OBSERVATION

Structural Changes in Acute Macular Neuroretinopathy Revealed With Adaptive Optics Optical Coherence Tomography

Acute macular neuroretinopathy (AMN) is a rare retinal disorder characterized by acute-onset paracentral scotomas with reddish-brown wedge-shaped lesions, with apices pointing toward the fovea in a teardrop or petalloid configuration.[1]

Adaptive optics (AO) imaging systems enable cellular-level resolution imaging of the human retina, achieving a transverse resolution of approximately 2 to 3 µm by compensating for ocular optical aberrations and permitting direct visualization of the individual cone photoreceptor mosaic and cell bodies in the human eye.[2] In previous AMN case studies using AO imaging,[3,4] photoreceptor damage at the AMN lesions was reported; however, the origin of hyporeflectivity in infrared reflectance (IR) has not been revealed.

Herein, we present a case of a patient with AMN with retinal structural changes using AO imaging to elucidate the origin of the IR hyporeflectivity lesion.

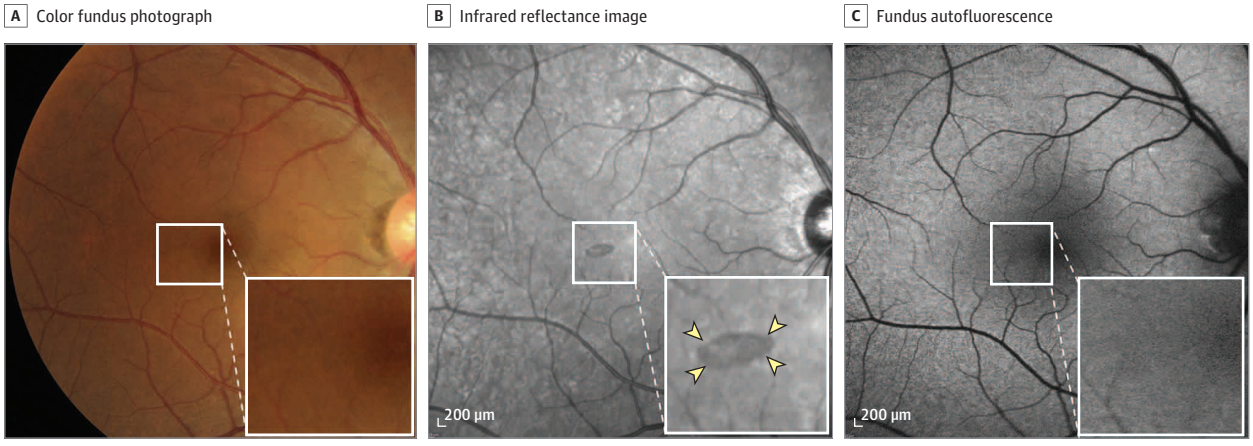
Report of a Case | A 33-year-old man presented to our clinic with a 3-day subacute history of a paracentral scotoma in the right eye. He reported a viral prodrome 2 weeks prior to the initiation of visual symptoms. The best-corrected visual acuity of the right eye was 20/20. Results of the anterior segment examination were normal. A classic dark-gray teardrop-shaped lesion was detected in the IR image but was unremarkable in the color fundus photograph and fundus autofluorescence images (**Figure 1**).

A horizontal spectral-domain optical coherence tomography (SD-OCT) B-scan showed focal reflectivity reduction of the ellipsoid zone (EZ), corresponding to a dark-gray lesion and hyperreflectivity at the Henle fiber layer (HFL) and outer nucleus layer (ONL) (**Figure 2**A). He also underwent examination using prototype confocal AO scanning laser ophthalmoscopy (AO-SLO) and AO-OCT imaging systems (Canon). The lateral resolution of AO-SLO and OCT imaging was approximately 3 µm, and the axial resolution of AO-OCT was 3.4 µm at the retina.[3] Confocal AO-SLO imaging showed disruption of the cone photoreceptor mosaic, which corresponded to the AMN lesion in the IR image (Figure 2A and B). AO-OCT revealed hyperreflective dots at the HFL and ONL and showed signal attenuation in the EZ and interdigitation zone (IZ; Figure 2B).

