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case report

True Posterior Ischemic Optic Neuropathy Associated with Herpes Zoster Ophthalmicus

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ABSTRACT

Although previous reports of ischemic optic neuropathy resulting from herpes zoster have appeared in the literature, these reports have not been convincing of a true optic neuropathy. The case presented is a true posterior ischemic optic neuropathy due to inflammation of the medial posterior ciliary artery, diagnosed on the basis of a deep, steep-sided altitudinal visual field defect. The herpes zoster infection also resulted in retinitis, damage to the iris sphincter, and corneal scarring. The effects of herpes zoster on the visual system are reviewed.

Key Words: herpes zoster opthalmicus, ischemic optic neuropathy

The herpes zoster virus is a round DNA virus responsible for causing 1 to 2% of all dermatologic disease.[1, 2] It affects both sexes[2–4] and all racial groups with approximately equal frequency,[2] with the majority of cases occurring in middle-aged or older patients.[2–5] Children can suffer from herpes zoster infection; however, the course of the disease is usually shorter than in adults, and the pain is less severe.[1, 4] Children are most likely to contract varicella (chickenpox), a self-limited infection caused by the varicella zoster virus. Approximately 20 to 30% of these patients later develop herpes zoster infection caused by either re-exposure to the zoster virus or reactivation of the latent virus.[2, 6] Herpes zoster infection occurs more commonly in patients whose immune system has been compromised by immunosuppressive therapy, malignancy, or disease.[2]

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In adults, the herpes zoster virus shows a predilection for the thoracic, cranial, cervical, lumbar, and sacral dermatomes, in that order of frequency,[1] whereas children most often have cervical or lumbosacral involvement.[7] The most commonly involved single nerve is the fifth cranial nerve (trigeminal nerve), especially in older patients.[7, 8] Herpes zoster opthalmicus, which constitutes 7% of all herpes zoster infections, ensues when the first or ophthalmic division of the fifth cranial nerve (Gasserian ganglion) is involved. Less commonly (by a ratio of 1:20), the second or maxillary division of the fifth cranial nerve is involved,[4] and even more rarely the mandibular division.[1] It is believed that the ophthalmic division is affected more frequently than the maxillary inasmuch as the area innervated by the ophthalmic division may be more often traumatized, resulting in reactivation of the virus.[4] The herpes simplex virus commonly affects the maxillary and mandibular division, and localization of the herpes simplex virus in the portions of the ganglion that supply these two divisions may result in an "interference effect."[4]

Herpes zoster ophthalmicus most frequently involves the supraorbital and supratrochlear branches of the frontal nerve,[1, 7] resulting in the appearance of vesicles on the skin of the upper eyelid and the forehead.[1, 2] Ocular involvement is usually preceded by the appearance of vesicles on the medial aspect and tip of the nose (Hutchinson's sign), an area innervated, as is the cornea, by the nasociliary nerve.[7] Lacrimal nerve involvement is the least common.[7] Although the infection is generally limited to a single sensory nerve, a transient viremia may cause isolated vesicles in scattered areas of the body.[7]

The onset of herpes zoster ophthalmicus is usually marked by fever, malaise, nausea, and headache.[1, 3, 4, 7] This is followed 1 to 2 days later by neuralgic pain, due to the acute swelling and inflam-

mation of the nerves,[1] and 2 to 3 days later by edema and hyperesthesia of the affected dermatome.[1, 3, 4] In rare cases there is no pain.[4] A preauricular or submandibular lymphadenopathy tends to occur early in the course of the infection if there is ophthalmic or maxillary branch involvement.[3, 4]

Eventually groups of erythematous papules break out along the affected nerve at irregular intervals.[4] The papules form into vesicles, which contain clear fluid for 3 to 4 days, and then become turbid and yellow due to infiltration by leukocytes.[1, 3, 4] The zoster virus can be cultured from the papules or clear vesicles.[7] Ten to twelve days after the onset of the disease, the vesicles become crusty and dry.[7] Scarring is common because of deep involvement of the dermis[4, 7] and frequent secondary infection with *Staphylococcus aureus*.[4]

