Paracentral Acute Middle Maculopathy
A New Variant of Acute Macular Neuroretinopathy
Associated With Retinal Capillary Ischemia

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IMPORTANCE With the advent of more sophisticated imaging systems, such as spectral domain optical coherence tomography (SD-OCT), disruption of the inner segment/outer segment (IS/OS) band, and thinning of the outer nuclear layer (ONL) have been identified in association with acute macular neuroretinopathy (AMN).

OBJECTIVES To characterize a new SD-OCT presentation of AMN as a paracentral acute middle maculopathy and to describe multimodal imaging findings that implicate an underlying pathogenesis related to retinal capillary ischemia.

DESIGN, SETTING, AND PARTICIPANTS Retrospective observational case series (January 1, 2012, to January 1, 2013) reviewing clinical and imaging data from 9 patients (11 eyes) with AMN at 6 tertiary referral centers. Lesions were classified as type 1 or 2 in relation to the SD-OCT location of the lesion above (type 1) or below (type 2) the outer plexiform layer (OPL) at 6 tertiary referral centers.

RESULTS Of the 9 patients, 5 were female and 4 were male (mean age, 47.6 years; range, 21-65 years). All patients presented with an acute paracentral scotoma and demonstrated a classic dark gray paracentral lesion with near-infrared imaging. Visual acuity ranged from 20/15 to 20/30. Six eyes (5 patients) had type 1 SD-OCT lesions, also referred to as paracentral acute middle maculopathy, and 5 eyes (4 patients) had type 2 SD-OCT lesions. Although type 1 lesions lead to inner nuclear layer (INL) thinning, type 2 lesions resulted in ONL thinning. Type 2 lesions were always associated with significant outer macular defects, including disruption of the inner segment/outer segment and outer segment/retinal pigment epithelium bands, whereas type 1 lesions spared the outer macula.

CONCLUSIONS AND RELEVANCE Paracentral acute middle maculopathy may represent a novel variant of AMN that affects the middle layers of the macula above the OPL as diagnosed with SD-OCT imaging. Two types of AMN lesions may be seen with SD-OCT occurring above and below the OPL. Type 1 refers to hyperreflective bands in the OPL/INL region with subsequent INL thinning. Type 2 is hyperreflective bands in the OPL/ONL region with subsequent ONL thinning. Type 2 lesions may be associated with concomitant defects of the inner segment/outer segment layer. We propose that each of these lesions may be explained by occlusion of either the superficial capillary plexus (type 1) or deep capillary plexus (type 2) located in the innermost and outermost portion of the INL, respectively, immediately adjacent to each corresponding lesion type.

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In the original description of acute macular neuroretinopathy (AMN), Bos and Deutman proposed that the characteristic red, wedge-shaped paracentral lesions of AMN involved the inner layers of the macula. With the advent of more sophisticated imaging systems, such as spectral domain optical coherence tomography (SD-OCT), disruption of the inner segment/outer segment (IS/OS) band was identified in association with AMN, and it was proposed that this disorder be renamed acute macular outer retinopathy. More recently, Fawzi et al performed complex multimodal imaging of 8 patients with AMN. Although outer macular lesions, including IS/OS and outer segment/retinal pigment epithelium (OS/RPE) defects and outer nuclear layer (ONL) thinning, developed in most of these eyes, 2 eyes in their series demonstrated more superficial involvement at the levels of the outer plexiform layer (OPL) and the Henle fiber layer (HFL) early in their course. Ischemia of the deep capillary plexus (DCP), located in the outermost portion of the inner nuclear layer (INL), was proposed as the cause of these early OPL lesions.

This report describes 6 eyes (5 patients) with a novel SD-OCT presentation of AMN in which lesions occurred above the OPL in the middle macular region that we have descriptively referred to as a paracentral acute middle maculopathy. We have also included in this study an additional 5 eyes (4 patients) with SD-OCT lesions identified below the OPL, affecting the outer macula and with multimodal imaging evidence of a vasculopathic or ischemic origin. We propose that retinal capillary ischemia affecting either the superficial capillary plexus (SCP) or the DCP may explain the development of either lesion, and we have classified each as either a type 1 (above the OPL) or type 2 (below the OPL) SD-OCT finding.

