

# HERPES ZOSTER OPHTHALMICUS COMPLICATED BY COMPLETE OPHTHALMOPLEGIA AND SIGNS OF PILOCARPINE HYPERSENSITIVITY. A CASE REPORT AND LITERATURE REVIEW.

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## ABSTRACT

We report a case of zona ophthalmica complicated with a complete ophthalmoplegia. In the literature only 19 cases have been reported the last 30 years, with a variety of possible pathophysiological mechanisms. Our patient's mydriasis reacted to diluted pilocarpine 0.125% which is a sign of Adie's pupil and is not supposed to occur in mydriasis caused by a third nerve palsy. We review the literature on the possible pathogenesis of this hypersensitivity.

## SAMENVATTING

We beschrijven een casus van zona ophthalmica, gecompliceerd met een complete oftalmoplegie. In de literatuur zijn enkel 19 gevallen beschreven in de laatste 30 jaar, met verschillende mogelijke pathofysiologische oorzaken. Onze patient vertoonde een mydriase die reageerde op verdund 0,125% pilocarpine. Dit is een teken van Adie's tonische pupil en kadert niet in een N III parese. We bespreken hier de literatuur en onderzoeken de verschillende mogelijke oorzaken van deze cholinergische hypersensitiviteit.

## RÉSUMÉ

Nous rapportons un cas de zona ophtalmique compliqué par une ophtalmoplégie complète. Dans la littérature il n'y a que 19 cas décrits dans les 30 der-

nières années, avec plusieurs causes pathophysiologiques possibles. Notre patient montrait une mydriase qui réagit à la pilocarpine diluée (0,125%). Ceci est un signe d'une pupille tonique et non pas d'une paralysie du nerf oculomoteur. Nous discutons la littérature afin de déterminer les causes de cette hypersensitivité cholinergique.

## KEY WORDS

Herpes zoster ophthalmicus - Ophthalmoplegia - Pilocarpine 0.125% hypersensitivity

## MOTS-CLÉS

Herpès zoster ophtalmique - ophtalmoplégie - hypersensibilité à la pilocarpine 0,125%

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## OBSERVATION

We report the case of a 74-year-old woman who presented to our department with a vesicular cutaneous eruption in the first ophthalmic division of the trigeminal nerve on the right side of her face as well as a complete ptosis. In the general medical history an ovarian carcinoma stage 4, treated with surgery, hyperthyroidism and Alzheimer dementia were noted. There was no significant ophthalmic history. During the ophthalmologic examination we found the following:

- Vesicular cutaneous eruption in the first ophthalmic division of the trigeminal nerve on the right side of her face as well as a complete ptosis.
- Conjunctival injection, superficial epithelial keratitis and corticonuclear cataract of the right eye.
- A best corrected vision of 1/10 at the right eye and 6/10 at the left eye.
- Normal intraocular pressure and normal ophthalmoscopy.
- The mental state of the patient did not allow proper testing of the colour vision and visual fields. Only testing of the confrontational visual fields was possible, which were normal.
- An anisocoria with a pupil diameter of 5 mm in the right eye and 3 mm in the left eye under mesopic conditions. The right pupil showed no reaction to light or convergence. Instillation of a pilocarpine 0.125% solution induced miosis of the right pupil, and no reaction of the left pupil.
- A complete ophthalmoplegia of the right eye (Fig. 1).
- Flash VEP showed normal and symmetrical P1 responses. The P2 responses of both eyes

were also symmetrical but a slightly prolonged latency time was noted.

- Magnetic resonance imaging showed bilateral normal orbits and visual pathways.
- A lumbar puncture was performed and the results were consistent with a mild meningoencephalitis.

The patient was treated with intravenous acyclovir 3x600mg during 14 days, after which oral acyclovir was given in tapering doses during 1 week. Oral methylprednisolone was administered at a dose of 64mg during 4 days, after which the dose was gradually tapered over a period of 1 month. Local treatment consisted of gancyclovir ointment 5 times a day. The patient experienced improvement of her vesicular eruption after 2 weeks, but no improvement of her ophthalmoplegia, her ptosis, or her vision was observed, even 2 months after the start of the vesicular eruption. Unfortunately the patient did not attend later appointments.

When examining the difference in vision we might easily imagine that it is caused by an optic neuritis (13). The results of the flash VEP showed a normal and symmetrical P1 response of both eyes. The P2 latency time was slightly prolonged and symmetrical in both eyes, which is probably caused by cataract. Because both the right and left eye flash VEP responses occurred with a normal pattern and were perfectly symmetrical, no optic neuritis could be diagnosed at that time. The same symmetrical responses were observed when the VEP was repeated 15 days later. Although optic neuritis is a possible cause of vision loss in our patient, our tests did not clearly prove this.

We suppose that a combination of factors caused the 1/10 vision at the right eye: a cataract and the mild keratitis. The possibility of an ambly-



Fig. 1: Complete ophthalmoplegia of the right eye.

opia at the right eye exists, because of an anisometropia of 2 diopters, present at the time of examination. No earlier data about her vision could be obtained.

