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Review

Unnoticed dysautonomic syndrome of the face: Harlequin syndrome

Nida Tascilar [a,*], Nilgün Solak Tekin [b], Zuhal Erdem [c], Atilla Alpay [d], Ufuk Emre [a]

[a] *Department of Neurology, Zonguldak Karaelmas University Medical Faculty, Zonguldak, Turkey*
[b] *Department of Dermatology, Zonguldak Karaelmas University Medical Faculty, Zonguldak, Turkey*
[c] *Department of Radiology, Zonguldak Karaelmas University Medical Faculty, Zonguldak, Turkey*
[d] *Department of Ophthalmology, Zonguldak Karaelmas University Medical Faculty, Zonguldak, Turkey*

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Abstract

Harlequin sign and harlequin syndrome, which are used interchangeably in the literature, are characterized by sudden onset of hemifacial sweating and flushing, induced by exercise and heat. Hemifacial sweating and flushing with normal ocular sympathetic innervation, known as harlequin syndrome, is rarely associated with tonic pupils, parasympathetic oculomotor lesion and pre- or postganglionic sudomotor sympathetic deficit. In the literature, hemifacial sweating and flushing in patients with apparently abnormal ocular sympathetic innervation has been defined as harlequin sign. To date, a few reports of excessive hemifacial sweating and flushing in structural lesion have been documented. Herein, we report five patients with excessive hemifacial sweating and flushing, two of whom had a syrinx. In presenting the patients, we have attempted to distinguish harlequin syndrome from harlequin sign. With this in mind, Case 1 can be described as harlequin syndrome resembling Ross syndrome, Case 2 as harlequin syndrome with normal ocular sympathetic innervation, Case 3 as harlequin sign with congenital Horner syndrome, Case 4 as harlequin sign with sympathetic and parasympathetic denervation sensitivity, and Case 5 as harlequin syndrome associated with occult sympathetic denervation sensitivity. These cases are discussed together with a review of the literature.

Keywords: Harlequin sign; Harlequin syndrome; Horner syndrome; Syringomyelia; Autonomic nervous system

Contents

* Corresponding author. Fatih sitesi Hizmet Yapı Koop. Kat:4 No:9, Kozlu Zonguldak, 67600 Turkey. Tel.: +90 3722667375; fax: +90 3722610155.
E-mail address: doga24@yahoo.com (N. Tascilar).

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1. Introduction

Harlequin syndrome (HSD) is the sudden onset of unilateral flushing and sweating in adults and was first described by Lance et al. (1988) (Turco and Farber, 1996). HSD is an autonomic syndrome of heat-, emotion- and exercise-induced flushing and sweating on the contralateral side of the face or arm, or both, with normal ocular sympathetic innervation (Turco and Farber, 1996; Carroll and Zajicek, 2004; Drummond and Lance, 1993). However, it has been reported recently that it might also present with tonic pupils, parasympathetic oculomotor lesion and pre- or postganglionic sudomotor sympathetic deficit (Magnifico et al., 2002).

Unilateral sweating may occur in some other disorders such as Holmes–Adie syndrome (HAS) (tonic pupil and areflexia) and Ross' syndrome (RS) (segmental anhidrosis, hyporeflexia and tonic pupils) (Drummond and Lance, 1993; Magnifico et al., 2002; Mathias, 2003; Shin et al., 2000). Hemifacial loss of sweating and flushing has also been reported in association with ocular sympathetic deficit (Horner syndrome) (Drummond and Lance, 1993). Hemifacial excessive sweating and flushing contralateral to Horner syndrome [harlequin sign (HSG)] is supposed to be a compensatory reaction to the lack of sweating on the sympathetically denervated side. In HSG, the areas that do not flush are always identical to the anhidrotic areas in Horner's syndrome (Morrison et al., 1997).

In the last 6 years, HSD had been suggested as part of a spectrum of disorders including RS and HAS (Carroll and Zajicek, 2004; Shin et al., 2000). In the literature, HSD and HSG have been used interchangeably, i.e. by Lombardi et al. (2004). Drummond and Shin reported hemifacial loss of sweating and flushing in patients with apparently normal ocular sympathetic innervation as HSD (Drummond and Lance, 1993; Shin et al., 2000). We also prefer to use HSD only in patients with apparently normal ocular sympathetic innervation. A few reports of HSG in structural lesion (multiple sclerosis, mediastinal neurinoma, and brainstem infarct, etc.) have been documented (Lance et al., 1988; Carroll and Zajicek, 2004; Noda, 1991).

We report five patients with hemifacial excessive sweating and flushing: one case of HSD resembling RS, one pure HSD, two cases of HSG in Horner syndrome possibly due to a syrinx, and one of HSD after operation. We discuss the cases together with a review of the literature.

2. Methods

2.1. Sudomotor testing

A starch-iodine preparation was applied to the whole face, chest and arms in an air-conditioned laboratory maintained at 22±1 °C in order to demarcate sudomotor function; the preparation turned blue on the side of intact sweating function, showing that sympathetic innervation to the non-sweating side was impaired (Haerer, 1992). Gustatory sweating and flushing were induced by tasting a teaspoon of hot chili sauce, which was held in the mouth for 1 min (Drummond and Lance, 1993). After the routine sudomotor testing, in order to determine whether the non-sweating side remained anhidrotic, facial flushing and sweating after vigorous exercise (stair climbing or jumping for about 20 min) was also tested in all patients.

2.2. Pharmacologic studies

The pharmacologic tests were applied on separate days. The patients were examined in a semi-dark room, sitting 56 cm away from the focus of the camera, with their gaze at a distant point and the observer off to one side. The photographs were then taken in dim light (2 lux) and in moderate bright light (153.5 lux) at baseline and 40–45 min after the instillation of the drug. Pupil diameter was later measured from the film negative magnified six times by ruler.

Parasympathetic innervation of the pupils was investigated through administration of a single drop of a dilute (0.125%) solution of pilocarpine in each eye in dim light. An absolute pupillary constriction of 1.5 mm or greater was considered abnormal (Shin et al., 2000). Dilute pilocarpine causes constriction of denervated pupils only and thus tests the integrity of parasympathetic innervation (Drummond and Lance, 1993; Shin et al., 2000).

1% phenylephrine eyedrops were used to investigate pupillary sympathetic activity in moderate bright light. Phenylephrine stimulates postjunctional α-adrenergic receptors, and in dilute solutions tests for sympathetic denervation supersensitivity (Drummond and Lance, 1993). Dilatation of more than 1.0 mm was considered abnormal according to the normal values of the ophthalmology clinic of our university.

2.3. Electrophysiologic studies

Sympathetic skin response (SSR) was recorded from both hands and soles by the delivery of 1 ms, high-current painful electric stimulus at an intensity of 30 mA by surface stimulating electrodes from the median nerves. An absent response was considered abnormal (Shin et al., 2000).

2.4. Heart rate response

As a marker of autonomic modulation of the heart, heart rate variability (HRV) was used. Analysis of HRV is a simple, non-invasive method to evaluate the sympathovagal balance (Sztajzel, 2004). HRV can be measured on the basis of 24-hour Holter recordings or on shorter periods ranging from 0.5 to 5 min, particularly in the field of dynamic electrocardiography. Measures of HRV in our patients by 24-hour Holter ECG showed similar results with healthy age-matched controls of the cardiology clinic of our university.