Congenital Cases of Concomitant Harlequin and Horner Syndromes

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We report three pediatric cases of concomitant congenital Horner and Harlequin syndromes. This association suggests a lesion at the superior cervical ganglion or just inferior. Often, no underlying lesion is documented. *(J Pediatr 2017;182:389-92).*

Harlequin color change is a transient manifestation of vasomotor instability, described first among newborns born preterm in 1952 by Neligan and Strang and reported as hemibody flushing. Historically, in 1988 Lance et al[1] named a dysautonomic syndrome "Harlequin syndrome" affecting the face. Harlequin syndrome is now defined as a paroxysmal hemifacial flushing and sweating, induced by exercise, emotional stress, or heat, whereas the other side of the face remains pale and dry. Harlequin syndrome is rare and has been reported mostly in adults, secondary to a lesion along the sympathetic nerve pathway. The syndrome can be associated with other autonomic system disturbances, such as Horner syndrome, reflecting a localized sympathetic dysfunction. The natural history is unknown in idiopathic cases. We report herein 3 pediatric cases of congenital Horner syndrome associated with Harlequin syndrome, to highlight this rare and striking association in infants and to discuss the underlying pathogenesis.

Case 1

A 15-month-old boy with no previous abnormal birth or medical history was referred to the dermatology service after his mother had noticed sudden and transient flushing of the left hemiface. Episodes had recurred since he started walking, after exertion, or in hot weather. The left side of his face showed erythema and sweating, with a clear demarcation at the midline, whereas the contralateral side remained pale and dry (**Figure 1**, A). The symptoms resolved spontaneously after 15-30 minutes of rest. The patient was known to have right ptosis, miosis, and enophthalmos, consistent with Horner syndrome, since birth. There were no other symptoms or neurologic defects. Findings of brain, cervical spine, and upper thoracic magnetic resonance imaging (MRI), with fluid-attenuated inversion recovery sequences and time-of-flight magnetic resonance angiography, were normal. Because of the patient's age and lack of other symptoms, no treatment was proposed. After 4 years of follow-up, the mother reported that the paroxysmal symptoms were less frequent and milder.

Case 2

A 2-year-old boy had a 10-month history of flushing and sweating of the right hemiface. During pregnancy, his mother received methadone. He was born at full-term gestation with no prenatal or birth complications. His psychomotor development was normal. Once he started walking at 14 months of age, he experienced asymmetrical reaction with erythema of the right hemiface and sweating of the right side of the scalp, after exercise or in hot weather. The symptoms resolved spontaneously after about 30 minutes of rest. Physical examination revealed a slight narrowing of the left palpebral fissure and miosis that the mother had noticed since birth. Findings of carotid auscultation, the neurologic examination, and general examinations were otherwise normal. Brain, cervical spine, and thoracic MRI with gadolinium, including supra-aortic angiographic views, excluded a tumoral or vascular etiology. After several months of follow-up, the exertion-induced symptoms persisted with no other symptoms.

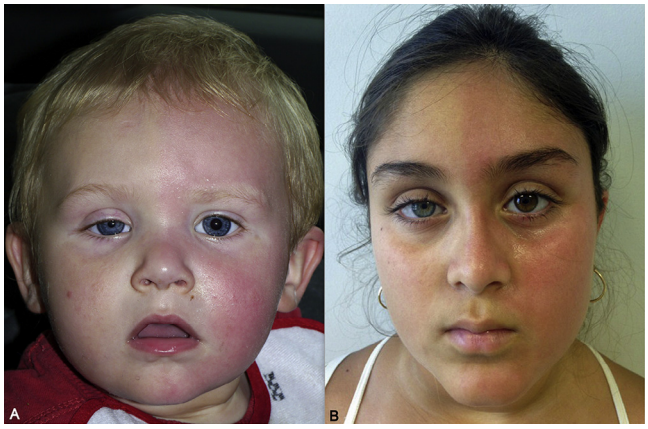

Figure 1. **A,** Patient 1. Erythema and hyperhidrosis of the left hemiface with a sharp demarcation at the midline (Harlequin syndrome), associated with obvious right miosis, ptosis, and enophthalmos (Horner syndrome). **B,** Patient 3. Clear-demarcated vasomotor erythema and sweating of the left hemifacial at heat with right Horner syndrome and heterochromia iridis.

