

CLINICAL CHALLENGES

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A Shot of Adrenaline

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(In keeping with the format of a clinical pathological conference, the abstract and key words appear at the end of the article.)

Case Report

A 21-year-old white woman presented to her allergist because of a skin reaction she described as generalized hives. She had several similar episodes in the past but with no specific diagnosis given or known inciting factor. While at the allergist's office she was given an injection of epinephrine and suddenly became dizzy, nauseous, and developed uncontrollable arm and leg shaking associated with head pain. Immediately following these symptoms she noted blurred vision in each eye. Subsequently she was given an injection of devalproex sodium (Depakote, Sanofi-Aventis, Paris, France). She had some difficulty with breathing and continued to have a headache for approximately four hours. She was sent home from the allergist's office, but because of her continued blurred vision she went to a local emergency room and was admitted to hospital for overnight observation. An MRI (magnetic resonance imaging) with contrast was reported to be normal. She was discharged the next day with no diagnosis.

Aside from the hives she was a healthy young woman matriculated at a local college. She was taking an oral contraceptive on a daily basis and

denied any illicit drug, tobacco, or alcohol use. Her family history was unremarkable.

Six days later she was seen in the Duke University Neuro-Ophthalmology clinic because of continued blurred vision in each eye, which she described as looking through black spots. On examination, blood pressure was 106/61 with a heart rate of 70 beats/min and regular. Visual acuity was 20/40 OD and 20/30 OS. Color vision with the Ishihara pseudochromatic plates was 9.5/10 OD and 7/10 OS. Pupillary reflexes were normal without a relative afferent pupillary defect. Ocular adnexa, slit-lamp (including intraocular pressures), ocular motility, and cranial nerve examinations were all normal. The fundus is seen in Fig. 1, and automated visual field testing in Fig. 2.

Where is the most likely anatomical location of the visual loss in this patient?

Comments

COMMENTS BY MICHAEL S. VAPHIADES, DO

The appearance of the visual field showing bilateral central defects usually localizes to either

bilateral optic nerve or bilateral macula, however, the fundus appearance argues for a bilateral maculopathy. On inspection of the macula (especially OD), a reddish-brown flower petal-shaped abnormality is noted. Both right and left macula are clearly abnormal and perfectly localize to the central defects on the automated visual field. Given this, further testing should be geared toward defining macular anatomy and function.

What further testing would you like to perform?

Comments (Continued)

COMMENTS BY DR. VAPHIADES

I would obtain a fluorescein angiogram. If normal, then optical coherence tomography (OCT) may help define the macular abnormality.

Case Report (Continued)

A macular photostress test showed a recovery time of 50 sec OD and 60 sec OS. OCT (Carl Zeiss Meditech, Dublin, CA) demonstrated a small area of abnormal signal at the level of the outer retina with normal thickness of the retinal nerve fiber layer and

macula (Fig. 3). Intravenous fluorescein angiography (IVFA) was normal in each eye.

What other test(s) would you recommend?

Comments (Continued)

COMMENTS BY DR. VAPHIADES

A multifocal electroretinogram (mfERG) is an exquisite test to evaluate the macula. The test provides an electrical response of the retina in over 100 locations in the central 25 degrees of visual field. It has the appearance of multiple small waveforms similar to the full field ERG, each negative wave comprising components from the a-wave and each positive component being some combination of positive components of the full-field electroretinogram (ERG). In this case, the mfERG should show bilateral impaired responses centrally corresponding to a bilateral maculopathy.

Case Report (Continued)

An mfERG showed decreased tracings within the macula in each eye (Fig. 4).

What is the most likely diagnosis?



Fig. 1. Top: Digital fundus photographs of the right (left) and left (right) eye taken 6 weeks after presentation. Notice the blunted macular reflex in the right eye. Bottom: Digital red free fundus photographs of the right and left macula. Notice the subtle pigmentary changes more visible in the right than the left macula.

