ACUTE ZONAL OCCULT OUTER RETINOPATHY – A CASE WITH RAPID RETURN OF VISUAL FUNCTIONS IN TYPE 3 DISEASE

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SUMMARY

Acute zonal occult outer retinopathy is noninfectious zonal dysfunction of outer retina often adjacent to optic nerve. It is accompanied by temporary disappearance of retinal fotoreceptor layer, visual acuity drop and late pigmentary fundus changes. Authors present a case report of a patient with unilateral involvement and spontaneous visual acuity resolution followed by quick reappearance of photoreceptor layer on OCT.

Key words: AZOOR, photoreceptor cell layer, OCT, SLO

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CASE REPORT

A 43 year old female patient with an anamnesis of deterioration of vision in the right eye persisting for two days was sent by the district ophthalmologist to the above workplace for the purpose of diagnosis. The deterioration was of the character of blurring of vision with a blind spot in the visual field of a yellowish-brown colour, together with sporadic flashes of light. The patient stated no pain in the eye, and that in the last two weeks she had slept very little and suffered pronounced psychological stress. She had worn correction for short-sightedness since childhood. She had never been treated for ocular diseases, had never undergone eye surgery and her personal anamnesis also contained no remarkable features.

Refraction in the right eye was -2.00 Dsf -0.75Dcyl 163°, intraocular pressure 16 torr. Refraction in the left eye was -1.50 Dsf -0.50Dcyl 12°, intraocular pressure 22 torr. Best corrected visual acuity measured on Snellen's optotype in the right eye was 5/15, in the left eye 5/5. The finding in the anterior segment of the eye was commensurate to age, without any turbidity of the lens, the vitreous was clear. The disc of the optic nerve was well bordered, coloured, in the nasal part mildly hyperemic, capillaries commensurate to calibre, macular without foveal reflex with indication of thinning of RPE in the fovea (fig. 1), although without coarse pathology, periphery of retina without deposit changes, completely attached. The biomicrospic finding of the ocular fundus in the left eye was physiological (fig. 2). The OCT examination of the right eye demonstrated preserved stratification of the neuroretina without changes of the vitreoretinal interface or cystoid changes, but it detected a lack of outer segments of the photoreceptors, including the cilium of the cone cells whilst preserving the membrana limitans externa (fig. 3). On the SLO (scanning laser ophthalmoscopy) image, the area of the lacking photoreceptors created a dappled, darker area in the overall area of the fovea and parafovea. OCT of the left eye did not demonstrate any pathological changes (fig. 4). The finding was concluded as maculopathy in the right eye in the differential diagnosis, the patient was administered betamethasone depot parabulbarly in a dose of 0.4 ml and was ordered for a follow-up examination two days later.

On the fourth day after the beginning of the symptoms, vision in the right eye improved slightly to 5/12, OCT finding negative, identical to the last examination. An exami-