Two months later, the patient reported a slight persistent scotoma, and his best-corrected visual acuity had not decreased. A slight AMN lesion was detected in the IR image (Figure 2C). The SD-OCT scan showed almost complete restoration of the EZ. However, the reflectivities of the ONL and HFL were still prominent (Figure 2C). Confocal AO-SLO imaging showed recovery of the cone photoreceptor mosaic (Figure 2D), and AO-OCT showed recovery of the EZ; however, the IZ was not well restored and a few hyperreflective dots at the ONL and HFL were still observed (Figure 2D).

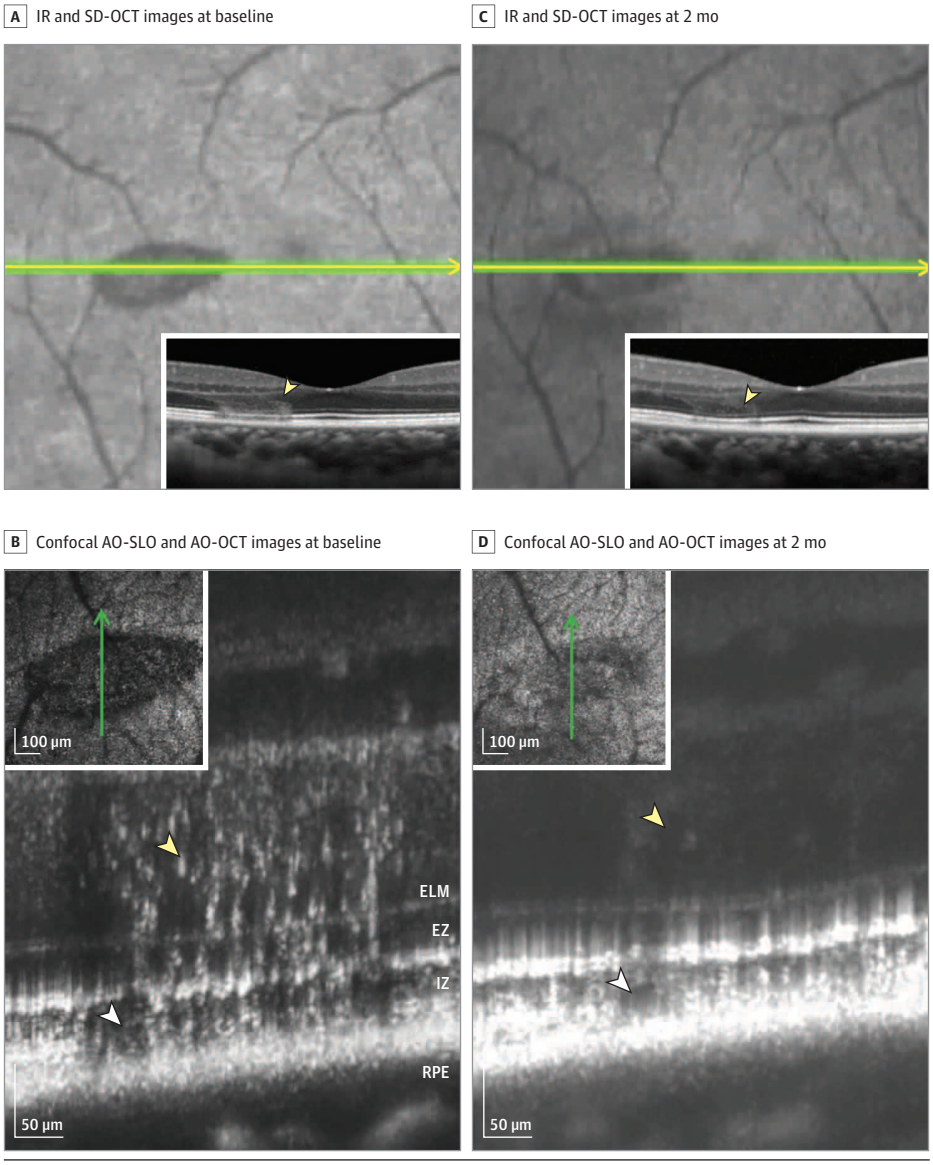
Discussion | We report a case of AMN using AO-SLO and AO-OCT imaging. We observed photoreceptor damage in the AO-SLO image, which appeared to be identical to the dark IR lesion. Moreover, cross-sectional AO-OCT imaging revealed IZ damage rather than EZ damage in the photoreceptor damaged area seen in the AO-SLO image. Although the hyperreflective dots in the HFL may attenuate the reflectivity of the IZ, we speculated that the hyporeflectivity in the IR image represents the cone outer segment tip damage. The HFL contains bundles of unmyelinated cone photoreceptor axons terminating in the