Methods

Institutional review board approvals were obtained commensurate with the respective institutional requirements. Research adhered to the tenets of the Declaration of Helsinki and was conducted in accord with regulations set forth by the Health Insurance Portability and Accountability Act.

We retrospectively reviewed the clinical and imaging data from 9 patients (11 eyes) with AMN evaluated at 6 tertiary referral centers, primarily focusing on multimodal imaging correlations. The diagnostic criteria of AMN included a history of acute-onset paracentral scotoma with or without decline in visual acuity and a nonprogressive course. All patients demonstrated classic parafoveal, dark gray, wedge-like lesions with near-infrared (NIR) reflectance and characteristic abnormalities with SD-OCT. We devised a simple classification system to reflect the primary location of SD-OCT lesions in AMN that affected the OPL/INL region of the middle macula (type 1) vs the OPL/ONL region of the outer macula (type 2) (Figure 1).

High-resolution digital color imaging, red-free (RF) photography, and fluorescein angiography (FA) were performed at the time of presentation for each patient. Initial NIR reflectance and SD-OCT examinations (Heidelberg Spectralis HRA+OCT; Heidelberg Engineering) were correlated with subsequent follow-up scans during each patient’s follow-up visit. We used the registration feature specific to the Heidelberg Spectralis HRA+OCT, which allows each OCT B scan to be coupled to its exact location on the NIR image, facilitating point-to-point correlations of the retinal findings between the NIR and OCT images.

In addition, patient 9 underwent adaptive optics (AO) imaging using the rtx1 AO retinal camera prototype (Imagine Eyes). The protocol used to capture images with this system has been previously described.

Report of Cases

Case 1

A 61-year-old white man presented with a 2-week history of a “gray spot” in his right eye just above fixation. He reported significantly higher levels of stress and increased consumption of coffee (10 cups daily compared with his previous amount of 5-7 cups daily) around the time of symptom onset.

His best-corrected visual acuity (BCVA) was 20/25 OD and 20/20 OS. Amsler grid testing elucidated a small paracentral scotoma superior to fixation in the affected eye. Ophthalmoscopic examination of the right eye revealed no obvious disease and a normal foveal reflex (Figure 2A). Similarly, the results of FA were unremarkable. However, RF photography revealed a subtle, wedge-like, dark gray lesion at the inferior fovea, which was better delineated with adjunct NIR imaging (Figure 2B and C). The registered SD-OCT through the lesion revealed a hyperreflective, plaquelike band at the junction of the OPL and INL that extended into the INL (Figure 2D and E), consistent with a type 1 lesion. The IS/OS was entirely intact.

![Figure 1. Proposed Classification of Acute Macular Neuroretinopathy](image-url)

<table>
<thead>
<tr>
<th>Level of Involvement</th>
<th>Outcome</th>
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<td>Type 1</td>
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<tr>
<td>OPL/INL junction</td>
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<td>Type 2</td>
<td>Atrophy of ONL</td>
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<td>OPL/ONL junction</td>
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OPL indicates outer plexiform layer; INL, inner nuclear layer; and ONL, outer nuclear layer.

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and the OS/RPE appeared attenuated because of a shadowing effect from the type 1 lesion above.

Follow-up SD-OCT examination 4 months after the patient’s initial presentation revealed a zone of severe INL thinning and markedly attenuated OPL where the hyperreflective lesion had been previously located (Figure 2 G and H). The deeper HFL had lost its optical reflex and appeared hyporeflective compared with the surrounding unaffected HFL. In addition, the dark lesion on NIR, as well as the shadowing it induced on SD-OCT, had dissipated (Figure 2F). The patient’s BCVA remained 20/25 OD, and the scotoma persisted, although it had decreased in size.