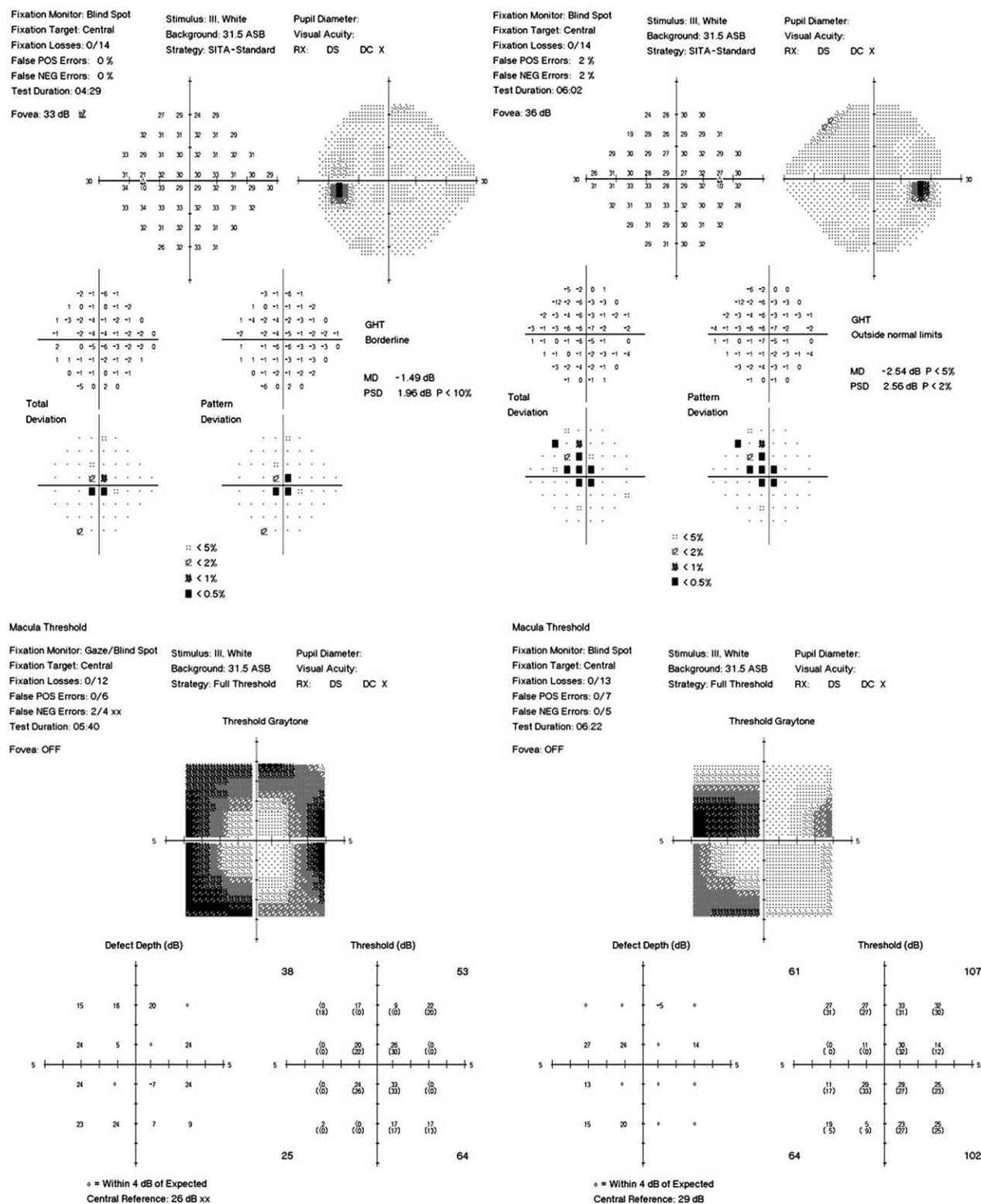


Fig. 2. Top: Humphrey visual field, SITA standard, 24-2, showing paracentral scotomas in the right (right) more pronounced than the left eye (left). Bottom: Humphrey visual field, macula full threshold, of the right eye (right) and left eye (left). Note the sparing of the central vision.

