

News in Review

COMMENTARY AND PERSPECTIVE

RETINA

Acute Macular Neuroretinopathy and COVID-19

ACUTE MACULAR NEURORETINOPATHY (AMN) is a rare, poorly understood retinal disease that most commonly occurs in young, healthy women. Now, based on findings of the largest case series to date, researchers report a possible association between AMN and COVID-19.¹

Although the relationship between the two processes remains theoretical, both have been associated with microthrombi as well as being preceded by respiratory or influenza-like illness. Established associations with AMN include the use of oral contraceptives, antecedent trauma, injections of epinephrine and pseudoephedrine, and pregnancy-induced hypertension.

“AMN has not been confirmed to be a sequela of COVID infection, but we believe it may be in certain individuals, which is why we felt it important to publish these data,” said Brian K. Do, MD, who practices in Chevy Chase, Maryland.

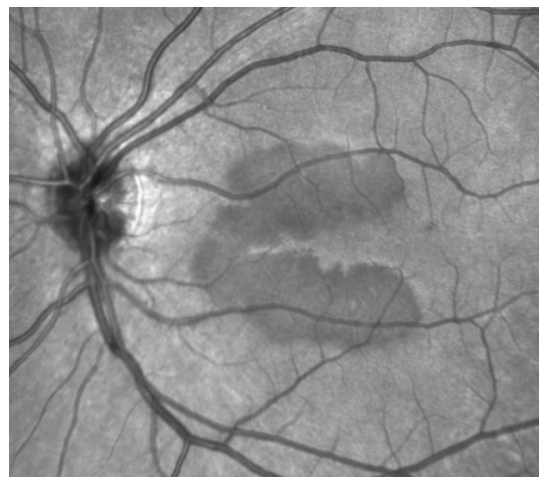
Retrospective case series. The findings are based on data from 25 eyes of 15 patients seen at eight referral centers from November 2020 to June 2022. All had concomitant symptomatic COVID-19 infection and AMN, which was diagnosed by one or more imaging modalities.

The patients’ mean age was 24 years, and most (80%) were female. All had

paracentral scotomas. Ten (67%) had bilateral disease, and four (27%) also presented with headache. All but one (93%) had symptoms of COVID-19 within two days of onset of symptoms of AMN. On average, their ocular symptoms began one day after they began experiencing COVID-19 symptoms.

Only two patients presented with decreased VA. One was a 19-year-old woman who was on oral contraceptives. Two weeks after she tested positive for SARS-CoV-2, she presented with central scotomas and VA of 20/125 in her right eye and 20/450 in her left. She stopped taking the oral contraceptives and was managed with prednisone; within a week, her vision was 20/25 in both eyes. The second case involved an 11-year-old girl with VA of 20/125 in both eyes. She was concurrently diagnosed with panuveitis, which the researchers suspect was the main contributor to the visual loss.

Building on earlier data. The report includes data from earlier case series, thus creating the largest compilation of cases to date—43 eyes in 29 patients. Earlier reports had far fewer bilateral events and fewer female patients; in addition, some cases were noted months after COVID-19 infection. Nevertheless, the rates from the different series were not markedly different, Dr. Do said. “The point is that there are relatively high rates of bilateral involvement, and that these problems can arise in anyone.”



SEQUELA OF COVID? Near-infrared imaging demonstrating a large perifoveal lesion in an individual with acute macular neuroretinopathy associated with COVID-19 infection.

More than coincidence? While the report involves only a small number of cases, the authors noted that the association is strengthened by the short time frame between the onset of ocular symptoms and COVID diagnosis.

They acknowledged that, because of AMN’s rarity, it is difficult to assess whether its incidence truly increased during the COVID pandemic. However, they cited an earlier retrospective study that found AMN diagnoses rose from .66 per 100,000 visits in 2019 to 8.97 per 100,000 in 2020.²

Dr. Do stressed that the latest study does not suggest a causal relationship between COVID-19 and AMN. However, he said, the temporal relationship between COVID-19 symptoms and the onset of visual symptoms and associated retinal imaging findings suggests that AMN “may be more than just a coincidence.” —Miriam Karmel

1 Dinh RH et al. *Ophthalmol Retina*. Published online Oct. 7, 2022.

2 Azar G et al. *J Clin Med*. 2021;10(21):5038.

Relevant financial disclosures: Dr. Do—None.

OCT Centers: Role in Glaucoma Screening?

COULD OCT READING CENTERS BE useful for determining glaucoma referability and increasing agreement among glaucoma specialists? The answer may be yes, according to recent research out of New York University.¹

In this retrospective exploratory study, researchers compared glaucoma referral patterns of three independent glaucoma specialists based upon a comprehensive teleophthalmology screening protocol.² They then compared these patterns to referrals made by two OCT report specialists on the sole basis of the OCT.