Case 2
A 65-year-old African American woman presented with a 1-week history of paracentral scotoma that she described as a “purplish pair of ragged lips” affecting her left eye. She denied any other visual symptoms or precipitating illnesses and had no significant medical history.

Her BCVA was 20/20 in the symptomatic left eye, whereas the fellow eye had a history of posterior staphyloma and amblyopia, with a BCVA of 20/60. The results of the remainder of her clinical examination were within normal limits. However, NIR imaging and near-infrared autofluorescence uncovered a dark, well-demarcated, nummular lesion at the nasal fovea in the left eye (Figure 3A and B). As in the previous case, the SD-OCT scan through this dark area revealed a hyperreflective band at the junction of the OPL and INL that extended into the INL (Figure 3C), consistent with a type 1 lesion, which similarly induced a shadowing effect on the deeper retinal layers. The IS/OS band was entirely intact.

The patient was followed up closely with serial SD-OCT examinations performed up to 30 weeks after the initial presentation (Figure 3D-G and J). The sequential scans demonstrated gradual resolution of the hyperreflective lesion, with subsequent progressive atrophy and severe thinning of the involved OPL and INL. These resulting atrophic changes induced a partial collapse of the overlying retinal structures, leading to the irregular foveal architecture observed, which was best appreciated on the final scan 30 weeks later (Figure 3J). At that visit, the visual acuity in the affected eye was stable at 20/20, and the NIR and NIA images were unremarkable (Figure 3H and I). As in the previous case, the underlying HFL again appeared to have lost its optical reflex and was hyporeflective relative to the normal adjacent HFL.

Case 3
A 56-year-old white man was referred for evaluation of paracentral scotomas in the left eye greater than the right eye of 6 weeks’ duration. Several days before the onset of his symptoms, he underwent a total left hip arthroplasty with an operative time of 6 hours, during which he required transfusion of 2 U of packed red blood cells because of severe blood loss. The patient had a complicated postoperative course that necessitated prolonged inpatient hospitalization. It was unknown whether he received pressor support during this period. Otherwise, his medical history was noncontributory.
Seven weeks later, the patient's subjective symptoms had improved. His BCVA was stable at 20/15 OD and had improved to 20/20 OS. With NIR reflectance, the macular lesions were lighter and less distinct (Figure 4G and O). The correlating SD-OCT scans revealed that the hyperreflectivity of the OPL and INL, although still present in both eyes, had decreased in size and intensity (Figure 4H, I, and P).

Case 4
A 60-year-old white man presented with a 2-day history of para- central scotoma in the right eye. He reported having symptoms consistent with a flulike illness approximately 1 week prior. His BCVA was 20/20 OU at the time of evaluation. Ophthalmoscopic examination of the symptomatic right eye revealed an ill-defined intraretinal white lesion (Figure 5A), which appeared similar with RF photography (Figure 5B). However, with NIR reflectance, the lesion appeared dark and more precisely delineated (Figure 5C). The SD-OCT imaging through the defect revealed a hyperreflective plaque at the junction of the OPL and INL that extended into the INL (Figure 5D), which cast a shadow over the outer retinal layers, consistent with a type 1 lesion. The IS/OS and OS/RPE bands were entirely intact.

Four weeks later, the patient returned and had improved symptomatically, although his BCVA remained stable at 20/20 OD. On follow-up NIR imaging, the dark lesion had dissipated (Figure 2E). Corresponding SD-OCT revealed a zone of severe INL thinning and an irregular, attenuated OPL (Figure 5F). The HFL underlying this OPL appeared hyporeflective compared with the adjacent unaffected HFL, similar to patients 1 and 2. Meanwhile, the shadowing of the outer retinal layers had resolved.

