SHORT REPORT

Acute zonal occult outer retinopathy and multiple sclerosis

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J Neurol Neurosurg Psychiatry 2006;77:1373–1375. doi: 10.1136/jnnp.2006.090415

The case of a 30-year-old woman who had two episodes of photopsia along with sudden-onset monocular visual field defects, developing into bilateral tunnel vision within 4 years, is reported. She also had episodes of a right hemiparesis and right-sided hypoaesthesia, accompanied by severe fatigue. This patient fulfilled the criteria for both clinically definite multiple sclerosis and acute zonal occult outer retinopathy (AZOOR). AZOOR can have an onset with monocular visual field loss, and can be distinguished from optic neuritis. In addition, some observations suggest common neuropathological and inflammatory mechanisms between multiple sclerosis and AZOOR.

Acute zonal occult outer retinopathy (AZOOR) is a rare, newly recognised retinal disorder occurring predominantly in young Caucasian women.¹ Its aetiology remains unknown, but an inflammatory origin is suspected.^{1,2} In a previous series of 51 patients, a considerable number of patients (n = 6) had multiple white matter lesions on magnetic resonance imaging (MRI) of the brain and some had transverse myelitis (n = 4), but no further clinical neurological details were provided.¹ Here we describe a patient with AZOOR who fulfilled the criteria of clinically definite multiple sclerosis.

Case report

A 30-year-old woman at 5 months of pregnancy noted a sudden-onset visual field defect in her left eye with photopsia, which expanded over the months into unilateral tunnel vision and then stabilised. Routine ophthalmological examination did not show abnormalities. After delivery, there was no progression and the photopsia stopped. Three years later, during a second pregnancy, photopsia appeared in her right eye and dark-adaptation problems occurred. One month later, she developed a paresis of the right arm and leg, gradually worsening in 1 day and lasting for 2 weeks. Neurological examination showed a right hemiparesis (grade 4/5) with ipsilateral hyper-reflexia and Babinski sign.

Since then, visual field defects further expanded also in this right eye over the months, ending in tunnel vision. One year after the onset of the hemiparesis, she was seen with a sudden hypoaesthesia of the right half of the body lasting for 2 weeks. At the same time, she had severe fatigue. The neurological signs and symptoms recovered without immunomodulatory treatment.

Ophthalmological, blood and MRI studies

The visual acuity at the time of the second pregnancy was 0.8 in the right eye and 0.4 in the left eye. There was a relative afferent pupillary defect of the left eye. A trace of vitreous cells was seen in both eyes. Funduscopy showed areas with depigmentation of retinal pigment epithelium and scattered

Figure 1 (A) Funduscopy showing areas with depigmentation of retinal pigment epithelium, a few intraretinal pigmentations, attenuated arterioles and a pale optic nerve with peripapillary atrophy. (B) T2-weighted magnetic resonance image showing an infratentorial (pontine) lesion.

Abbreviations: AZOOR, acute zonal occult outer retinopathy; CSF, cerebrospinal fluid; MRI, magnetic resonance imaging

Figure 2 Goldmann perimetry was carried out under standardised conditions using targets V-4e, I-4e and I-1e. It showed a concentric scotoma in the left eye (A) with an annular scotoma in the right eye (C) at the beginning of the second episode with photopsia. This evolved into bilateral asymmetric concentric scotoma 1 year later (B, D). OS: left eye, OD: right eye.

intraretinal pigmentation, narrowed retinal vessels and a pale optic nerve in both eyes (fig 1A). The macular region of the left eye showed an epiretinal membrane with cyst-like changes. The changes were confirmed by optical coherence tomography.