“The literature has demonstrated interobserver variability in glaucoma referral, approximately 15% on average,” said coauthor Lama Al-Aswad,

MD, MPH, CEO of Visi Health Technologies and EnVision Health Technologies in New York City. “This is a problem in community screening because, in general, we don’t want a lot of false positive or unnecessary referrals.”

Mobile screening project. The study included data on 243 individuals (483 eyes) who were evaluated during a mobile van community screening project that took place in 2017 in several New York City neighborhoods. The participants (mean age, 59.4 years) were predominantly Black or Hispanic, and 50% were female. They underwent comprehensive ophthalmic evaluations, including anterior segment OCT to evaluate the angle and posterior segment OCT to evaluate the macula and optic nerve.

For this study, three glaucoma specialists independently evaluated the collected data to determine whether they would recommend a further glaucoma workup. To simulate a reading center, two OCT report specialists evaluated

only the OCT image for each eye using the commercial report and a specialized custom report. They then looked at the effect of making the OCT specialist custom reports available to the glaucoma specialists.

Results. Intergrader agreement between glaucoma specialists and between OCT report specialists was 60% ($k = 0.43$) and 95% ($k = 0.77$), respectively. The glaucoma specialists determined that 25% of cases were referable for further workup, while the report specialists recommended that 1% be referred. With the availability of the OCT report specialist’s judgments in the second phase of the analysis, overall agreement increased to 85% ($k = 0.53$).

Surprising findings. “In our study, we showed that there is less variability in the interpretation when adding a customized OCT report,” Dr. Al-Aswad said. “These findings were unexpected.” Moreover, she said, “I personally did not think that having a customized

CATARACT

Emergency Visits After Cataract Surgery

WHY DO SOME PATIENTS SEEK EMERGENCY CARE AFTER their cataract surgery? According to a Duke University study, younger age, longer case times, and retrobulbar or general anesthesia plus monitored anesthesia care (MAC) were significantly associated with visits to the emergency department (ED) within 30 days of cataract surgery.¹

“Recognizing the risk factors for ED visits after cataract surgery can help us manage patients in the early postoperative period to prevent unplanned health care utilization and reduce treatment costs,” said Sahil Aggarwal, MD, at Duke Eye Center in Durham, North Carolina. “Mitigating these risk factors can also reduce complications and improve patient satisfaction after cataract surgery.”

Study rationale. “Prior to this study, we saw a small number of patients who had ophthalmic surgeries and presented to the ED within a few weeks, but almost none of these patients were admitted,” said Dr. Aggarwal.

To better understand this phenomenon, the team investigated the risk factors for postoperative ED visits in 34,246 patients who underwent cataract surgery from 2013 to 2021. “We hypothesized that most ED visits would result from nonocular causes and that the

complexity of surgery might predict the risk of postoperative ED visitation,” Dr. Aggarwal said.

Who’s at risk? Only 607 (1.77%) of the cataract patients visited the ED within 30 days of surgery. Most of these visits were due to cardiovascular complaints (24.4%). Only 15.4% of ED visits were associated with ocular issues, most commonly high IOP, rebound iritis, and posterior vitreous detachment.

Younger patients (<70 years of age) were more likely than older patients to seek emergency care (OR, 1.39). This may be because younger patients are less likely to have a primary care provider and thus are more likely to turn to the ED when they need care, Dr. Aggarwal noted. Longer case length (>30 minutes) also increased the odds of ED visits (OR, 2.1), as did the combination of MAC and retrobulbar or general anesthesia (OR, 2.98). Case length provides an indication of complexity, and “longer cases may lead to greater inflammation, IOP variability, and anesthesia-related complications,” Dr. Aggarwal said.

Looking ahead. “Prospective studies of the preoperative history of patients are needed to validate risk factors for postoperative ED visits,” Dr. Aggarwal said. He added that the Duke team plans to examine risk factors for ED visits after glaucoma, cornea, and retina surgeries.

—Christos Evangelou, PhD

1 Aggarwal S et al. *Am J Ophthalmol*. 2023;245:1-7.

Relevant financial disclosures: Dr. Aggarwal—None.

report or an OCT specialist would differ from the glaucoma specialists' decision, because we are experts in OCT readings. I didn't think that would affect our decision-making or increase interobserver agreement."

Future implications. Based on the findings, Dr. Al-Aswad said, "If you are going to use one tool for glaucoma screening in a large community screening, OCT may be the tool to use."

Dr. Al-Aswad said the findings "suggest a role for an OCT reading center, similar to a radiology reading center," and she highlighted the importance of community glaucoma screening to decrease the burden of eye disease. "There is still a lot of work to be done in this field," she noted. "In addition, we really need to better define glaucoma as a disease for us to be able to create protocols and standards for glaucoma referrals."