Comments (Continued)

COMMENTS BY DR. VAPHIADES

Most compelling about this case is the acute onset of the visual dysfunction following an injection of epinephrine in a young woman. This history, coupled with the level of acuity loss, visual field appearance, characteristic reddish-brown flower petal-shaped macular abnormalities, and centrally depressed mfERG virtually assures the diagnosis of acute macular neuroretinopathy (AMNR).

Case Report (Continued)

Based on the clinical and paraclinical findings it was postulated that the patient suffered from AMNR. Nearly 1 year later vision had improved to 20/20 OU. Color vision was 10/10 in each eye. The optic nerves continued to remain normal in appearance and there were only subtle pigmentary changes in each macula. The visual fields showed

subtle improvement of the paracentral scotomas bilaterally (Fig. 5).

Discussion

In 1975, Bos and Deutman¹ described AMNR in four women, between the ages of 24 to 33 years, presenting with acute unilateral or bilateral paracentral visual loss. Brownish-reddish, wedge-shaped parafoveal lesions pointing to the fovea were noted on the clinical examination. IVFA was either normal or showed capillary dilation with no leakage and visual recovery was either slow or non-existent. Nearly three decades later, an extensive review of the English-language literature by Turbeville et al²² analyzed 41 cases of AMNR reported from 1975 to 2002. Eighty-three percent of the cases were women in their reproductive years. Predisposing factors noted in these cases included oral contraception (17 cases), antecedent (1 week prior) upper respiratory/influenza-like symptoms (18 cases), trauma,