Case 5
A 54-year-old Middle Eastern man presented with a 2-day history of an inferonasal paracentral scotoma in the left eye. He denied any antecedent flulike prodromal illness and was otherwise healthy. His BCVA was 20/20 OU at the time of evaluation. Anterior segment examination results were within normal limits, but ophthalmoscopic of the left eye revealed a paracentral superotemporal intraretinal white lesion associated with a subtle intraretinal hemorrhage (Figure 6A). The remainder of the retinal examination findings were only remarkable for a few small macular drusen bilaterally. The RF photography helped better demarcate the borders of the white lesion (Figure 6B). Corresponding FA revealed a subtle blocking defect over the fovea of the intraretinal hemorrhage (Figure 6C) but other findings were otherwise unremarkable.

With NIR reflectance, the lesion appeared dark, with its borders more sharply outlined (Figure 6D). The registered SD-OCT image through the defect revealed a hyperreflective plaque at the junction of the OPL and INL that extended into the INL (Figure 6E), which cast a shadow over the outer retinal layers, consistent with a type 1 lesion. The IS/OS and OS/RPE bands were entirely intact.

Two weeks later, the patient returned and had improved symptomatically, whereas his BCVA remained stable at 20/20 OS. On follow-up NIR imaging, the dark lesion appeared lighter.
and less distinct than previously (Figure 6F). Similarly, the SD-OCT hyperreflective band was still present, although not as intense as it appeared on presentation (Figure 6G) and with associated thinning of the INL. The shadowing of the outer retinal layers had also resolved.

Case 6
A 33-year-old white woman was referred for a 5-day history of a central “spot” in her left eye. She denied any antecedent flu-like illness and was not taking any medications. Her medical history was significant for a previous episode of toxic shock syndrome.

Her BCVA at presentation was 20/20 OU. Ophthalmoscopic examination of the left eye revealed a pale, semitranslucent, teardrop-shaped lesion in the parafoveal region associated with a focus of intraretinal hemorrhage at its base (Figure 7A). A blocking defect secondary to the intraretinal heme was confirmed by FA, but otherwise the FA results were unremarkable (Figure 7B). The NIR reflectance better outlined the borders of the teardrop lesion, which appeared dark with this imaging modality (Figure 7C). The registered SD-OCT through the lesion revealed a hyperreflective band at the level of the OPL and ONL, with attenuation of the underlying IS/OS and OS/RPE layers (Figure 7D), consistent with a type 1 lesion. At 7-week follow-up, the lesions were lighter and less distinct on NIR (G and O). Corresponding SD-OCT (H, I, and P) revealed that the hyperreflectivity of the OPL and INL, although still present in both eyes, had decreased in size and intensity (arrows).

The patient was still symptomatic at her 2-month follow-up visit, whereas her BCVA remained intact at 20/20 OU. The pale lesion was no longer detectable by ophthalmoscopic examination, color photography, or FA, and the intraretinal hemorrhage had resolved (Figure 7, E and F). However, NIR imaging confirmed persistence of the lesion, although it appeared less prominent compared with the image obtained at her initial visit (Figure 7G). The SD-OCT revealed that the hyperreflective area had resolved, with subsequent thinning of the ONL overlying an attenuated IS/OS and OS/RPE complex (Figure 7H).
Case 7
A previously healthy 43-year-old white woman presented with a 4-day history of a paracentral scotoma she described as a “claw-shaped gray area” just temporal to fixation in her right eye. On examination, her BCVA was 20/20 OU. Ophthalmoscopy of the symptomatic right eye revealed a paracentral, well-circumscribed (arrow) lesion within the foveal avascular zone that appeared dark and well circumscribed on SD-OCT. Baseline color ophthalmoscopic (A) and red-free (B) images of the right eye revealed an ill-defined intraretinal white lesion, which appeared dark and well circumscribed (arrow) with near-infrared (NIR) reflectance (C). Corresponding SD-OCT revealed a zone of severe INL thinning (between top solid arrows) and an irregular, attenuated OPL (between bottom interrupted arrows), where the hyperreflective lesion had been previously located. The Heidelberg retina tomograph now appeared moderately hyperreflective compared with the surrounding unaffected HFL, whereas the shadowing effect on the deeper retinal layers had resolved.