Scarring and pitting of the forehead and eyelid tends to be more severe than lesions from herpes zoster occurring elsewhere on the body.[7] Scarring of the lids may lead to cicatricial entropion or ectropion, trichiasis, loss of eyelashes, or poliosis.[2, 4, 7] Exposure keratitis may develop in association with cicatricial retraction of the upper lid.[9] Dacryoadenitis and canaliculitis are rare complications.[2, 4]

Herpes zoster involvement of the ophthalmic and maxillary divisions is accompanied frequently by infiltrative conjunctivitis and hyperemia.[1, 4] Usually papillary in nature, the conjunctivitis may also be follicular or involve the formation of pseudomembranes.[1, 4]

Corneal involvement is common if the nasociliary nerve is affected,[4] with keratitis occurring in some 40% of patients.[1] The corneal lesions tend to develop after the onset of the skin lesions and are usually characterized by a punctate epithelial keratitis.[6, 9] Epithelial keratitis may occur with or without stromal edema and cellular infiltration.[1, 4, 9] The stromal opacities are usually distributed in the superficial stroma just under Bowman's layer.[9] The interstitial inflammation may induce corneal neovascularization[1, 4] and cholesterol-like deposits, resulting from abnormal metabolism of injured keratocytes or deposited by the bloodstream, may induce further corneal opacification.[4]

The epithelial keratitis may also take the form of a dendrite. Although dendrite formation is commonly associated with herpes simplex, the dendrite of herpes zoster is usually slightly more elevated and does not have the knobs at the ends of the dendrite, which are typical of their appearance in herpes simplex keratitis.[4] Disciform keratitis may also occur 1 to 9 months after acute herpes zoster ophthalmicus and is believed to be due to a delayed hypersensitivity reaction.[9] It is characterized by a large, round, central opacity caused by corneal edema and folds in Descemet's membrane, and is associated usually with deep corneal vascularization and severe corneal scarring.[4]

Neurotrophic keratitis often develops, resulting in corneal thinning, scarring, and perforation.[9] With herpes zoster keratitis corneal sensation is usually severely reduced, may remain so for 6 to 12 months after the episode,[1, 4] and is often diminished permanently.[4]

Next to the cornea, the anterior uveal tract is the most frequently affected structure[1, 3] with iridocyclitis occurring in approximately 40% of herpes zoster patients.[7] The anterior uveitis is generally accompanied by keratitis and/or scleritis,[1, 4, 7] the iritis is characterized by photophobia, ciliary flush, miosis, intense ocular pain, decreased vision, fine keratic precipitates, iris hyperemia, and peripheral anterior and posterior synechiae formation.[1, 4, 7, 10] With the keratic precipitates, cells, and flare in the aqueous, in severe cases there may be anterior chamber hemorrhage or hypopyon.[1, 4, 7] The iritis is usually self-limiting, lasting from 6 to 12 months.[4] Herpes zoster vasculitis may lead to sectorial iris atrophy with damage to the sphincter, and minimal stromal damage.[1, 4, 5, 7, 10, 11] Heterochromia iridis,[1] sympathetic ophthalmia,[1, 3] or phthisis bulbi may result from a severe anterior segment ischemia.[1, 4, 7]

Initially hypotonia may be seen with herpes zoster because aqueous production is decreased by the inflammed pars plicata.[1, 11] However, secondary glaucoma frequently ensues because of the decreased aqueous outflow resulting from the accumulation of pigment and cellular debris in the trabecular meshwork, acute trabeculitis, and/or angle closure resulting from the formation of synechiae.[1, 4, 7, 12] The glaucoma is characterized by pupillary dilatation, pericorneal injection, and intense deep pain.[4]

A diffuse scleritis may be associated with the keratitis or iritis, or more rarely a nodular scleritis may occur 2 to 3 months after the onset of the disease.[1, 3, 4, 8] The nodules, which are small and painful, resolve slowly, frequently leading to scleral thinning and staphyloma formation.[1, 4, 8] Less common is a diffuse or localized posterior scleritis.[7]