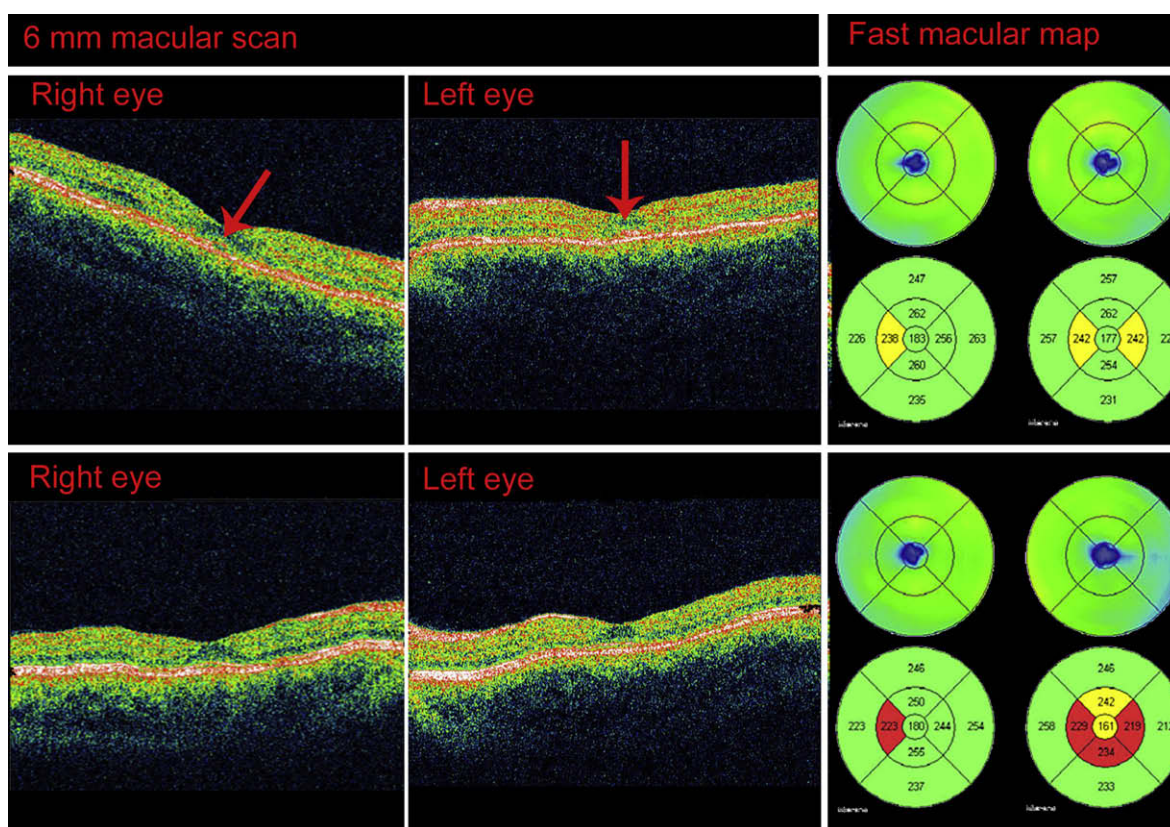


Fig. 3. Top: Optical coherence tomography, 60 mm scan (left) and fast macular map (right) protocols, on initial presentation. Notice the abnormal increased signal in both eyes located at the outer segment–inner segment junction of the photoreceptor cells (red arrow). The fast macular map shows a focal area of relative thinning at the level of the inner macular ring in both eyes. Bottom: Optical coherence tomography, 6-mm scan (left) and fast macular map protocols (right), at 6-week follow-up. Notice that the increased signal has disappeared and is replaced by focal atrophy located at the outer segment of the photoreceptor cell layer. The fast macular map shows further thinning at the level of the inner macular ring.

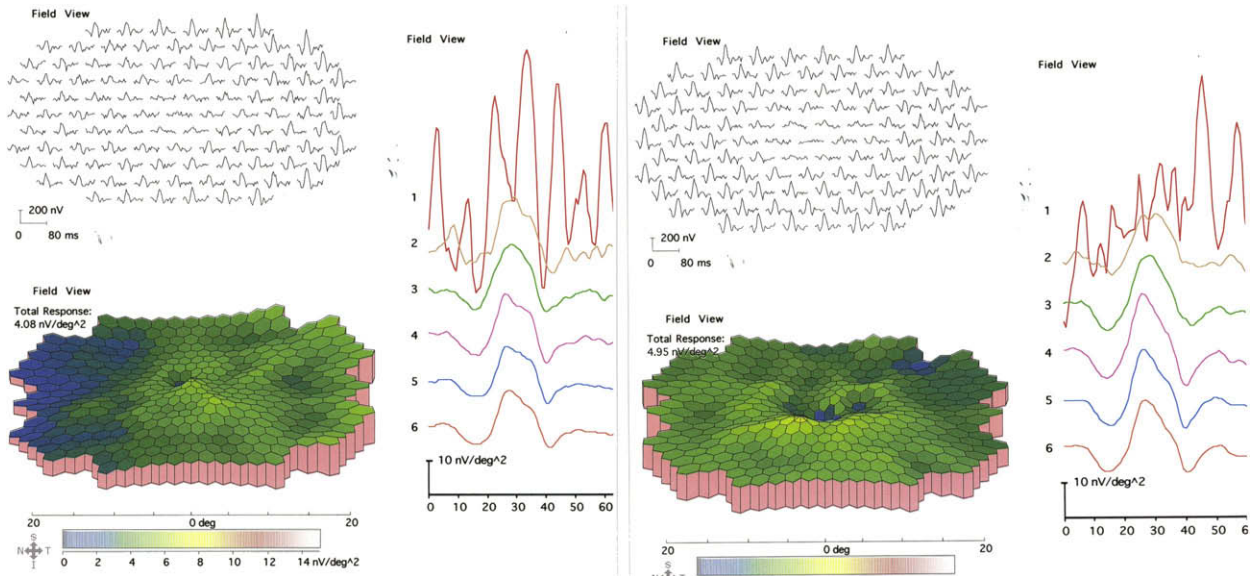


Fig. 4. Multifocal electroretinogram of the right eye (left) and left eye (right). There are decreased foveal peaks and decreased central wave forms in each eye.

