

## NEUROLOGICAL RARITY

# Harlequin syndrome

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Arlecchino (Harlequin) was a character in the travelling improvisational theatre originating in Venice in the 16th century, known as *Comedia Dell' Arte*. This remained popular until the 18th century, but many of the characters are still recognizable today – Columbine, Pagliacci and Pulcinella, a woman-chasing hunchback who was the forerunner of Punch. The first Harlequin masks were grotesque and the term Harlequin syndrome was therefore applied to a severe form of congenital ichthyosis with rudimentary ears, ectropion and 'fish mouth' appearance. But later, Harlequin masks became less sinister and more sophisticated with diamond-shaped colourful patterns, or blackening of one half of the face (Fig. 1). This appearance came to mind when my colleagues and I observed five patients who flushed and sweated excessively on one side of the face in hot weather, or after exercise, particularly obvious when the sweating area was demonstrated by the application of alizarin powder (Fig. 2) (Lance *et al.* 1988). Although the term 'Harlequin colour change' had been applied by paediatricians to vasomotor instability in the newborn, causing flushing of the dependent half of the body, it was difficult to avoid evoking the name of Harlequin again when we described the sudden onset of hemi-facial flushing and sweating, one of the most dramatic and colourful of the autonomic disorders.

The question arose 'which is abnormal – the red side or the pale side?' The history of one of our patients gave a clue because her problem started at the age of 58 years while she was walking in the sun with her daughter and grandchildren. She experienced sudden vertigo after which the left side of her face immediately became red and sweaty and her right eyelid drooped as part of a Horner's syndrome.

We were aided in our interpretation by parallel studies by which we demonstrated that the sympathetic outflow to facial

vessels contained vasodilator as well as vasoconstrictor fibres. In patients with unilateral lesions of the sympathetic pathway there was often flushing at first from the release of vasoconstrictor tone but heating then caused the intact side to become red and increase in temperature while the denervated side remained at the previous temperature (Fig. 3). It thus became clear that our patient described above had suffered a limited



Figure 1 Harlequin.



**Figure 2** Harlequin syndrome. Sweating on the right half of the face delineated by the application of alizarin powder. From Lance *et al.* (1988) by permission of the publisher of *Journal of Neurology, Neurosurgery and Psychiatry*.



**Figure 3** Absence of thermoregulatory facial flushing on the right side of the face after cervical sympathectomy. From Drummond & Lance (1987); by permission of the publisher of *Brain*.

lateral medullary infarct with a right Horner's Syndrome and a right facial sympathetic deficit. Because she had a naturally pale skin, being of Dutch ancestry, her affliction was a great embarrassment to her, causing her to stay indoors during the warm Australian summer. In her case, a surgical lesion of the cervical sympathetic on the flushing side proved to be the answer and the resulting ptosis matched the other side, an appearance not unbecoming.

Our other four patients were different because there was no obvious Horner's syndrome, indicating that the sympathetic lesion was localized to those fibres emerging from the spinal cord with the second or third thoracic roots, as ocular sympathetic fibres leave via the first thoracic root. There were two women aged 39 and 73, years and two men aged 29 and 42 years. In all cases the unusual facial appearance was observed after exposure to heat such as gardening, working strenuously in the sun, or exercise such as playing squash. Because squash had precipitated the onset in three of these four patients we entertained the notion that the anterior radicular artery at the third thoracic segment may have been occluded by torsion of the thoracic spine during a hard-fought match. To throw some light on this we studied the latency from stimulation of the motor cortex and the thoracic spinal cord to the third intercostal muscle, but this was delayed in only one patient.

A later investigation (Drummond & Lance 1993) showed supersensitivity of one or both pupils to the constrictor effect of a

dilute solution of pilocarpine (0.0625%) as well as excessive dilatation to 1% phenylephrine eye drops, indicating that there was a partial ocular parasympathetic lesion as well as a subclinical pupillary sympathetic deficit in 3 out of 4 of our patients with Harlequin syndrome. This suggested the diagnosis of an acute autonomic neuropathy in these instances, inviting comparison with Holmes–Adie syndrome, Ross's syndrome (with additional segmental anhidrosis) and the persistent autonomic defect which occasionally follows the Guillain–Barré Syndrome.

Magnetic resonance imaging in our patients showed no abnormality of the upper thoracic spine but Harlequin syndrome has been described with a superior mediastinal neurinoma at the level of the third thoracic vertebra, transiently after removal of a cystic mass from the

neck of a 2-year-old child, and after internal jugular vein catheterization in an adult. One author stated that the syndrome 'usually results from interruption of postganglionic sympathetic fibres secondary to malignant invasion' but this has not been our experience. It has been reported as an accompaniment of a congenital Horner's syndrome in 4-month-old and 7-year-old boys. It does of course result from surgical division of the second and third thoracic roots, or thoracoscopic sympathectomy for facial hyperhidrosis.

In summary, Harlequin syndrome results from compromise of vasomotor and sudomotor sympathetic nerve supply to one side of the face with over-reaction, presumably compensatory, of the corresponding fibres on the intact side. If a Horner's syndrome is not apparent, the cause must be sought in the preganglionic or postganglionic sympathetic fibres at the second and third thoracic levels of the spinal cord. If the onset is sudden and a structural lesion has been excluded, then probably the diagnosis is a restricted autonomic neuropathy with a benign prognosis.

## REFERENCES

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