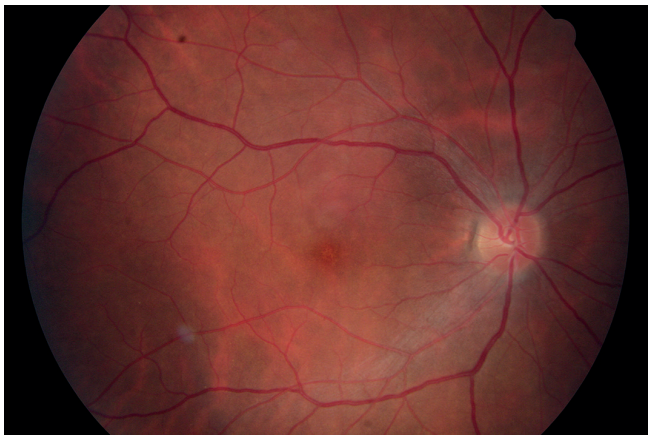

Fig. 1 Photograph of fundus o. dx: slight atrophy of RPE in fovea

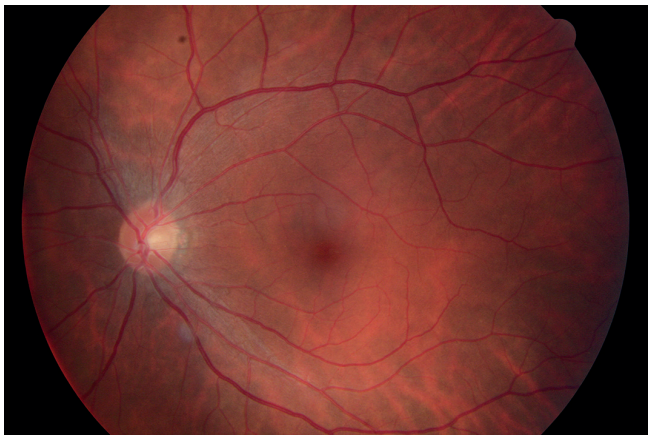

Fig. 2 Photograph of fundus o. sin – physiological finding

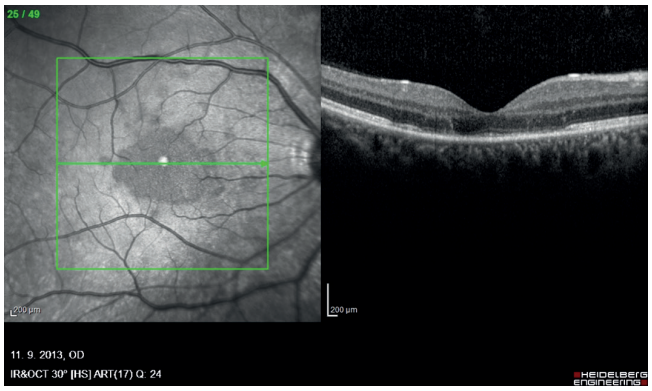

Fig. 3 OCT finding o. dx: discontinuity of line of outer segments of photoreceptors, corresponding with darker, dappled area parafoveally on SLO image in left part of image

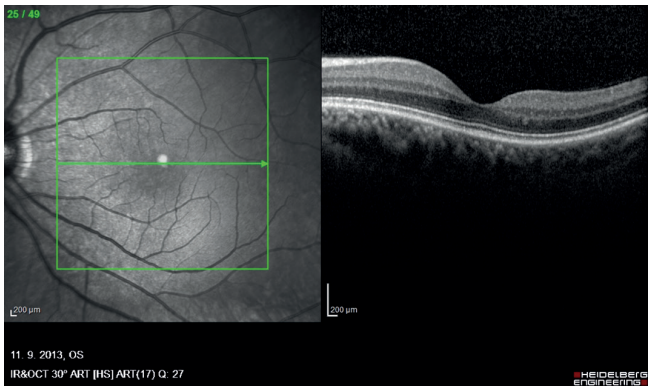

Fig. 4 OCT finding o. sin: physiological finding

nation of the visual field was conducted using a computer perimeter (Octopus brand), by the full-threshold method. The examination recorded a reduction of sensitivity in the small region of the fovea by 13 decibels (fig. 5). We considered extramacular scotoma localised superior to be clinically insignificant. The patient was proposed admission to the department for the purpose of further differential diagnosis of the disease, but refused hospitalisation on that day.

On the fifth day after the beginning of the symptoms, the patient was admitted to the department with a conclusion of maculopathy in the right eye with possible development of retrobulbar neuritis. Vision in the right eye had improved since the previous day to 5/5 partially. The patient was administered methylprednisolone venously in a bolus dose of 1000 mg, with continuation for a further two days and subsequent transition to methylprednisolone administered per os in a dose of 1 mg/kg/day. A blood sample of the patient was taken for basic blood count, biochemical screening and inflammation markers. We ordered the patient for an electro-physiological examination at the Department of Ophthalmology of St. Michael's Hospital in Bratislava.

On the sixth day after the beginning of the symptoms of the disease, visual evoked potentials were examined, which did not demonstrate a change of amplitude and speed of the progression of disturbance by the right optic nerve, on the basis of which we eliminated retrobulbar neuritis from the differential diagnosis. The results of the blood test did not demonstrate an increase of the inflammation parameters, and all were within the norm limits.

During hospitalisation we conducted an examination by fluorescence angiography. In the first minute of the examination we observed an intimation of mild transmitted hyperfluorescence in the fovea (fig. 6) in the right eye, with pronounced staining of the disc of the optic nerve in the fifth minute (fig. 7). This finding was very discrete, and we concluded it as clinically insignificant. The finding in the left eye was physiological (fig. 8). On the tenth day after the beginning of the symptoms, the finding on OCT was practically unchanged in comparison with the finding upon identification of the disease (fig. 9). The patient now had full vision on a level of 5/5, was discharged from the department, and we concluded the finding as acute zonal occult outer retinopathy, and we continued to observe the patient in outpatient care.

