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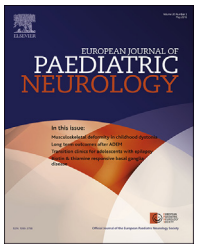

Case Study

Congenital Harlequin syndrome as an isolated phenomenon: A case report and review of the literature

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ABSTRACT

Harlequin syndrome (HS) is a rare autonomic disorder due to a hemifacial cutaneous sympathetic denervation. It is characterized by unilateral diminished sweating and flushing of the face even though after heat or prolonged exercise. It is typically acquired. Congenital cases only represent a 6% of all individuals with HS. All congenital HS cases reported so far showed a concomitant Horner syndrome, probably due to a stellate ganglion involvement. HS represents an uncommon autonomic disorder due to a hemifacial cutaneous sympathetic denervation. It is clinically characterized by a dramatic alteration in facial appearance: ipsilateral denervated pale and dry half from the other intact red and moist half. *Conclusion:* We present, to the best of our knowledge, the first case of a patient with a congenital HS as an isolated phenomenon.

1. Introduction

Harlequin syndrome (HS), first described by Lance et al. in 1988 represents an uncommon autonomic disorder due to an hemifacial cutaneous sympathetic denervation.[1,2] It is clinically characterized by a dramatic alteration in facial appearance, in

List of abbreviations: SD, Standard deviation; ESR, Erythrocyte sedimentation rate; HS, Harlequin syndrome; MR, Magnetic resonance.

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"What is known"

- Harlequin syndrome represents an uncommon autonomic disorder due to a hemifacial cutaneous sympathetic denervation.
- It is clinically characterized by a dramatic alteration in facial appearance: ipsilateral denervated pale and dry half from the other intact red and moist half.

"What is New"

- We present the first case of a patient with a congenital HS as an isolated phenomenon. Our observations indicate that congenital HS could appear without a concomitant Horner syndrome.
- To our knowledge, all congenital HS cases reported so far showed a concomitant Horner syndrome, probably due to a stellate ganglion involvement.

which a distinct line divides the ipsilateral denervated pale and dry half from the other intact red and moist half.

This bipartite facial discoloration is named harlequin syndrome after the classical character in the Italian improvisational theater, the *Commedia dell'Arte*. In the recent literature the terms harlequin syndrome and harlequin sign have been used interchangeably. Moreover, the term harlequin color change is used to describe the transient hemibody flushing often seen in premature neonates due to immadurity of the hypothalamic centers.[3]

Congenital cases represents approximately a 6% of all the HS patients.[4,5] To date it was thought that Horner syndrome was an obligatory concomitant syndrome in patients presenting a congenital HS.

We present, to the best of our knowledge, the first case of a patient with a congenital HS as an isolated phenomenon.

2. Case report

A 14-month-old male who was referred to our neuropediatric outpatient clinic due to a history of anhidrosis and pallor affecting the right side of his face which contrasted with the flushing and sweating on the left side provoked by physical exercise. Relatives noticed this peculiar pattern of facial flushing since he started to walk.

The male infant was born with spontaneous eutocic delivery at 38 weeks of gestation. He was the first child of a healthy, young Caucasian couple. Three previous first-trimester miscarriages were reported. Rest of family history was unremarkable. The pregnancy history was normal and there was no known exposure to teratogens during pregnancy. The infant's birth weight was 2942 g, length was 50.5 cm and head circumference was 33.5 cm (p39, −0.29 SD). All within the standard range (10th–90th centile) for male Spanish neonates. His psychomotor development was normal. His medical history was uneventful. He did not use any medication.

On examination at rest no asymmetric facial flushing or sweating was noted. Blood pressure and heart rate were normal for his age. Neurological examination did not reveal any other abnormalities. Cranial nerves, deep tendon reflexes of extremities, and pupil responses were normal. Signs of ptosis were absent.

After physical exercise, progressive flushing and profuse sweating was seen on the left side of his face. The right side of his face remained pale and anhidrotic (Fig. 1). No asymmetric patterns were present on the upper limbs or chest. The clinical picture was compatible with the HS.

His hemogram, glucose, electrolytes, ESR, renal, hepatic and thyroid function were normal as well as chest radiograph, cranial, cervical and thoracic spine MR, and MR angiography of the circle of Willis and vertebrobasilar circulation.

Ophthalmologic examination at the age of 3 revealed an physiological anisochoria of 0.4 mm. It was identified as physiological since the difference between pupils was less than 1 mm, it was not more exacerbated in the dark than in light, and both pupils reacted normally to light stimulation: after a light stimulus, the pupils returned to their original darkness diameter in less than 8 s. Visual acuity and pupillary reflexes were normal in both eyes.

After being diagnosed with HS, the family's concerns were relieved by explaining the benign nature of the condition. The patient is currently 7 years-old. Symptoms have remained unchanged, showing right-sided anhidrosis and pallor even though after prolonged exercise (Fig. 1).

Ophthalmologic evaluation was completed at the age of 7. Autonomic pupillary function was assessed with pupillography and pharmalogical testing with topical apraclonidine. Horner syndrome was not detected: pupillary dilation lag in the dark was absent and the apraclonidine test was negative.

3. Discussion

This patient represents an example of probable congenital HS. We assume that it is a congenital phenomenon as the clinical picture was noted as soon as the patient acquired ambulation and started to sweat profusely. He had never practiced physical exercise before and he had never shown a so generous sweating so it is unlikely that a congenital HS would be noted previously. Moreover, he was born after a non-instrumental delivery, no trauma history was reported and no structural underlying lesions could be found.

Localization of the lesion in HS must be based on both the patient's clinical history and his constellation of symptoms.[6,7] The site of the pathology can be anywhere along the sympathetic outflow to the face (Fig. 2). The first neuron of the sympathetic fibers begins in the posterior hypothalamus, traverses the midbrain and reticular substance of the pons, and ends in the anterior lateral gray substance of the spinal cord. It synapses somewhere between C8 and T2, at the ciliospinal center. The second neuron (preganglionic fibers) leaves the spinal cord at T2–T3 and synapse with the third neuron (postganglionic fibers) in the superior cervical ganglion. Postganglionic fibers that supply the medial forehead