Baseline color ophthalmoscopic (A) and red-free (B) images of the right eye revealed a well-demarcated wedge-shaped opacification nasal to fixation in the patient’s symptomatic right eye. On examination, her BCVA was 20/20 OU. Ophthalmoscopy revealed an ill-defined intraretinal white lesion, which appeared dark and well circumscribed (arrow) with near-infrared (NIR) reflectance (C). Corresponding SD-OCT revealed a zone of severe INL thinning (between top solid arrows) and an irregular, attenuated OPL (between bottom interrupted arrows), where the hyperreflective lesion had been previously located. The Heidelberg retina tomograph now appeared moderately hyperreflective compared with the surrounding unaffected HFL, whereas the shadowing effect on the deeper retinal layers had resolved.

Case 8
A 45-year-old white woman primigravid with twins was admitted during the 33rd week of pregnancy for observation and treatment of preeclampsia. Her blood pressure on admission was 150/90 mm Hg and became increasingly difficult to manage during the hospitalization, necessitating early induction of labor. Shortly after, the patient began to experience “blurry vision” in both eyes, prompting an inpatient ophthalmology consultation. Her BCVA was 20/25 OD and 20/30 OS at the time of evaluation. Amsler grid testing revealed a central scotoma in the left eye. Anterior segment examination results were within normal limits. Ophthalmoscopy demonstrated bilateral cotton-wool spots and red-brown discoloration of the central macula, greater in the left eye than in the right eye (Figure 9A and I). The NIR imaging revealed bilateral, well-demarcated, petaloid-shaped, dark gray macular lesions (Figure 9B and J). The SD-OCT corresponding to these areas revealed involvement of the HFL and ONL and patchy dropout of the IS/OS and OS/RPE lines in the right eye and pronounced attenuation of both layers in the left eye consistent with bilateral type 2 lesions (Figure 9C, D, K, and L). The results of FA were only remarkable for late, faint hyperfluorescent areas corresponding to the cotton-wool spots seen clinically (Figure 9E and M).

One month later, the patient thought her vision was improved but not yet back to baseline. Her BCVA was stable, and the scotoma in her left eye had decreased in density. Follow-up NIR imaging revealed persistence of the macular lesions, although the lesions appeared less intense with less distinct margins (Figure 9F and N). On SD-OCT, there was notable atrophy and thinning of the ONL bilaterally, and although the IS/OS and OS/RPE layers were still largely compromised, both eyes demonstrated patches of regenerating IS/OS (Figure 9G, H, O, and P).

Case 9
A previously healthy 21-year-old white woman was referred for evaluation of a central “bright spot” in the left eye for the previous 18 days. She had already been seen by a local retina specialist and neuro-ophthalmologist before her presenta-
tion and was told that the results of her ophthalmologic examination were normal.

Her BCVA was 20/20 OD and 20/25 OS. Anterior segment and retinal examination findings were grossly unremarkable, but color ophthalmoscopic imaging of the left eye revealed a barely detectable dark paracentral lesion (Figure 10A). The NIR reflectance of the left eye uncovered a small, wedge-shaped, dark-gray lesion that involved the superotemporal fovea (Figure 10B). The SD-OCT corresponding to the NIR defect revealed a subtle hyperreflective lesion that involved the OPL and ONL with associated focal disruption of the IS/OS and OS/RPE layers (Figure 10, D and E), which was consistent with a type 2 lesion.

A montage of 3 images of the left eye was acquired with the rtx1 AO retinal camera (Figure 10C). The dark lesion visualized on the NIR image corresponded to an area where fewer cones were visualized in the AO montage. Notably, the area of disruption of the cone mosaic on the AO montage was more widespread (Figure 10C) than the lesion visualized on the NIR image (Figure 10B). The cone mosaic reflectivity, contiguity, and spacing around the lesion appeared normal (no quantitative evaluation performed).