On the thirteenth day after the first symptoms, the patient underwent an ERG and EOG examination at the Department of Ophthalmology at St. Michael's Hospital in Bratislava (fig. 10 and 11). The Arden quotient in the right eye was within the suspect zone, in the left eye within the norm. An adaptation curve to light exposure was present, a little flatter upon good co-operation of the patient. The finding did not confirm damage to the cone cells, there was highly

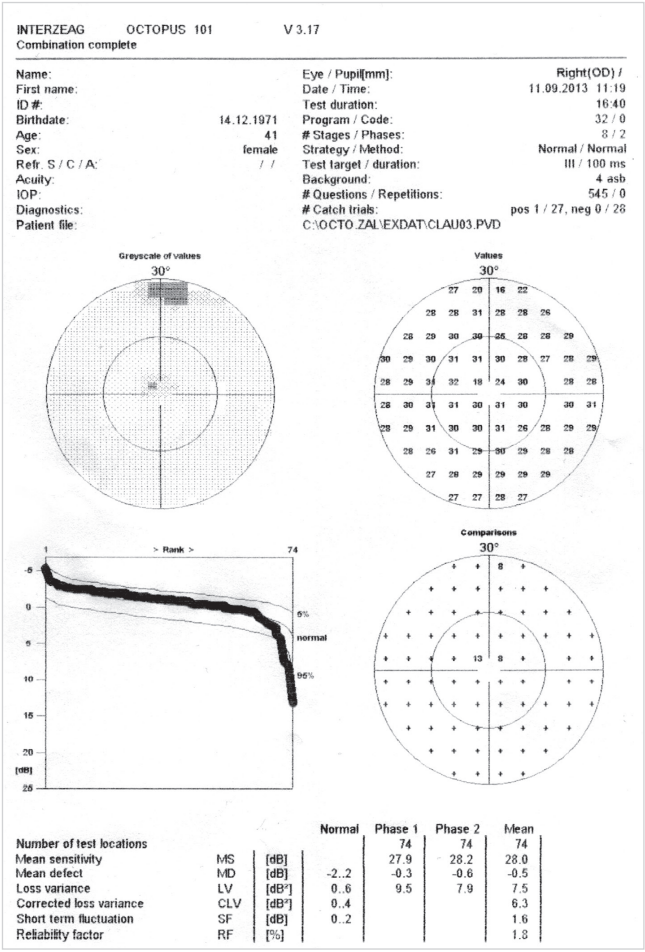

Fig. 5 Result of examination of visual field of right eye by computer perimeter. Reduction of sensitivity of small region in fovea

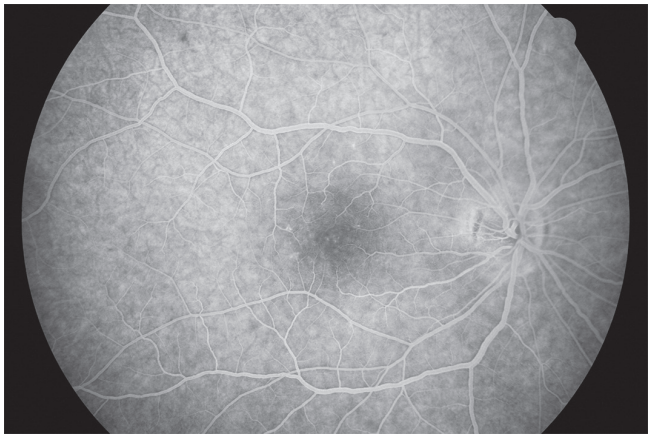

Fig. 6 FAG from 1st minute – slightly increased transmitted hyperfluorescence in fovea

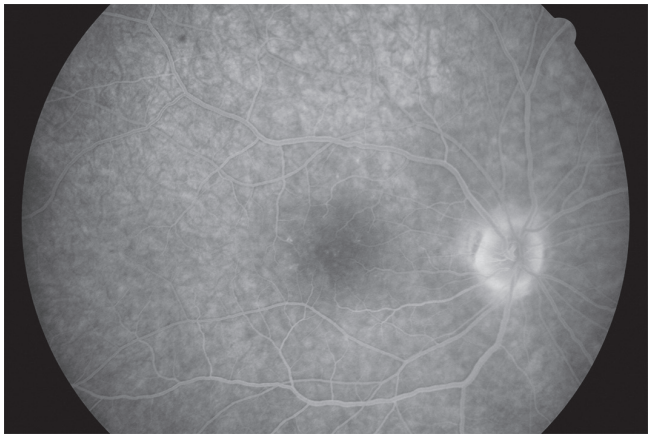

Fig. 7 FAG examination from 10th minute – pronounced staining of disc of optic nerve