The severe ocular abnormalities seen in some patients with herpes zoster are due to direct viral invasion and a granulomatous or nongranulomatous inflammation and ischemia secondary to vasculitis.[7, 11, 13]

Choroiditis and retinitis are seen occasionally, and may be associated with vitreous opacities, occlusion of the central retinal artery or vein, and partial or complete retinal detachment.[1, 4, 7, 11, 14] Recently herpes zoster virus has been implicated as one of the causative agents of the acute retinal necrosis syndrome, a devastating visual disorder characterized by retinal arteritis, necrotizing retinitis, vitritis, and rhegmatogenous retinal detachment,[15] often necessitating enucleation of the involved eye.

Optic neuritis or retrobulbar optic neuritis resulting in secondary optic nerve atrophy may also accompany herpes zoster ophthalmicus.[1, 3, 4, 16–21] Involvement of the optic nerve in herpes zoster may be associated with meningioencephalitis leading to

blindness.[1, 4, 7, 12] The optic neuropathy has been suggested as being ischemic[4, 7, 21] resulting from neural inflammation and vascular insufficiency secondary to arteritis.[21] However, Hayreh[22] noted that most cases reported in the literature[23–25] were in fact more likely to be either an optic atrophy, perhaps secondary to retinal artery occlusion, or retrobulbar optic neuritis. Optic nerve involvement might follow the transmission of the zoster virus to the optic nerve by branches of the trigeminal nerve via the ciliary ganglion, or by direct migration of the virus from the fifth to the second cranial nerve.[1]

In rare cases, the extraocular muscles become paralyzed; there may be partial or complete third nerve palsy, resulting from direct spread of the herpes virus from the fifth to the third cranial nerve.[1] Less commonly these patients have sixth or fourth nerve palsies.[1, 3, 4] Muscle function usually returns within 2 months; only rarely is the patient left with a residual paresis.[4, 7] Palsies are usually seen in patients over 40 years of age,[7, 26] and they may be bilateral or contralateral.[26]

Disturbance of the sympathetic nerves by the herpes zoster virus can result in Horner's syndrome.[1, 2] Argyll-Robertson pupil may occur as a result of a ciliary ganglion lesion,[1, 3] internal ophthalmoplegia from ciliary ganglion involvement,[1] and exophthalmos from inflammation of retrobulbar tissues and/or lid retraction.[1, 3]

Both cutaneous and visceral dissemination are more common with herpes zoster ophthalmicus than with herpes zoster infection elsewhere in the body.[7] Bell's palsy, encephalitis, myelitis, peripheral sensory neuropathy, or a motor neuropathy may result from direct viral invasion and inflammation of the spinal cord, brain stem, or cavernous sinus.[7] A serious neurological complication of herpes zoster ophthalmicus includes segmental granulomatous arteritis affecting the carotid arteries or branches of the internal cerebral arteries, resulting in fever, headache, mental confusion, and contralateral hemiplegia.[7, 13]

Postherpetic neuralgia, caused by scarring of the affected nerves, is a frequent sequela of herpes zoster infection.[1, 4] Its occurrence is related to age, being rare in children, but common in patients over 50 years of age.[4, 7] Its frequency increases until the age of 70 years, at which age it affects approximately one-half of all herpes zoster sufferers.[4] It is not related to the severity of the initial disease, but is particularly common and severe in patients with herpes zoster ophthalmicus.[4, 7, 8]

CASE REPORT

A 22-year-old Caucasian male was seen at the University of Waterloo for a routine eye examination. The patient reported that he had suffered from "shingles" (herpes zoster) at the age of 14 years and that "scar tissue had affected the vision in his left eye." The patient had no other complaints regarding his vision, and he was in excellent general health and on no medications.

Uncorrected visual acuities were 6/4.5 OD, 6/9 OS at 6 m, and 0.37 M OD, 1.00 M OS at 40 cm. Pinhole improved the acuity in the left eye to 6/6. Static retinoscopy revealed an insignificant refractive error of OD −0.25 D and OS +0.50 −0.50 × 180.