migraines, and hypotension. The diagnosis was established based on the clinical presentation, characteristic visual field defects, and a flower-petal arrangement of lesions in the macula that corresponded to the central-paracentral visual field defects. The macular lesions were thought to

represent well-defined areas of outer or inner retinal thinning similar to the changes seen in other disorders that cause focal retinal thinning such as retinal holes or following the resolution of Berlin edema or retinal hemorrhage. IVFA and indocyanine green angiograms were normal in

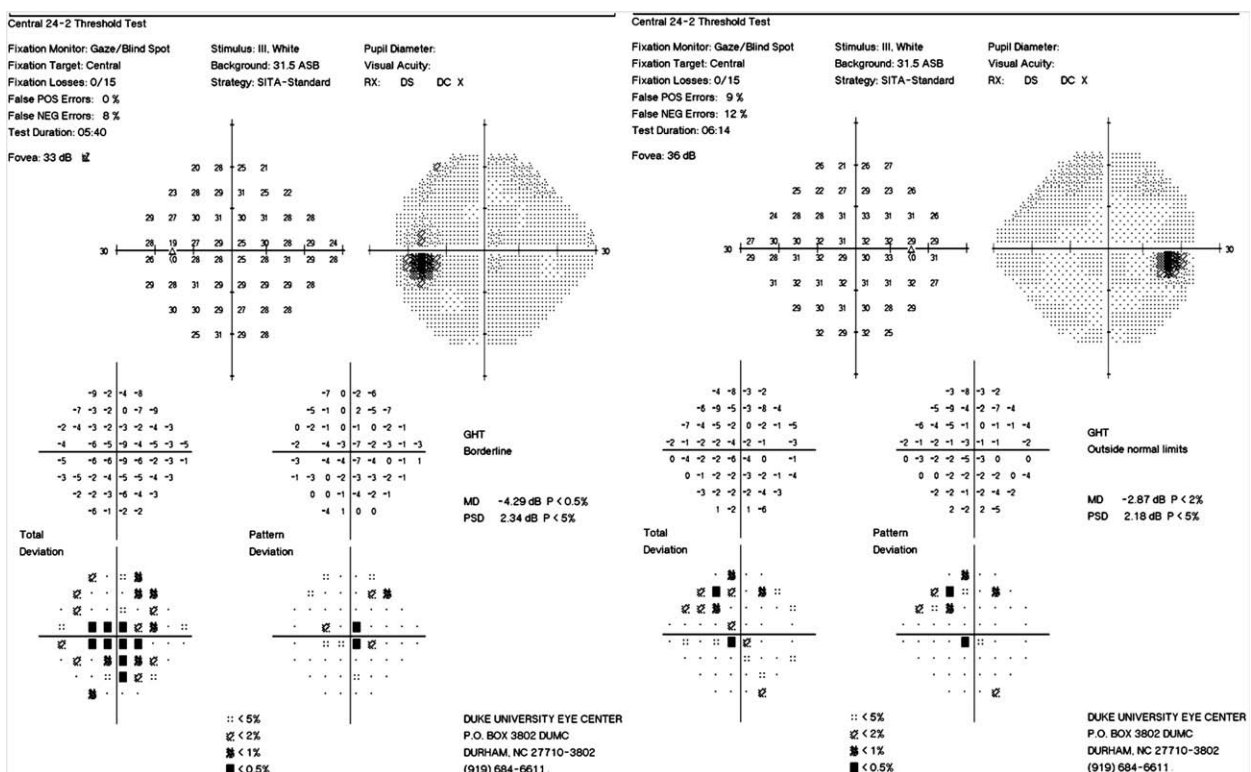


Fig. 5. Follow-up (approximately 1 year after presentation) Humphrey visual field 24-2. Bilateral paracentral scotomas are still present but improved from initial presentation.

many of the cases expect for possible hypofluorescence of some of the lesions.