Electroretinography showed markedly reduced photopic and scotopic responses in the right eye. The responses were non-detectable in the left eye. The visual evoked potential showed no abnormalities. Visual field analysis showed an annular scotoma in the right eye that evolved over a period of several months into a concentric scotoma with a nasal extension and a large temporal island (fig 2C,D). The field of the left eye was already severely constricted (fig 2A,B). Blood tests were negative for antinuclear antibodies; serology for syphilis, borrelia and toxoplasmosis was also negative. Cerebrospinal fluid (CSF) analysis showed no pleocytosis, total protein concentration 0.42 g/l (normal), immunoglobulin (Ig) G index 1.07 (increased) and oligoclonal IgG bands present in CSF but absent in blood. T2-weighted and fluid-attenuated inversion recovery-weighted cerebral MRI (obtained after the second pregnancy) showed more than nine white matter abnormalities localised around the

ventricles, juxtacortically and in the pons (fig 1B). A juxtacortical lesion showed enhancement with gadolinium, all fulfilling the MRI criteria for multiple sclerosis.³ In addition, T2-weighted MRI of the spinal cord showed a 3-cm size lesion at C3.

DISCUSSION

AZOR was diagnosed in this patient because of the combination of acute loss of visual fields with photopsia, sparing of central vision, specific fundoscopic abnormalities, reduced receptor cell amplitudes observed with electroretinography findings and a normal visual evoked potential.¹ No recovery of visual field was noted, which is another feature of this disorder.¹ The fundoscopic changes, including the attenuation of the vessels and the optic disc pallor, occur secondary to the massive loss of photoreceptor function.¹ Our patient also gradually developed multiple sclerosis, a diagnosis that was based on a combination of neurological examinations, the multiple sclerosis-compatible white matter lesions on MRI of the brain and spinal cord along with CSF findings (raised IgG index with oligoclonal bands).³

The known ophthalmic disorders associated with multiple sclerosis are optic neuritis, intermediate uveitis and retinal vasculitis. One could wonder whether the occurrence of AZOOR and multiple sclerosis in one patient is merely coincidental. Jacobson⁴ also observed signs of central nervous system inflammation in a patient with AZOOR.

The only available long-term follow-up study of patients with AZOOR showed the presence of (not further defined) white matter abnormalities on cerebral MRI in a substantial subgroup.¹ Both multiple sclerosis and AZOOR share common characteristics, such as a relapsing course, often followed by gradual worsening. Other characteristics shared by the two conditions are a skew to female sex, inflammatory lesions localised predominantly in areas around venules, together with signs of secondary neuronal cell loss.¹⁻³ Moreover, in both multiple sclerosis and AZOOR, onset or worsening is often observed after aspecific viral-like infections,^{1,5} and there seems to be an association with generalised autoimmune disorders.^{1,6} For both AZOOR and multiple sclerosis an autoimmune aetiology has been suggested, with central nervous system myelin as a suspected target in multiple sclerosis.²⁻⁴ Onset and worsening of the retinal disease during pregnancy, such as seen in our patient, has been reported more often.¹ This aspect is clearly different from what is generally seen in multiple sclerosis, which tends to ameliorate during pregnancy.³

Acute visual loss in a young woman has a broad differential diagnosis, but is most often caused by optic neuritis.⁷ A diagnosis of AZOOR should be suspected in cases of loss of one or more zones of visual field, particularly when associated with photopsia, absence of discomfort with eye movement, relatively spared visual acuity and without fundoscopic explanation for visual loss.¹ Electrophysiology should be carried out to differentiate AZOOR from optic neuritis and other lesions affecting the posterior visual pathways.^{1,7,8}

This knowledge can help to prevent incorrect diagnosis of optic neuritis in patients with multiple sclerosis who present with visual impairment in the absence of manifest ocular signs. This case illustrates a rare cause of acute visual field loss, with asymmetric involvement of the eyes. Moreover, it

may point to common neuropathological mechanisms shared between multiple sclerosis and AZOOR: two diseases with still largely enigmatic aetiologies.

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Funding: RQH is supported by the Dutch MS Research Foundation and by The Netherlands Organisation for Scientific Research (NWO).

Competing interests: None.

Consent was obtained for publication of the patient's details described in this report.

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Received 8 February 2006

Revised 4 July 2006

Accepted 12 July 2006

Published Online First 25 July 2006

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