Figure 1. Multimodal Imaging of Acute Macular Neuroretinopathy (AMN)



A, An AMN lesion is unremarkable in the color fundus photograph. B, Infrared reflectance image showing a classic dark-gray teardrop-shaped AMN lesion (arrowheads). C, The AMN lesion is not detectable in the fundus autofluorescence image.

Figure 2. Adaptive Optics (AO) Imaging of Acute Macular Neuroretinopathy (AMN)



A, At baseline, spectral-domain optical coherence tomography (SD-OCT) shows hyperreflectivity in the Henle fiber layer (HFL) at the AMN lesion (arrowhead). B, Confocal AO scanning light ophthalmoscopy (AO-SLO) visualizes the focal cone photoreceptor mosaic loss that appeared to be correlated with the infrared (IR) image (A). In the vertically scanned AO-OCT image (green arrow), reflectivity attenuation is observed both in the ellipsoid zone (EZ) and interdigitation zone (IZ). However, the signal attenuation is more severe in the IZ than in the EZ (B, white arrowhead). At the level of the HFL, multiple hyperreflective dots are observed (yellow arrowhead). C, Two months later, the hyperreflectivity in the HFL on SD-OCT did not recover well (arrowhead). C and D, In the IR and confocal AO-SLO images, the IR reflectivity and the cone photoreceptor mosaic became apparent again. However, the reflectivity was still attenuated. D, Unlike the more normal appearance of the EZ, the IZ was not readily apparent in the AO-OCT image (white arrowhead). The multiple hyperreflective dots observed in the HFL at baseline decreased but were still slightly visible (yellow arrowhead). ELM indicates external limiting membrane; RPE, retinal pigment epithelium.

pedicles and spherules that synapse in the OPL.[5] The vertically scanned AO-OCT revealed multiple hyperreflective dots within the HFL. We speculated that each hyperreflective dot might represent inflammation-related swelling of the photoreceptor axons propagated from IZ inflammation.

In conclusion, hyporeflectivity in the IR image represents IZ damage, and hyperreflectivity of the HFL on OCT may correspond to abnormalities of the photoreceptor axons potentially propagated from IZ inflammation, although no definitive inflammation was noted.

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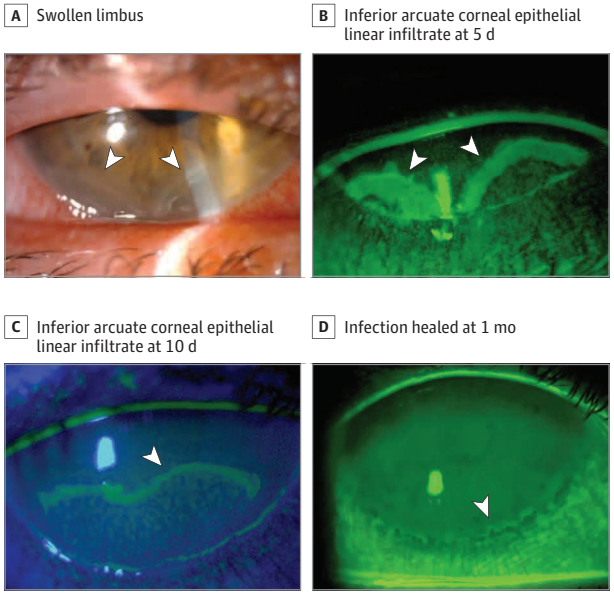
Severe Corneal Involvement Associated With Mpox Infection

Since April 2022, an outbreak of mpox (formerly monkeypox) has been unfolding. Ocular involvement seems rare[1] with mainly periocular vesicles, blepharitis, and ulcerative conjunctivitis.[1-4] We report 2 cases of severe corneal involvement during mpox infection.