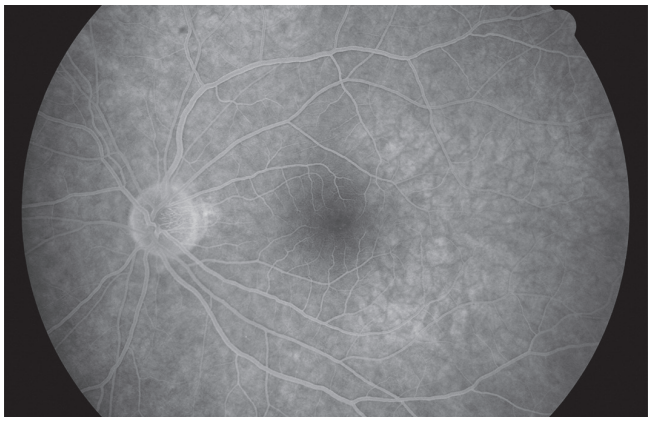

Fig. 8 FAG examination o. sin: physiological finding

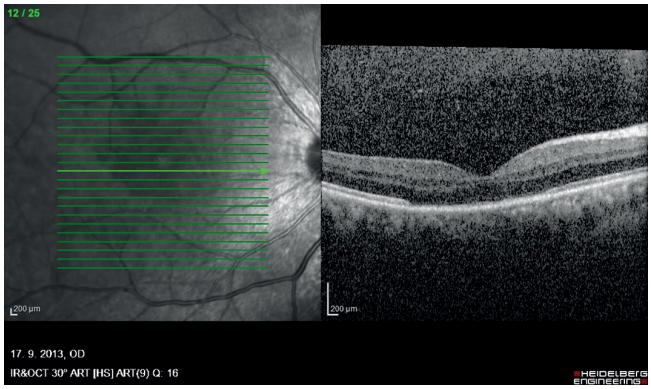

Fig. 9 OCT finding 10 days after the beginning of symptoms – lack of photoreceptors persists