—Patricia Weiser, PharmD

1 Ramachandran R et al. *Ophthalmol Glaucoma*. 2023;6(1):602-613.

2 Al-Aswad L et al. *Asia Pac J Ophthalmol*. 2021; 10(5):461-472.

Relevant financial disclosures: Dr. Al-Aswad—New World Medical: S; Research to Prevent Blindness: S; Russell Barrie Foundation: S; Save Vision Foundation: S; Topcon: S.

IMMUNOLOGY

Eyedrops Change Surface Microbiota

BENZALKONIUM CHLORIDE (BAK) IS the most frequently found preservative in eyedrops. Now researchers report a possible link between preservatives, which are intended to prevent growth of pathogenic bacteria in medication bottles, and microbial changes that may put the ocular surface at greater risk for inflammation.¹

For this study, the researchers evaluated the impact of topical glaucoma medications. "We found that glaucoma patients taking IOP-lowering drops [with preservatives] had an altered ocular surface microbiome compared to age-matched subjects without a history of glaucoma or use of eye-

drops," said Bryan J. Winn, MD, at the University of California, San Francisco. "These glaucoma patients had fewer of the normal commensal bacteria that we think are important for maintaining ocular surface homeostasis."

Comparing three groups. For this study, the researchers conducted ribosomal RNA sequencing on ocular surface swabs collected from both eyes of 17 participants. Ten patients had asymmetric/unilateral glaucoma and were being treated with a variety of topical eyedrops containing BAK on one eye. Seven age-matched healthy controls had no history of ocular disease or eyedrop use.

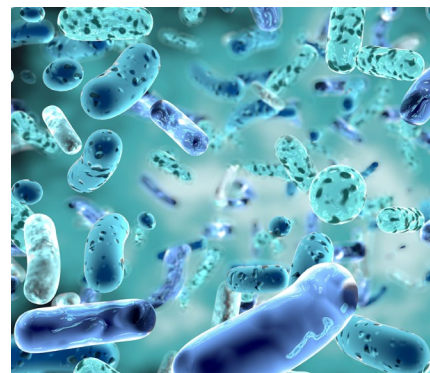
The samples were categorized into three groups: 1) patients' glaucomatous eyes treated with eyedrops (n = 10), 2) a control group of the patients' contralateral untreated eyes (n = 10), and 3) a secondary control group of healthy eyes (n = 14). The researchers compared microbial diversity and composition, with differences tested for association with ocular surface disease measures.

Effect on the microbiota. The microbial composition of treated eyes was distinct from that found in healthy controls. Specifically, treated eyes had a highly diverse array of bacteria that was significantly different from the less diverse microbes found on the eyes of healthy controls.

In an unexpected finding, ocular surface changes occurred in both treated and contralateral untreated glaucomatous eyes. This may indicate that the ocular surface microbiome is a "bilateral microbial niche," Dr. Winn said. In other words, changes or perturbations that occur in one eye may have bilateral effects.

Other findings. In other findings, treated eyes were found to have decreased tear meniscus height and tear break-up time. In addition, results of genome inference analysis suggested that the ocular surface microbes of treated eyes had a greater capacity for inducing inflammation than those of healthy controls.

Is BAK to blame? Patients were treated with a variety of eyedrop for-



MICROBIAL COMPOSITION. Treated eyes had a highly diverse array of microbes on their ocular surface, including *Bifidobacterium*.

mulations, yet all eyes exhibited similar changes to the ocular microbiome. In addition, neither the duration nor the frequency of glaucoma therapy was associated with differences in ocular bacterial diversity or microbiome composition. "These findings suggest that an ingredient common to all drops, and not the active medication ingredient, may be responsible for inducing the changes to the microbiota," Dr. Winn said.

Follow-up study. Are the findings relevant to other drops with preservatives, such as those recommended for dry eye? "That is one of our concerns and is an avenue we are investigating," Dr. Winn said. "The greatest number of drops used, including those available over the counter, are for the treatment of dry eye. If preservatives disturb ocular surface homeostasis via microbiome alterations, it may lend even more support for using nonpreserved alternatives."

Dr. Winn added, "We think the most plausible explanation for our findings is that a constant application of a detergent-like preservative to the ocular surface alters the ocular surface microbiome, but prospective studies are needed to confirm this."

—Miriam Karmel

1 Chang CJ et al. *Invest Ophthalmol Vis Sci*. 2022; 23(9):32.

Relevant financial disclosures: Dr. Winn—Columbia University: P.

See the financial disclosure key, page 8. For full disclosures, including category descriptions, view this News in Review at aao.org/eyenet.