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### Authors

Kaur, Sarabjit  
Aggarwal, Parul  
Jindal, Nidhi  
[et al.](#)

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**Photo vignette**

**Harlequin syndrome: a mask of rare dysautonomic syndromes**

**Sarabjit Kaur MD<sup>1</sup>, Parul Aggarwal MBBS<sup>1</sup>, Nidhi Jindal MD<sup>1</sup>, Surabhi Dayal MD<sup>1</sup>, Dr. Vijayeeta Jairath MD<sup>1</sup>, Vijay Kumar Jain MD<sup>1</sup>, Sunny Viridi MD<sup>2</sup>**

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**<sup>1</sup>Department of Dermatology, Venereology and Leprology , Pt. BDS PGIMS, Rohtak, Haryana, India.**

**<sup>2</sup>Department of Pulmonary and Critical Care Medicine, Pt BDS PGIMS, Rohtak, Haryana, India.**

**Correspondence:**

Dr.Sarabjit Kaur  
House no 401, sector 14, first floor, Rohtak  
Haryana, India  
drsarabjit14@yahoo.com  
08221935374

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**Abstract**

Harlequin syndrome (HS) is a rare disorder of the sympathetic nervous system which presents with unilateral decreased sweating and flushing of the face, neck, and chest in response to heat, exercise, or emotional factors. The contralateral side displays a compensatory overreaction to provide normal heat regulation of the face as a whole. In the literature, most of the cases are primary in nature and no underlying cause could be identified. Harlequin sign is used to denote these symptoms in patients who also exhibit associated oculosympathetic paresis, such as Horner syndrome, Adie syndrome, and Ross syndrome.

We report a rare case of a 13-year-old boy who presented with complaints of flushing and sweating of the left side of the face after exertion, while the right side remained dry and maintained its normal color. No structural abnormality was identified on detailed work up. Thus, diagnosis of classic idiopathic HS was made. Despite the rarity of this syndrome, dermatologists should be acquainted with this distinctive entity and should refer the patient for complete ophthalmological and neurological examination.

**Key words: Harlequin syndrome, unilateral hyperhidrosis, Horner syndrome.**

**Introduction**

Harlequin syndrome is a rare and dramatic condition in the category of the dysautonomic syndromes. It is characterized by asymmetric sweating and flushing of the face, neck, and sometimes upper thoracic region in response to heat, exercise, or emotional factors [1]. HS is mostly a primary or idiopathic condition, but can also be secondary to organic lesions or iatrogenic causes. Lance et al first described and named it based on resemblance of HS discoloration to colorful harlequin masks [1]. This analogy is also used to describe a severe form of congenital ichthyosis and these entities must not be confused. The term, Harlequin color change has also been applied in newborns to describe vasomotor instability (flushing of the dependent half of the body) [2]. Occasionally patients with HS also show other associated autonomic syndromes of oculosympathetic paresis, such as Horner syndrome, Adie syndrome, and Ross syndrome, referred as harlequin sign [3].

**Case synopsis**

A 13-year-old boy presented to the outpatient department of dermatology with complaints of 2 years of flushing and sweating of the left side of the face on prolonged physical exercise and during emotional stress (Figure 1). During these episodes, the

right side of the face remained dry and maintained its normal color. No history of migraine or cluster headache was present. No birth problems were identified. There was no history of undergoing any surgical procedure. There was no significant medical history. On examination, no asymmetric sweating and flushing was noted at rest. His vitals were normal. The unilateral flushing and sweating of the left side of the face was reproduced by asking the patient to climb upstairs and downstairs for 5 minutes. An iodine starch test clearly delineated the affected area (Figure 2).

Neurological and ophthalmological examination revealed no signs of ptosis or miosis and tendon reflexes were normal. Routine hematological and biochemical investigations were normal. Thyroid function tests were within normal limits.

Chest radiography, duplex ultrasonography of carotid arteries, and computerized tomographic scan of head and neck, thorax, and spinal cord revealed no underlying structural lesions.

The clinical picture was compatible with primary harlequin syndrome. The patient was reassured and counseled about the benign nature of his condition.



**Figure 1.** Unilateral hyperhydrosis of the left side of the face. **Figure 2.** Iodine starch test highlighted the affected area.