MRI	Magnetic resonance imaging

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Case 3

A 10-year-old girl was referred to the dermatology service for flushing and sweating of the left hemiface, which was noted after she started walking at the age of 18 months. She was born at full term with no obstetrical complications. Erythema and sweating episodes appeared several times a day after exercise (**Figure 1**, B), heat, or sun exposure. Episodes resolved after 1 hour of rest or in shade. Flushing was limited to the left hemiface, with no thoracic or arm involvement. She had a right Horner syndrome with enophthalmos, miosis, and ptosis. Her right iris was lighter in color than the left, consistent with heterochromia iridis, which is a common finding in congenital Horner syndrome. Findings of the physical examination were otherwise normal. Brain and cervical spine MRI with gadolinium plus angiography was normal. Although symptoms remained relatively unchanged for 8 years, the patient noticed an improvement in the past several months,

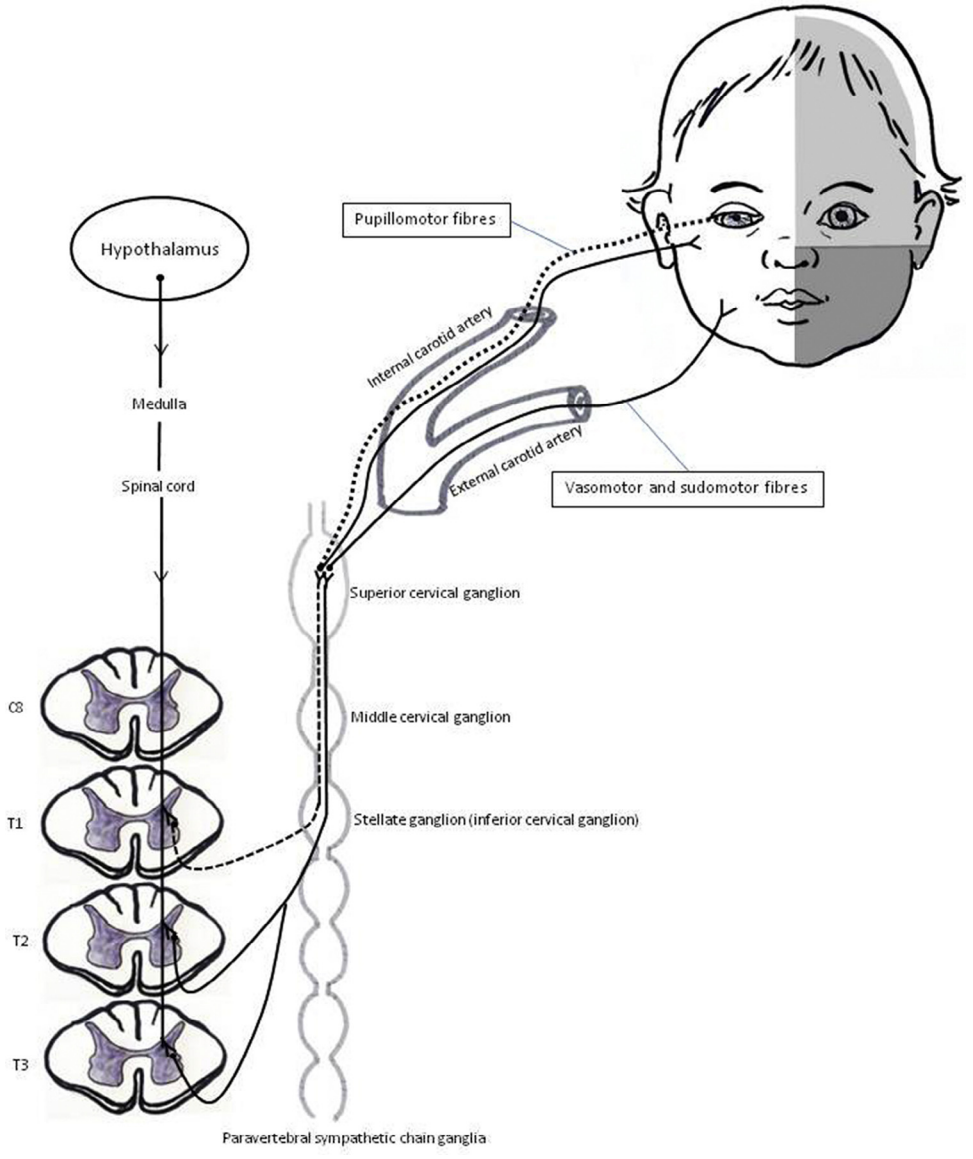

Figure 2. Schematic diagram of the sympathetic nervous system pathway of the eye and face. The sympathetic nerve pathway originates from the hypothalamus (first-order neuron) and synapse in the lateral horn of spinal cord, between C8 and T2 (second-order neurons). Second-order (preganglionic) oculomotor fibers leave the spinal cord in the first thoracic root (T1), whereas sudomotor and vasomotor fibers innervating the face leave inferiorly, at T2 and T3. These fibers then ascend along the paravertebral sympathetic chain to synapse in the superior cervical ganglion with the third-order (postganglionic) neurons. Fibers exit this ganglion in the third-order neurons and divide in rostral fibers, innervating the eye and the forehead by traveling along the internal carotid artery, and in caudal fibers to supply the lower one-half of the face, along the external carotid artery.