

CASE REPORT

Chlorpromazine and Horner's Syndrome

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Abstract

Horner's syndrome is characterized by an interruption of the sympathetic nerve pathway somewhere between its origin in the hypothalamus and the eye. We describe a case of Horner's syndrome in a 13-year-old girl during chlorpromazine therapy. Phenothiazines are strong α -adrenergic antagonists with consequent inhibitory action on sympathetic innervation. The low daily dose, 40 mg, suggests a complex etiology (German J Psychiatry 2005; 9: 33-35).

Keywords: Horner's syndrome, oculosympathoparesis, quetiapine, chlorpromazine, adrenergic alpha-receptors

Received: 15.5.2005

Revised version: 2.10.2005

Published: 13.1.2006

Introduction

Horner's syndrome is characterized by an interruption of the sympathetic nerve pathway somewhere between its origin in the hypothalamus and the eye. V.A., a thirteen-year-old girl, was admitted to our adult psychiatric unit due to increasingly disruptive behavior and panic attacks. In a previous admission to a child psychiatry unit, one month before, she had been started on a treatment with chlorpromazine 40 mg per day.

This treatment was not effective on symptomatology, and the patient showed progressively increasing ptosis, subtle anisocoria of the left eye and loss in eyelid crease of the right eye. On admission to our unit, there was conjunctival hyperemia of the left eye and dilation lag too. Laboratory tests, EEG, chest radiography and brain computed tomography (CT) scan were normal.

An ophthalmologic consultant diagnosed Müller's muscle paralysis, complete on the left and partial on the right.

Substitution of chlorpromazine with quetiapine gave fast remission of symptomatology. We consider this case to be exemplary of motor action of sympathetic innervation and how this can be affected by psychopharmacologic treatments.

Signs and Symptoms

In Horner's syndrome we find blepharoptosis owing to denervation of the sympathetically controlled Müller muscle. Müller's muscle acts as an accessory elevator of the upper eyelid, and loss of sympathetic input results in subtle ptosis and lower eyelid retraction, due to interest of analogous unnamed muscle. Paresis of Müller's muscle may lead to the loss of the upper lid crease. Enophthalmus is apparent due to combination of an often subtle upper eyelid ptosis with lower eyelid retraction that can result in narrowing of the interpalpebral fissure (Walton & Buono, 2003, Daroff 2005). Miosis and subtle anisocoria results from the imbalance of dilation and constriction forces from the sympathetically innervated iris dilator muscle and the parasymphatically innervated iris constrictor muscle.

We can find also slower pupil dilatation compared with the normal contralateral. Iris heterochromia occasionally accompanies Horner's syndrome, particularly in congenital lesions. The etiology of iris heterochromia in Horner's syndrome has not been firmly established; however, some investigators have suggested that postganglionic lesions in the sympathetic chain may disrupt the neurotrophic development of iris melanocytes.

In the acute phase of Horner's syndrome we find conjunctival hyperemia as a result of the loss of the vasoconstricting effects of sympathetic innervation (Walton & Buono, 2003).

Pathophysiology

The anatomic substrate for sympathetic innervation to the eye and ocular adnexae consists of a three neuron arc. First-order fibers descend from the ipsiposterolateral hypothalamus. There are probably some synapses in the brainstem at the level of the pons, but most of the fibers descend uncrossed to the synapse in the ciliospinal center of Budge-Waller, located in the intermediolateral columns of the spinal cord at the level of C8 to T2 (Walton & Buono, 2003, Marx et al. 2004). There, it synapses with second-order preganglionic pupillomotor fibers and exits the spinal cord at the level of T1. In close proximity to the pulmonary apex and the subclavian artery, second-order neurons synapse in the superior cervical ganglion, located between the internal jugular vein and the internal carotid artery (C3-C4).

Postganglionic pupillomotor fibers exit the superior cervical ganglion and ascend along the internal carotid artery.

The fibers responsible for sweat and piloerection of the face follow the external carotid artery. The pupillomotor fibers enter the skull base through the carotid canal and travel through the middle cranial fossa into the cavernous sinus.

The sympathetic fibers join the ophthalmic division of the trigeminal nerve on its course into the orbit, part of the sympathetic fibers follow the course of the nasociliary nerve through the superior orbital fissure. Other fibers pass through the ciliary ganglion, and via the short ciliary nerves, divide and innervate various anatomic structures: the middle ear, the orbital vasomotor fibers, the dilator muscle of the pupil, the accessory levator muscle of the upper eyelid (Müller's muscle) and its analog in the lower eyelid, and the lachrymal gland.

Causes

Frequently, Horner's syndrome results from a central, preganglionic or postganglionic lesion. Central Horner's syndrome is found in a small percentage of patients. Causes of central lesions are cancer, vascular lesion demyelinating disease, and trauma. Preganglionic lesions are caused by cancer, in particular Pancoast apical lung tumor, trauma, like birth trauma with injury to the lower brachial plexus, aneurysm or dissection of aorta, surgical lesion, central venous catheterization, radical neck dissection, thyroidectomy, carotid angiography, coronary artery bypass graft, chest tubes, and lymphadenopathy. Postganglionic lesions are caused by cancer, trauma, inflammation, cluster or migraine headaches, carotid cavernous fistula, internal carotid artery dissection, thrombosis or aneurysm (Walton & Buono 2003). Horner's syndrome can have a pharmacological aetiology involving central, preganglionic and postganglionic effects. In particular, phenothiazines including chlorpromazine, alkaloid extracted from rauwolfia, antihypertensive drugs like guanethidine and anesthetics like bupivacaine and lidocaine (Mathias 2003).

Discussion

In the described case, clinical enquiries did not show any pathology and suggested a pharmacological etiology. How-

ever, there are no reports in the literature specifically on chlorpromazine and Horner's syndrome, although Horner's syndrome related to phenothiazines is well documented, due to α -adrenergic antagonist activity with consequent strong inhibitory activity on sympathetic innervation (Fraunfelder 1996). Chlorpromazine replacement with quetiapine achieved remission of symptoms, which is plausible, considering that chlorpromazine K_i for α_1 receptor is 0,28 versus 22 for quetiapine. (PDSP 2005). In the described case, the symptoms occurred at a very low daily dose (40mg), considering that the usual daily dosage may vary from 300 mg to 600 mg per day and doses of up to 1000 mg per day are uncommon but possible (Hales & Yudofsky 2003). Though, in the literature, chlorpromazine sympathetic side-effects are not related to plasma concentration and the pharmacokinetic profile of chlorpromazine is less linear, compared to quetiapine, the daily dose seems too low to explain the symptoms satisfactorily (Midha et al. 1989; Chetty et al. 1999; DeVane 2001; McConville et al. 2000; Hirsch et al. 1996). A subjective sympathetic hypersensitivity due to young age or a hidden local cause, possibly an inflammatory process of the lid, brought to a head by chlorpromazine therapy, would seem to be a more exhaustive explanation (Sieb & Hartmann 2000; Petzold et al., 2001).

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