## Discussion

Harlequin syndrome was first described by Lance and Drummond in 1988. The name was inspired by the resemblance of patients' half-flushed faces to colorful harlequin masks used by the character of the classical Italian theatre, Comedia dell' Arte. The asymmetric sweating and flushing of skin may also involve the neck and upper thoracic region besides the face [1]. Women are commonly affected and social embarrassment is the chief factor in seeking medical advice [4]. Although HS is mainly primary or idiopathic, the condition can also relate to organic or iatrogenic causes (Table 1) [3,8]. In the case of organic lesions, the symptoms do not always resolve after surgical resection. The iatrogenic causes (medications and intraoperative trauma), on the other hand, are mostly temporary and except for cases secondary to sympathectomy, the symptoms generally resolve within a few hours [3].

The etiology of axonal damage in primary/idiopathic harlequin syndrome is yet to be elucidated. Occlusion of the anterior radicular artery at the third thoracic segment during strenuous exertion, microvascular ischemia, an autoimmune process, or an infective agent are the proposed mechanisms [2]. In our case this could be the possible etiology as no underlying

secondary lesion was detected. Primary HS can also be congenital with Horner syndrome which presents as a concomitant syndrome [5].

**Table 1.** List of causes of HS

<b>Primary or idiopathic</b>	
<i>No cause is identified</i>	
<b>Secondary</b> <sup>[3]</sup>	
<i>Organic lesions</i>	<i>Iatrogenic causes</i>
<ul style="list-style-type: none"> <li>• Mediastinal neurinomas</li> </ul>	<ul style="list-style-type: none"> <li>• Paravertebral thoracic blocks</li> </ul>
<ul style="list-style-type: none"> <li>• Cervical syrinx</li> </ul>	<ul style="list-style-type: none"> <li>• Jugular vein catheterization</li> </ul>
<ul style="list-style-type: none"> <li>• Intramedullary astrocytoma</li> </ul>	<ul style="list-style-type: none"> <li>• Resection of a neck mass</li> </ul>
<ul style="list-style-type: none"> <li>• Thoracic neurofibroma</li> </ul>	<ul style="list-style-type: none"> <li>• Thoracic sympathectomy</li> </ul>
<ul style="list-style-type: none"> <li>• Left apical lung cancer</li> </ul>	<ul style="list-style-type: none"> <li>• Surgical trauma</li> </ul>
<ul style="list-style-type: none"> <li>• Medullary infarction</li> </ul>	<ul style="list-style-type: none"> <li>• Neuropraxia</li> </ul>
<ul style="list-style-type: none"> <li>• Compressed thyroid artery</li> </ul>	<ul style="list-style-type: none"> <li>• Pharmacological blockade of the neural transmission</li> </ul>
<ul style="list-style-type: none"> <li>• Brachial plexopathies</li> </ul>	
<ul style="list-style-type: none"> <li>• Spontaneous dissection of cervical carotid artery</li> </ul>	
<b>Other causes</b> <sup>[8]</sup>	
<ul style="list-style-type: none"> <li>• Guillain-Barre syndrome</li> </ul>	
<ul style="list-style-type: none"> <li>• Pure autonomic failure</li> </ul>	
<ul style="list-style-type: none"> <li>• Multiple system atrophy</li> </ul>	
<ul style="list-style-type: none"> <li>• Diabetic neuropathy</li> </ul>	

An understanding of the anatomy and functioning of the autonomic nervous system is required to predict the possible sites of neural affection. The absence of Horner syndrome in our case indicates the pathology to be in the preganglionic (between the stellate and superior cervical ganglion) or the postganglionic sudomotor and vasomotor sympathetic fibers originating in the second and third thoracic levels of the spinal cord [6]. The sympathetic neural damage is present on the non-flushing/sweating side. The excessive flushing of the other side of the face, which earlier was considered to be the pathological site, is now understood to be a compensatory over-reaction [7].