The unilateral and alternating cover test indicated that the patient was nonstrabismic and orthophoric at distance and near. Stereoacuity was measured as 200 sec arc on the Randot test.

Color vision, assessed with the Farnsworth-Munsell 100 hue test, was normal for the right and left eyes.

The direct pupillary light reflex was normal for the right eye and diminished for the left, whereas the consensual light reflex was diminished for the right eye and normal for the left. A relative afferent pupil defect was present on the left side. Blotchy stromal lesions, presumably resulting from herpes zoster keratitis, were visible in the superior cornea of the left eye on biomicroscopy. There was no overt evidence of iris atrophy and the anterior chamber angles were open. Intraocular pressures were 15 mm Hg OD and 16 mm Hg OS by applanation tonometry. A slight distortion of the pupil was noted in the left eye.

Gross visual field testing by confrontation revealed a superior field defect in the left eye. The absolute nature of this superior altitudinal defect was confirmed and quantified by automated perimetry (Humphrey Field Analyser 30-2 threshold test) (see Fig. 1). The visual field for the right eye was within normal limits.

Pupils were dilated with 1 drop of 2.5% phenylephrine HCl plus 1 drop of 1% tropicamide each eye. There was an uneven dilatation of the left pupil, with the inferior temporal quadrant of this iris showing a poor response to the mydriatic agents (see Fig. 2).

Indirect ophthalmoscopy revealed a hyperpigmented inferior retina in the left eye with a dull foveal reflex. Pallor was evident in the inferior temporal quadrant of the optic nerve head (Fig. 3). The fundus appearance of the right eye was unremarkable.

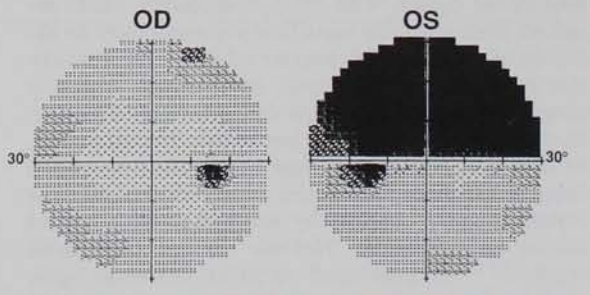

Figure 1. Automated visual fields (Humphrey Field Analyser 30-2 threshold test) showing the normal field for the right eye and the absolute superior altitudinal defect for the left eye.

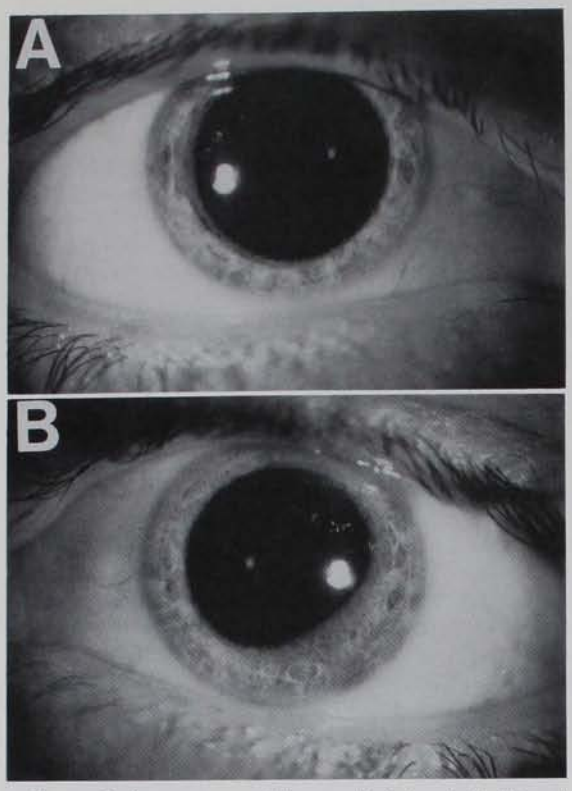

Figure 2. Appearance of the pupil of the right (A) and left (B) eyes after attempted dilation with 1 drop of 2.5% phenylephrine HCl plus 1 drop of 1% tropicamide OU. The left pupil showed irregular dilatation indicative of a sectorial defect of the iris sphincter muscle.