Report of Cases | *Case 1.* A 34-year-old immunocompetent man developed vesicles on the penis, perineum, and right eyelid. Results of polymerase chain reaction (PCR) test for mpox was positive. After 3 weeks, he developed unilateral red, painful right eye and was unsuccessfully treated with ofloxacin, 0.3%, and dexamethasone, 0.1%, eye drops 4 times a day and oral valaciclovir 3 g per day. He consulted our department after 5 days. Vision was 20/20 OU. Right eye examination showed inferior lid cutaneous ulceration, hyperemic swollen conjunctiva and inferior limbus, and 2 inferior arcuate epithelial corneal infiltrates that stained with fluorescein (**Figure 1**A and B). Left eye was normal. Corneal PCR test returned positive for mpox. Trifluridine, 1%, eye drops 4 times a day were prescribed and steroids stopped. Patient refused systemic treatment for mpox. After 5 days, the corneal lines had merged and progressed toward the center, leaving a grayish epithelium (Figure 1C). Because of ocular pain, the patient self-administered oral prednisone 30 mg per day for 7 days. The cornea healed after 3 weeks without visible scars but with mild limbal neovascularization and thickening (Figure 1D). Vision remained normal.

Case 2. A 30-year-old immunocompetent man was hospitalized in our infectious diseases department with fever, vesicles on the penis and the right eyelids, and a red right eye. Skin mpox PCR test result was positive. Nine days later, he was referred to our ophthalmic department because ocular symptoms worsened with intense pain, photophobia, and mucous discharge in the right eye, despite ganciclovir, 0.15%, eye drops 4 times a day. Vision was 20/25 OD and 20/20 OS. Left eye examination results were normal. Right eye examination disclosed vesicles on both eyelids, major conjunctival inflammation with ulcerations and pseudo membranes, and superior and inferior limbal swelling. Because of the eye, a single intravenous cidofovir infusion (5 mg/kg) was administered and topical dexamethasone, 0.1%, and trifluridine, 1%, 4 times a day were started. Systemic infection was controlled at day 16, but keratitis evolved with inferior and superior arcuate fluorescein positive epithelial lines that migrated from the limbus to the center (**Figure 2**A and B). Corneal mpox PCR test result at day 25 was positive, thus a new infusion of cidofovir and oral tecovirimat 1200 mg per day for 30 days were administered. Topical steroids were stopped but not for long because pain recurred rapidly. Epithelial lines merged inferiorly within 6 weeks (Figure 2C). After 2 months of evolution, ocular infection had resolved, leaving an inferior linear subepithelial corneal scar (Figure 2D), and superior and inferior limbal stem-cell deficiency with corneal neovascularization. Central corneal epithelium was hazy and visual acuity was 20/32.

Figure 1. Case 1



Right eye: swollen limbus and inferior arcuate corneal epithelial linear infiltrate (white arrowheads) at 5 days (A and B) and 10 days (C), after beginning of the ocular symptoms. Note the serpiginous centripetal evolution leaving a greyish irregular epithelium behind (A) and the inferior limbus thickening and neovascularization after infection healed at 1 month (D, white arrowhead).

Discussion. During the 2022 mpox outbreak, corneal infection seems rare[1] occurring in 2 of 588 patients with mpox (0.3%) at our infectious disease unit between May and October and in 4 of 26577 mpox cases in the US.[3] Only 4 cases have been reported in the literature:1 geographic ulcer,[5] 1 serpiginous linear centripetal keratitis,[6] and 2 undescribed cases.[3] Our cases suggest that arcuate serpiginous centripetal epithelial keratitis, as described by Finamor et al,[6] is specific to mpox. We have not observed such a pattern in other viral diseases. Delayed infection of the cornea may be caused by initial lid margin infection.