Three weeks later, the patient returned and had improved symptomatically, whereas the BCVA remained unchanged. Follow-up SD-OCT revealed partial reconstitution of the IS/OS and OS/RPE layers.

Results

The Table provides a detailed summary of the clinical data for each patient. Although type 1 lesions lead to thinning of the INL, type 2 lesions lead to thinning of the ONL. Type 2 lesions were always associated with significant outer macular defects, including obvious attenuation of the IS/OS and OS/RPE bands, whereas type 1 lesions failed to disrupt the integrity of the IS/OS junction. In our study, 6 eyes (patients 1-5) had type 1 lesions and 5 eyes (patients 6-9) had type 2 lesions. Note that although there was a significant age and sex difference between the 2 groups and a different level of OCT involvement, the demographic and clinical findings between the 2 groups were similar and consistent with the diagnosis of AMN for each case. Nevertheless, we have elected to describe type 1 lesions as a paracentral acute
middle maculopathy to reflect the unique SD-OCT level of
disease (Table).

Discussion

More sophisticated imaging systems have helped to redefine
the clinical presentation of AMN and have markedly en-
hanced diagnostic sensitivity. In some cases of AMN, ophthal-
moscopic abnormalities may be entirely absent, and color oph-
thalmoscopic photography findings may be essentially normal,
as in patients 1, 2, 3, and 9 in our study. Greater diagnostic re-
liance has shifted toward the use of NIR reflectance imaging
to demonstrate characteristic dark gray paracentral lesions that
typically point toward the foveal center.4,7-9 The SD-OCT may
reliably detect outer macular abnormalities, including IS/OS
and OS/RPE loss and ONL thinning.3,4,10

Recently, various authors4,7 have discovered that AMN le-
sions may develop at the junction of the OPL/ONL zones with
associated outer macular disruption. It is apparent from this
study that AMN lesions may even involve the middle layers of
the retina at the junction of the OPL and INL zones, a novel
SD-OCT presentation that we referred to as a paracentral acute
middle maculopathy. We identified 6 eyes with middle SD-
OCT lesions above the OPL (type 1) and 5 eyes with outer SD-
OCT lesions below the OPL (type 2).

Each lesion type may possibly be explained by retinal cap-
illary ischemia. In postmortem studies on human donor eyes,
Tan et al12 identified 4 different capillary networks in the hu-
man retina located in the following regions: nerve fiber layer,
retinal ganglion cell layer, junction of the inner plexiform layer
and superficial boundary of the INL (ie, the SCP), and junc-
tion of the deep INL and OPL (ie, the DCP) border. In our study
all type 1 lesions were noted on SD-OCT to extend from the bor-
der of the OPL to the most superficial edge of the INL, with sub-
sequent thinning of the INL. These type 1 lesions are pre-
cisely aligned with the SCP (Figure 11), and given the
vasculopathic risk factors associated with our patients with
type 1 lesions, we propose that occlusion of the SCP is the likely
origin for these lesions.

By contrast, type 2 lesions of the OPL/ONL region are more
closely aligned with the DCP. The OPL is composed of photo-
ceptor axon terminals, and this layer lies directly adjacent
to the DCP located in the outermost portion of the INL (Figure 11).
In the foveal and perifoveal areas, the HFL occupies a signifi-
cant portion of the outer OPL.12 The DCP provides 10% to 15% of the oxygen supply to the photoreceptor
population.13 The photoreceptor axon terminals are replete
with oxygen-dependent mitochondria as demonstrated by
Stone et al14 and may rely more heavily on the DCP for oxy-
gen supply than the photoreceptor inner and outer segments
located closer to the underlying choriocapillaris. A steady de-
crease of the diffusion gradient of oxygen from the choriocap-
illaris to the photoreceptor axons has been experimentally con-
firmed by Wangsa-Wirawan et al.15 As such, the OPL and the
region immediately below the OPL may act as a watershed zone
and may be especially vulnerable to ischemic insults to the DCP.
Subsequent axonal and outer segment disruption and death
may develop as evidenced by the IS/OS and OS/RPE abnormalities that develop with type 2 lesions (patients 6-9) on SD-OCT and is further confirmed by the presence of cone loss illustrated by AO imaging in patient 9.