## DISCUSSION

In the literature there are many different hypotheses as to the pathophysiology of this ophthalmoplegia. It has been suggested that a compression of the nerves is a possible mechanism for the ophthalmoplegia in herpes zoster. According to Chang-Godinich (3) intraorbital inflammation induces an elevated pressure in the orbit, giving rise to proptosis and ophthalmoplegia. Another compression mechanism is related to the inflammation of the extraocular muscles (10). The intraorbital inflammation then leads to myositis, which in turn compresses the nerves. Both these compression mechanisms are unlikely in our patient because of the normal magnetic resonance imaging of the orbits, showing no signs of intraorbital inflammation or myositis. Although simultaneous microinfarction of the nerves could be responsible for third, fourth, and sixth nerve palsy in patients with zona ophthalmica (6), we believe that this is unlikely in our patient because of the accompanying meningo-encephalitis. There is the possibility of an orbital apex syndrome secondary to zona ophthalmica (9). Orbital apex syndrome is described as a combination of ophthalmoplegia, optic neuropathy and anesthesia in the distribution of the ophthalmic nerve. These patients often show a mild meningo-encephalitis. When there is an ophthalmoplegia in combination with anesthesia in the distribution of the ophthalmic nerve, but no involvement of the optic nerve, an orbital fissure syndrome is diagnosed (15). According to Edgerton (5) and Yong (15) it is a continuous spread of inflammation from the trigeminal nerve to the cavernous sinus and the orbital fissure that causes ophthalmoplegia. The patient described by Yong also suffered from mild meningo-encephalitis.

Considering the fact that we could not prove the existence of optical neuritis in our patient, but that a mild meningo-encephalitis was present, we believe it to be more likely that our patient suffered from the orbital fissure syndrome rather than from the orbital apex syndrome. Like

Yong, we believe that the ophthalmoplegia is more likely to be the result of perineural inflammation at a specific location, due to a spread of the virus out of the fifth cranial nerve (15). As the third, fourth and sixth nerves course closely to the fifth nerve in the superior orbital fissure it is easy to imagine these nerves to be affected by the perineural inflammation. In addition a viral infection also affects the third, fourth and sixth nerves as viral particles are emitted from the fifth nerve in the surrounding area (1). Because the optic nerve runs through the foramen opticum and is anatomically separated from the other cranial nerves, the optic nerve is not affected. It is generally accepted that herpes zoster ophthalmicus may occur with motor cranial neuropathy, with the third nerve most frequently affected and the sixth nerve least frequently affected. However, complete ophthalmoplegia is rare. Only 19 cases have been reported during the last 30 years.

We demonstrated cholinergic hypersensitivity in our patient: after instillation of 0.125% pilocarpine the affected iris sphincter contracted more than the fellow normal pupil. This is a sign of tonic pupil (Adie's pupil). The parasympathic fibers that innervate the iris sphincter synaps in the ciliary ganglion. Postganglionic fibers then provide innervation to the iris sphincter and the ciliary body. Adie's pupil is hypersensitive to low concentration of pilocarpine due to a postganglionic parasympathic denervation, which leads to an up-regulation of the receptors at the nerve - sphincter synaps (2,4). In our patient the mydriasis is not caused by a postganglionic damage but by a third nerve denervation. So why does this patient react to a diluted pilocarpine solution? Preganglionic hypersensitivity was described by Jacobson and Vierkant (8) who found no difference between 11 patients with third-nerve palsy and 11 patients with Adie's pupil for their cholinergic hypersensitivity. Several mechanisms might account for this: transsynaptic degeneration may explain cholinergic hypersensitivity (8), but this is unlikely in our patient because tests were conducted 5 days after the onset of mydriasis. Another possibility, proposed by Slamovits (12), is that a decrease in efferent input in the ciliary ganglion, caused by presynaptic damage, leads to less tonic input in the sphincter muscle. Consequently less acetylcholine is present

at the muscle synaps. Slamovits described this as a relative cholinergic denervation, which stimulates an up-regulation of the muscarine receptors at the sphincter muscle. This increase of muscarine receptors leads to cholinergic hypersensitivity. Westheimer proposed the existence of nonsynapsing axons passing the ciliary ganglion (14). This may explain the cholinergic hypersensitivity in our patient, but this theory has already been strongly criticised.

## CONCLUSION

Herpes zoster ophthalmicus may occur with motor cranial neuropathy (7), with the third nerve most frequently affected and the sixth nerve least frequently affected (1,11). However, complete ophthalmoplegia is rare. Only 19 cases have been reported during the last 30 years.

It is assumed that only patients with an Adie's pupil have cholinergic hypersensitivity. The fact that this case had a cholinergic hypersensitivity with a third-nerve palsy, which has also been reported in the literature, proves that this is not exceptional, and that the mechanism should be further investigated.

Physicians who use low concentration pilocarpine to test pupillary hypersensitivity should be aware of the fact that a denervational hypersensitivity response may occur, both in preganglionic and postganglionic parasympathetic lesions.

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