The first report of mfERG in AMNR found the results to be unexpectedly normal.⁶ Following this initial report, however, multiple other reports described areas of decreased retinal function. These areas of electroretinographic depression corresponded to the visual field defects detected.^{2-4,13,24} Based on the findings from the mfERG the pathology in AMNR was believed to be localized to the outer retina or at the level of the photoreceptor cells.

The use of OCT in the setting of AMNR was first described by Feigl and Haas.⁶ The authors were able to show a high reflectivity band measuring about 115 μm situated in the inner most retinal zone, corresponding to the retinal pigment epithelium-choriocapillaris complex. This band was not consistently reported in subsequent cases of AMNR, however, focal macular thinning was noted.¹¹ Chan et al³ identified, in the acute phase, a thin back-scattering band between the photoreceptor cell outer and inner segments suggesting either outer segment swelling or localized collection of subretinal fluid. This finding disappeared on follow-up and was replaced by a localized thinning. Recently, Monson et al¹⁵ used ultra-high-resolution OCT in a case of AMNR and found that there was focal thinning of the outer retina, possibly at the level of the photoreceptor cell outer segments with distortion of the inner segment/outer segment junction.

Despite the many well-described clinical observations in AMNR, the cause of the disorder remains unknown. Some cases have been described in the setting of an upper respiratory tract (flu-like) illness prior to the visual loss suggesting a viral or immunological process.^{1,3,7,11,14,17-23} Other associated conditions have included shock,¹² postpartum hypotension,¹⁰ trauma,⁸ and heavy caffeine consumption.¹⁰ Kerrison et al¹⁰ speculated transient ischemia may be the culprit in the five cases they reported. They speculated that the central vision is spared due to the fact that the affected macular area has a high metabolic activity and benefits from a dual blood supply. In contrast, according to Turbeville et al,²² the fact that the retinal pigment epithelium adjacent to the red lesions is spared argues against a choroidal vascular problem.

Epinephrine has been identified as a potential causative agent of AMNR in four cases.^{5,16} Guzak et al⁹ reported two additional cases of AMNR following the administration of an intravenous contrast agent and intravenous sympathomimetics. However, in both cases the visual symptoms began prior to the administration of epinephrine. In addition, a review of 902 cases reported by the Federal Drug

Administration's adverse events reporting system regarding epinephrine from 1980 to 1997, disclosed three cases that were listed as "retinal disease" or "vision abnormality".² Desai et al⁵ speculated that an immunological reaction due to epinephrine may be occurring at the level of the photoreceptor cells rather than ischemia.

In summary, AMNR is a rare disorder characterized by the acute onset of unilateral or bilateral paracentral and/or ring scotomas sparing the central vision that occurs mostly in young women. It is often characterized by wedge-like macular lesions. The exact cause is unknown but viral, immunological, as well as ischemic etiologies have been hypothesized. The pathology is thought to be at the level of the outer retina or photoreceptor cells as demonstrated by mfERG and OCT. There is currently no treatment for the condition and the prognosis, as suggested by the available reports in the literature, is variable. Similar to what has been reported previously, our patient had areas of decreased macular function on the mfERG that corresponded to the perimetric visual field defects. Also on OCT there was a small focal area of an increased signal in the outer segment of the photoreceptor cells on presentation that was replaced, in a few weeks, by focal thinning and atrophy.

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Abstract. Acute macular neuroretinopathy is a rare disorder characterized by the sudden onset of unilateral or bilateral paracentral scotomas with relative sparing of the central vision that occurs mostly in young women. It is often characterized by wedge-like macular lesions. The cause of acute macular neuroretinopathy is unknown but viral, immunological, and vascular etiologies have been proposed. There is no current treatment and the visual prognosis is variable. We describe a young woman in whom this disorder was associated with the administration of epinephrine. (*Surv Ophthalmol* 54:618–624, 2009. © 2009 Elsevier Inc. All rights reserved.)

Key words. acute macular neuroretinopathy • epinephrine • OCT • paracentral scotoma