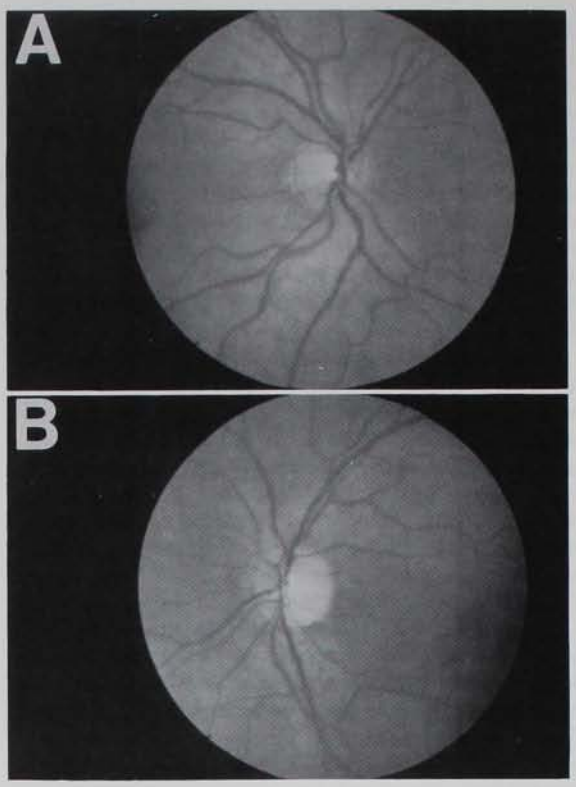

Figure 3. Posterior poles of the right (A) and left (B) eyes illustrating pallor of the inferior temporal aspect of the optic nerve head of the left eye.

DISCUSSION

The patient's clinical findings are consistent with a diagnosis of ischemic optic neuropathy, resolved retinitis, damage to the iris sphincter muscle, and stromal scarring of the left eye resulting from herpes zoster ophthalmicus. Unlike typical anterior ischemic optic neuropathy in which the altitudinal visual field defect is usually an inferior defect due to nonperfusion of the lateral posterior ciliary artery, in the present example, nonperfusion of the medial posterior ciliary artery leads to a superior altitudinal defect. The optic neuropathy likely resulted from vascular insufficiency secondary to arteritis of the medial posterior ciliary artery, unlike the anterior ischemic optic neuropathy which is commonly caused by giant cell arteritis or nonarteritic causes such as arteriosclerosis, hypertension, or diabetes. We believe that the patient described here is an example of the rarely described true ischemic optic neuropathy associated with herpes zoster ophthalmicus. Hayreh[22] noted that most reports[23-25] of presumed anterior ischemic optic neuropathy resulting from herpes zoster were in fact more suggestive of either optic atrophy, perhaps secondary to retinal artery occlusion, or retrobulbar neuritis.

Vasculitis of the medial posterior ciliary artery with ischemia of the inferior temporal choroid also resulted in retinitis with hyperpigmentation of the inferior temporal retina of the left eye. Involvement of the anterior uveal tract is suggested by the subtle distortion of the natural pupil, and the irregular pupillary dilatation observed with the topical instillation of 1 drop of 2.5% phenylephrine HCl and 1 drop of 1% tropicamide. This phenomenon likely represents sectorial damage to the iris sphincter muscle such that tropicamide, a parasympathetic blocker which produces mydriasis by inhibiting sphincter activity through competition with acetylcholine at the myoneural junction,[27] is rendered less effective.

As there is no treatment for the patient's visual field defect or other ocular sequelae of the herpes zoster infection, patient management consists of regular eye examinations including quantitative field analysis.

In summary, we believe that our patient is an example of a true posterior ischemic optic neuropathy associated with herpes zoster ophthalmicus.

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ANNOUNCEMENT

Dr. Merton C. Flom has been appointed Dean of the College of Optometry, University of Houston, Houston, Texas. A nationwide search for a permanent Dean has begun. Dr. Flom replaces Dr. W. R. Baldwin who has been Dean since 1979.