It is well known that AMN is a disorder associated with various pressor agents or vasoconstrictors, including sympathomimetics, such as epinephrine, norepinephrine, ephedrine, or caffeine. It is possible that the use of sympathomimetics, as in patient 1 who admitted to heavy caffeine intake, may induce vasoconstriction of the SCP, leading to ischemia and development of the hyperreflective OPL/INL band (type 1 lesion) associated with AMN. Similar type 1 lesions developed bilaterally in patient 3, perhaps because of systemic hypotension and severe blood loss causing ischemia of the SCP. Thinning of the INL and ONL that ensues with type 1 and 2 lesions, respectively, appears to be a long-standing change that further reinforces the ischemic theory.

Retinal capillary ischemia is further supported by the presence of a dilated DCP as demonstrated by high-magnification FA in patient 7. Moreover, some cases of AMN may demonstrate an isolated intraretinal retinal hemorrhage in association with the wedge-shaped AMN lesion as illustrated in patients 5 and 6, further supporting a vascular occlusive or vasculopathic origin. In addition, patient 8 had classic paracentral petaloid NIR lesions diagnostic of AMN, likely the result of toxemia of pregnancy and associated hypertension. This
patient also demonstrated cotton-wool spots due to occlusion of the precapillary arterioles and infarction of the inner retina, and it is likely that the bilateral type 2 AMN lesions may be explained by capillary ischemia of the outer retina due to vaso-occlusion of the DCP.

If the ischemic insult is severe enough, photoreceptor and outer segment loss may ensue, as evidenced by OS/RPE and IS/OS defects (type 2 lesion) with SD-OCT and cone loss with AO imaging (patient 9). Ischemic infarcts may lead to permanent INL (type 1) or ONL (type 2) thinning and even outer segment loss (type 2) and may explain persistent paracentral field defects in some patients with AMN, including all of our patients, although follow-up was limited in some cases. Other ischemic insults to the SCP or DCP may be potentiated by trauma,24 shock,20,25 hypotension,26 or severe blood loss, as occurred in patient 3.

Limitations of our study include the retrospective nature of the case review and the small number (n = 11) of eyes studied, although this is one of the largest case series of AMN to date. Although we have provided clinical and anatomical evidence to support retinal capillary ischemia as the cause of AMN, this proposed mechanism has not yet been proven. Showing causality would require animal models of retinal capillary occlusion and subsequent demonstration of the characteristic findings of AMN with multimodal imaging.

The mean age of the 5 patients with type 1 lesions was 59.2 years (range, 54-65 years), whereas the 4 patients with type 2 lesions had a mean age of 33 years (range, 21-43 years). Moreover, patients with type 1 lesions tended to be male, whereas those with type 2 lesions tended to be female. Therefore, it is possible that the eyes that we have described as a paracentral acute middle maculopathy, or type 1 variant of AMN, may represent a novel macular disease altogether.

However, patients with type 1 and 2 lesions harbored many similar features of AMN, including demographic risk factors, such as vasopressor exposure; presenting symptoms, such as paracentral scotoma; presenting clinical findings, such as paracentral macular lesions that were dark gray with NIR; and hyperreflective SD-OCT lesions that affected
the OPL junction and could be explained by ischemia of the adjacent SCP (type 1) or DCP (type 2). It is more difficult to explain when a type 1 vs type 2 lesion will develop, but it is possible that younger patients may be more resistant to middle macular ischemia and may only be prone to watershed ischemic insults that affect the OPL/ONL region and the outer macula due to more severe vasculopathic injury. The consistent development of both type 1 and 2 lesions focally in the parafoveal region may be attributed to the greater density of the capillary network in this area.

