw anisocoria with a trace of ptosis of the upper eyelid, but careful scrutiny showed reverse ptosis of the lower eyelid.

Figure 1. Case 1 showing left-sided Horner syndrome with miosis and ptosis of the left upper eyelid with reverse ptosis of the left lower eyelid.
At other times, we observed significant ptosis without anisocoria (Figure 4). The mother was informed that this manifestation was rare and most likely physiological in nature. We recommended a computed tomographic (CT) scan of the neck and thorax to be certain there was no tumor. The mother was reluctant to approve a CT scan because of concerns about radiation exposure. Ultimately, she consented. The radiology department preferred a CT to a magnetic resonance image as calcium, which is sometimes seen in neuroblastoma, is easier to see with a CT. The CT revealed a neck mass, and 5 days later surgery was performed for a neuroblastoma of the paravertebral sympathetic chain. The tumor was completely removed and no chemotherapy was required. At the 6-month follow-up appointment, this patient had persistent left-sided Horner syndrome.

Case 2. A 4-month-old boy had a small left pupil observed by his mother during a 2-week period. Ptosis was not present, and the child was in good health. The mother was advised that although the eye examination results were normal, she should call us immediately if a droopy eyelid developed. Ten days later, the child’s mother reported that her son had developed ptosis on the same side as the miosis. An appointment was promptly scheduled for that same day. The child did indeed have ptosis, and positive results on an apraclonodine hydrochloride (Iopidine), 0.5%, test showed dilation of the miotic pupil and reversal of the ptosis 30 minutes after the apraclonidine was administered (Figure 5 and Figure 6). A CT scan of the neck and thorax revealed a tumor of the paravertebral sympathetic chain in the neck. Results of a biopsy were positive for neuroblastoma, and the child was successfully treated with chemotherapy.

Case 3. A 12-month-old boy had a 2-week history of a smaller pupil on the left side. The eye examination showed subtle anisocoria with a left miotic pupil. The anisocoria was greater in dark than in light (Figure 7). There was no ptosis and the cocaine test was negative. Four months later, the child returned with 2.5 mm of ptosis on the left side combined with the miosis. A diagnosis of Horner syndrome was made. A CT scan showed a mass impinging on the carotid artery on the same side as the Horner syndrome. A biopsy showed an enlarged benign lymph node.

Comment. Smolin1 described a 30-year-old man with congenital Horner syndrome who had episodes of intermittent pupil dilation on the side of the Horner syndrome. The patient had positive results on a cocaine test. Mutalib et al2 reported acquired Horner syndrome secondary to a spontaneous pneumothorax in a 14-year-old boy. The Horner syndrome lasted for 3 years and required no treatment.
syndrome was believed to be secondary to pressure on the sympathetic fibers in the area of the apical pleura. After the pneumothorax resolved, the miosis disappeared but the patient was left with a small residual ptosis.

In 2000, Slavin3 described a 47-year-old man who developed a 2-mm ptosis of the left upper eyelid with inverse ptosis of the ipsilateral lower eyelid with equal pupils. Positive results on a hydroxyamphetamine hydrobromide, 1%, test localized the Horner syndrome to the third neuron. Hydroxyamphetamine stimulates the release of nor epinephrine from nerve endings. This drug will dilate a first- or second-neuron Horner syndrome but not a third-neuron Horner syndrome. The Horner syndrome in this patient was believed to be associated with cluster headaches. During the next 2 weeks, the ptosis improved to only a 1-mm difference between the 2 sides, but then the right pupil was 3.5 mm and the left was 4.0 mm in the light. The right pupil was 4.0 mm in the dark and the left was 4.5 mm. Slavin surmised that the patient had developed Horner syndrome on the same side as a physiologically larger pupil, causing the 2 sides to be equal at the time of the initial visit. Hopf4 described a 32-year-old man with an alternating Horner syndrome. The syndrome first appeared on his left side, and 2 weeks later it appeared only on the right side. Five days later, it rotated again to his left side. He had an intramedullary papillary ependymoma extending from the C5 to the C8-T1 level, and it was successfully removed.

Rosenkranz et al5 described several patients who developed transient Horner syndrome after stent placement for carotid stenosis. They felt that a carotid wall hematoma caused stretching or compression of the periarterial sympathetic fibers. One of their patients had partial Horner syndrome with only pupillary involvement but no ptosis.

In a literature search, Mokri6 found a case of incomplete Horner syndrome in children. We have found no reports of incomplete or varying Horner syndrome in children.

These cases illustrate the variability in the manifestation of Horner syndrome. The fact that the miosis might precede the ptosis by 1 week to several months is a critical consideration. Physicians should consider cocaine or apraclonidine, 0.5%, pupil testing in infants with anisocoria even if ptosis is absent. If pharmacological testing results are negative or if the testing is not done, the family of an infant with anisocoria must be advised to look for the subsequent development of ptosis. If that should occur, the child must return for an immediate evaluation.

Computed tomography was chosen as the best diagnostic modality for demonstrating neuroblastoma radiologically. Calcification has been reported to appear between 50% and 90% of neuroblastoma tumors, with CT being the most sensitive for showing this.7-8 Calcifications are less commonly seen with magnetic resonance imaging.9 Calcification is far more frequent in neuroblastoma than in any other pediatric tumor.

Time is of the essence when elucidating the cause of Horner syndrome so that diseases that are potentially life-threatening can be treated. One should also be aware that Horner syndrome can be intermittent.
Remember that heterochromia is usually associated with congenital Horner syndrome but can occur in lesions with the onset before 2 years of age (Figure 8). The lighter-colored iris is on the side of the Horner syndrome as the sympathetic innervation is needed for the deposition of pigment in the stroma of the iris.

An additional caveat alerts the physician that just as anisocoria can at times be present without ptosis in infantile Horner syndrome, ptosis can sometimes be present without anisocoria. And lastly, Horner syndrome in infants may be present intermittently.

While our 3 cases do not fit the classic description of Horner syndrome, they do represent 33% of the infantile Horner syndrome cases seen in our pediatric ophthalmology practice in the past 5 years. Although these cases could represent a rare clumping of atypical findings, it is also possible that such nonclassic findings may be more common than previously recognized.

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