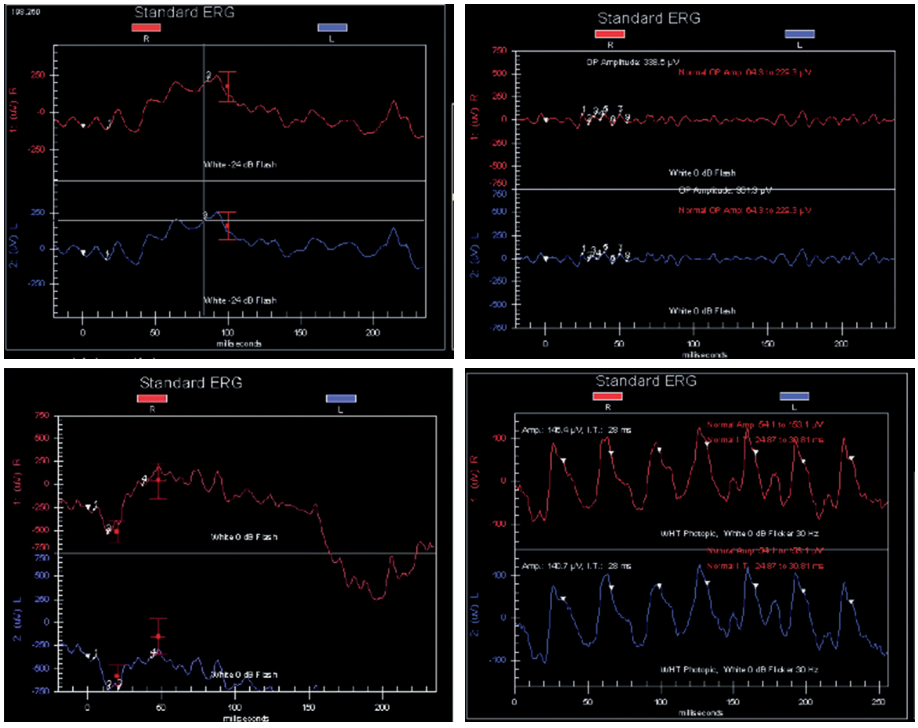

Fig. 10 Electroretinogram in scotopic and photopic image, flicker ERG

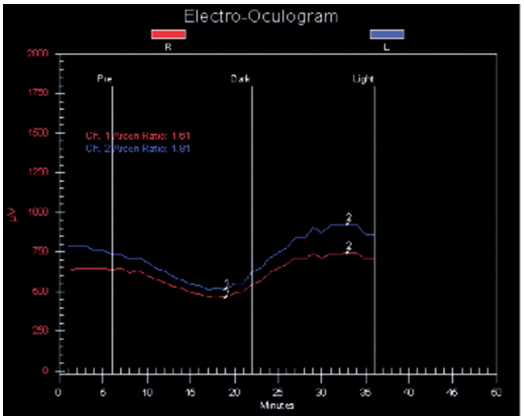

Fig. 11 Electrooculogram

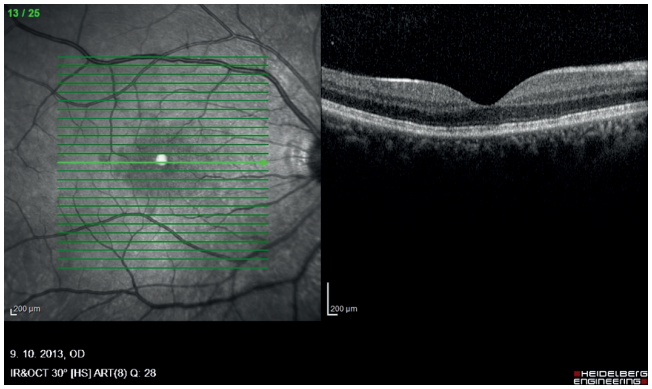

Fig. 12 OCT finding 1 month after the beginning of symptoms – renewed line of photoreceptors with reduced dark stain on SLO image

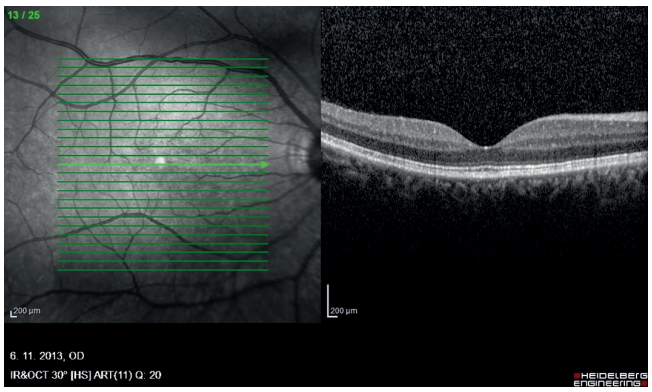

Fig. 13 OCT finding 2 months after the beginning of symptoms – complete restitution of photoreceptors without dark stain on SLO image

probably a deficit of rod cells.

One month after the beginning of the symptoms there was complete renewal of the outer segments of the photoreceptors on OCT (fig. 12) and a reduction of the dark stain on the SLO image. One month later the dark stain had disappeared completely and the OCT finding was practically physiological (fig. 13).

At the last follow-up examination approximately one year after the onset of the symptoms, the patient was asymptomatic, both the biomicroscopic and OCT examination were without a pathological finding and visual acuity with correction was 5/5 bilaterally.

DISCUSSION

Acute zonal occult outer retinopathy – AZOOR) is a syndrome characterised by a sudden loss of visual functions in one or more zones of the central part of the retina. Scotoma may be recurrent, or may increase in size and often merges with the optic nerve, and is most commonly accompanied by photopsias. AZOOR occurs more frequently in young myopic women, in which the return of visual functions rarely occurs (3). The disease begins unilaterally and frequently afflicts both eyes. The first to describe this disease was Donald Gass, in a group of 13 patients with central scotoma without the corresponding changes on the fundus, in whom changes of pigmentation of the retina and atrophy of the choroidea developed over time in the place of the scotoma (2). He used the acronym AZOOR, which summarises the fundamental clinical features of the disease:

A – acute: sudden uni- or bilateral loss of vision with photopsias.

Z – zonal: loss of visual functions appear in one or more areas of the retina with or without accompanying enlargement of the blind spot.

O – occult: minimally initial biomicroscopic finding or complete lack of changes on the retina in the areas corresponding with scotoma.

O – outer: primarily afflicts the outer part of the retina – layer of photoreceptors with abnormal response to ERG. Cone cells are more afflicted than rod cells.

R – retinopathy.

The etiology of the disease is unknown, in which an infectious or autoimmune origin is considered. A virus or infectious agent may enter the eye along the optic nerve or the ora serrata, and provoke an immune response to viral antigens, which are similar to antigens produced by the photoreceptors, by which zones of dysfunction to loss of photoreceptors originate (3). However, to date no unusual antibodies against photoreceptors have been found in patients with AZOOR (6). An alternative possibility of the origin of the disease is a genetic predisposition of certain individuals to autoimmune and inflammatory response against cells of the retina, in which the ocular symptoms originate through exposure to specific triggers from the external environment (7).