Our suggested pathogenesis of focal retinal capillary ischemia would imply that AMN has little in common with any

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<th>Patient No./ Sex/Age, y</th>
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<td>6/F/33</td>
<td>Left</td>
<td>White</td>
<td>None</td>
<td>20/20</td>
<td>Paracentral</td>
<td>Semitranslucent teardrop lesion with hemorrhage</td>
<td>Teardrop, dark OPL/ONL, IS/OS, OS/RPE</td>
<td></td>
</tr>
<tr>
<td>7/F/43</td>
<td>Right</td>
<td>White</td>
<td>None</td>
<td>20/20</td>
<td>Paracentral</td>
<td>Wedgelike, white lesion</td>
<td>Wedgelike, dark OPL/ONL, IS/OS, OS/RPE</td>
<td></td>
</tr>
<tr>
<td>8/F/35</td>
<td>Right</td>
<td>White</td>
<td>Toxemia of pregnancy</td>
<td>20/25</td>
<td>Paracentral</td>
<td>Red-brown macular discoloration</td>
<td>Petoind, dark HFL/ONL, IS/OS, OS/RPE</td>
<td></td>
</tr>
<tr>
<td>F/35</td>
<td>Left</td>
<td>White</td>
<td>Toxemia of pregnancy</td>
<td>20/30</td>
<td>Paracentral</td>
<td>Red-brown macular discoloration</td>
<td>Petoind, dark HFL/ONL, IS/OS, OS/RPE</td>
<td></td>
</tr>
<tr>
<td>9/F/21</td>
<td>Left</td>
<td>White</td>
<td>None</td>
<td>20/25</td>
<td>Paracentral</td>
<td>Subtle, wedgelike, dark gray lesion</td>
<td>Wedgelike, dark OPL/ONL, IS/OS, OS/RPE</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AMN, acute macular neuroretinopathy; BCVA, best-corrected visual acuity; HFL, Henle fiber layer; INL, inner nuclear layer; IS, inner segment; NIR, near-infrared reflectance; ONL, outer nuclear layer; OPL, outer plexiform layer; OS, outer segment; RPE, retinal pigment epithelium; SD-OCT, spectral-domain optical coherence tomography.
of the other acute zonal occult outer retinopathy complex disorders, one of the hypotheses proposed by Gass,22,27-29 with which it has occasionally been grouped. Although the acute zonal occult outer retinopathy complex group includes conditions that are associated with IS/OS loss and subsequent reconstitution (eg, multiple evanescent white dot syndrome),30-32 it is clear from this case series and the one by Fawzi et al4 that middle macular disease involving the OPL region as demonstrated by SD-OCT may be a prominent form of the disease. These characteristic middle macular lesions and the association with various ischemic causes serve to clearly distinguish AMN from the acute zonal occult outer retinopathy complex group of disorders that are more likely autoimmune or inflammatory mediated. In summary, it appears that AMN is not nearly as rare a disorder as previously thought. The diagnosis of AMN has vastly improved with the use of multimodal imaging, including NIR imaging and SD-OCT. Two types of AMN lesions may be appreciated with SD-OCT analysis occurring above and below the OPL. Type 1 refers to hyporeflective bands in the OPL/INL region with subsequent INL thinning, which we describe as a paracentral acute middle maculopathy. Type 2 refers to hyporeflective bands in the OPL/ONL region with subsequent ONL thinning and outer macular disruption. We propose that each of these lesions may be explained by vasoconstriction or occlusion of the SCP (type 1) or DCP (type 2) located in the innermost and outermost portion of the INL, respectively, immediately adjacent to each corresponding lesion type.

ARTICLE INFORMATION
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Critical revision of the manuscript for important intellectual content: Sarraf, Rahimy, Fawzi, Sohn, Barbazetto, Mittra, Klancnik, Mrejen, Goldberg, Soerson, and Freund.
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Patient examinations: Beardsley.
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REFERENCES
Paracentral Acute Middle Maculopathy

Original Investigation Research