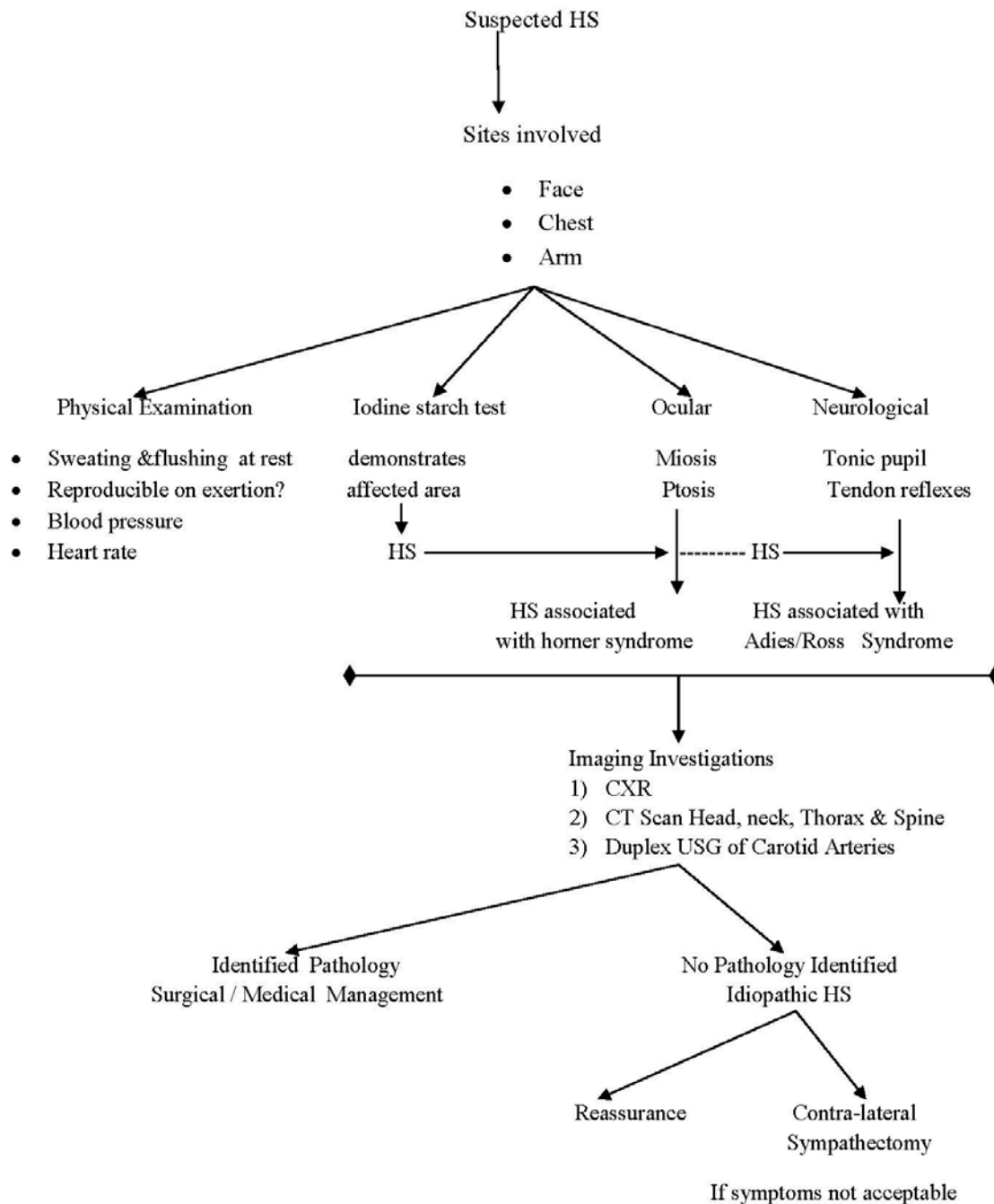
The harlequin sign must be considered in the differential diagnosis. The co-existence of HS and Horner syndrome - a triad of ptosis, miosis, and anhidrosis, suggests pathological lesions of the superior cervical ganglion. The combination of HS with Adie syndrome/Ross syndrome- triad of tonic pupils, hyporeflexia, and segmental anhidrosis, implicates an abnormality of postganglionic cholinergic parasympathetic and sympathetic fibers projecting to the iris and sweat glands [3]. Another consideration, that of unilateral hyperhidrosis, the Frey syndrome, is characterized by recurrent episodes of facial flushing and/or sweating, limited to the cutaneous distribution of the auriculotemporal nerve in response to gustatory stimuli [9].

Thus, a definite diagnosis of primary harlequin syndrome can be considered after excluding the structural and iatrogenic causes. Its benign nature that does not require treatment must be clearly explained to the patients. There is generally no need for follow-up visits. To alleviate severe social embarrassment, contralateral sympathectomy can be considered to interrupt facial flushing. However, side effects like compensatory flushing and sweating of other parts of the body must be kept in mind. To make it more comprehensible, the management algorithm of HS has been presented in the flow chart [6].

## Conclusion

This case report emphasizes that any patient presenting with a unilateral decreased or increased sweating and flushing of the face, should undergo a complete ophthalmological and neurological examination. Detailed history and imaging investigations should be done to detect any hidden underlying pathology. Also, considering the anxiety that this syndrome can cause, patients with idiopathic disease must be counseled about the benign nature.

### Flow chart. Management algorithm in patients of HS



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