Sudden loss of sight does not correlate with the biomicroscopic finding on the retina, which is mostly negative, or minimal changes of pigmentation of the fundus are visible in the areas of scotoma. Examination by fluorescence angiography in most cases also does not detect a marked pathology with the exception of discrete window defects. In later phases of angiography it is possible to observe accentuated physiological identification of contrast in the optic nerve – late staining of the disc. This observation led Gass to the assumption that the disease is of infectious origin, and that the place of entry of the virus into the eye is the area around the papilla (4). Spaide (13) highlights the significance of autofluorescence of the fundus upon determination of the precise area of affliction of the retina, in which this area is hypoautofluorescent. Electro-physiological examinations virtually always demon-

strate abnormalities (3).

The pathology is perhaps most emphatically demonstrated by the OCT examination. In the afflicted areas of the retina which correlate with scotoma, we see a discontinuity to complete lack of a line of photoreceptors. The OCT examination also includes a display of the position of individual tomograms with regard to the topography of the retina, which represents an image digitally created with the help of SLO (scanning laser ophthmoscopy). The light emitted by the laser, reflected from the retina, is recorded via an exceptionally narrow slit, thus ensuring display of the structures on one level of focalisation. The emitted laser ray of SLO is reflected from the cells of the RPE. The properties of the reflected light are altered primarily by changes in the RPE itself, as well as in the transparent layers of the neuroretina. As a result, in the areas of lacking photoreceptors, which together with the Müller cells form "functional retinal columns" (11) and function as optic fibres, on SLO we see a display of a dappled dark area. We see a similar darkening in the centre of the traces after treatment by laser. These observations were definitively confirmed recently by the published use of SLO with adaptive optics (AOSLO) for the measurement of the density of photoreceptors in the case of AZOOR (10).

In older findings it is possible to observe a thinning of the neuroretina on OCT.

The disease is classified amongst white spot syndromes. Some patients beginning as MEWDS (multiple evanescent white dot syndrome) may progressively manifest symptoms of diffuse damage to the layer of photoreceptors, which is consistent with AZOOR (1). In other patients who come within the spectrum of punctate inner choroidopathy (PIC) or multifocal choroiditis (MCH), serious affliction of the outer layers of the retina may develop – again consistent with AZOOR (14). There are therefore a number of types of AZOOR as a clinical unit: type 1 – without the presence of other white spot syndromes and type 2 – beginning as other white spot syndrome. A minimal amount of patients do not manifest any clinical abnormalities of the retina, but only a malfunction of the photoreceptors – type 3.

Within the framework of differential diagnostics, it is necessary to differentiate sudden loss of sight in the case of AZOOR from neuropathy of the optic nerve, including retrobulbar neuritis (12), which is helped by the finding of a focal lack of photoreceptors. Dystrophic diseases of the retina are mostly bilateral, symmetrical and slowly progressing, which safely differentiates them from AZOOR. Patients with retinopathy in connection with cancer associated retinopathy (CAR) or melanoma associated retinopathy (MAR) may also manifest signs of damage to the outer layers of the retina, even with a finding of antibodies (5).

To date no demonstrated therapy exists for the disease. Successes have been reported with corticoids and immunosuppressive substances (9). Antiviral and antibacterial preparations have also been tried. Recently Mahajan and Stone described success in three patients with the administration of Valcyclovir (8). However, the patients were in an early stage, and the clinical picture was not entirely typical of AZOOR.

Our patient manifested all the symptoms typical for acute phase of the disease – sudden loss of sight with photopsias, blind spot in the visual field, negative biomicroscopic finding and discrete pathology on fluorescence angiography. There was an evident pathognomonic lack of photoreceptors on OCT, determined by the scope of the dark, dappled area on the SLO image. We explain the unconvincing finding on the electro-physiological examination by means of the lack of identification of the acute phase of the disease, inasmuch as the patient had practically full vision on the day of the examination. The applied therapy by bolus doses of corticoids was directed primarily at the potential diagnosis of retrobulbar neuritis, which however was not confirmed by the VEP examination. **On the basis of the above facts, the patient comes within the category of type 3 AZOOR, although such a sudden improvement of visual functions, as well as anatomical restitution of photoreceptors are unusual in this group of patients.**

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