GETTING A GOOD LOOK AT UVEITIS WITH MULTIMODAL IMAGING

Many options for use in diagnosing and treating patients with inflammatory conditions.

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Uveitis is one of the major causes of visual impairment and blindness, accounting for 10% to 25% of worldwide total blindness.[1] Uveitis most commonly affects the working-age population, with a prevalence estimated to be approximately 114.5 per 100,000 general population.[1-3] If left untreated, the condition can result in significant vision loss in roughly 35% of affected individuals.[2]

Given the high burden of disease, timely diagnosis and treatment is of utmost importance. Evaluation of patients begins with a thorough clinical examination and comprehensive medical history. Multimodal imaging plays an important role in establishing a diagnosis and in monitoring a patient's response to treatment.[4] Multimodal imaging provides important information by displaying and documenting subtle retinal or choroidal lesions, inflammation of retinal vessels and the optic nerve, retinal ischemia, and cystoid macular edema (CME).[5] This article reviews the most common imaging modalities used by retina specialists in patients with infectious and noninfectious uveitis.

Figure 1. Widefield fundus photo of the left eye of a 56-year-old woman with a 3-week history of blurriness and pain. Polymerase chain reaction of aqueous humor revealed the presence of varicella zoster virus particles.

AT A GLANCE

- Multimodal imaging plays an important role in establishing a diagnosis of uveitis and monitoring response to treatment.
- Multimodal imaging enables visualization of subtle retinal and choroidal lesions, inflammation of retinal vessels and the optic nerve, retinal ischemia, and CME.
- Further research is needed to automate quantification of posterior and anterior segment inflammation.

SURVEYING THE OPTIONS

Color Fundus Photography

Color photos are helpful in documenting anterior segment, retinal, and choroidal lesions. They can also be helpful in monitoring progression of

Figure 2. A 37-year-old man presented with decreased vision and photopsia in his left eye. Fundus imaging showed an area of fibrosis with protrusion of larvae into the vitreous. Serologies were positive for *Baylisascaris procyonis*.

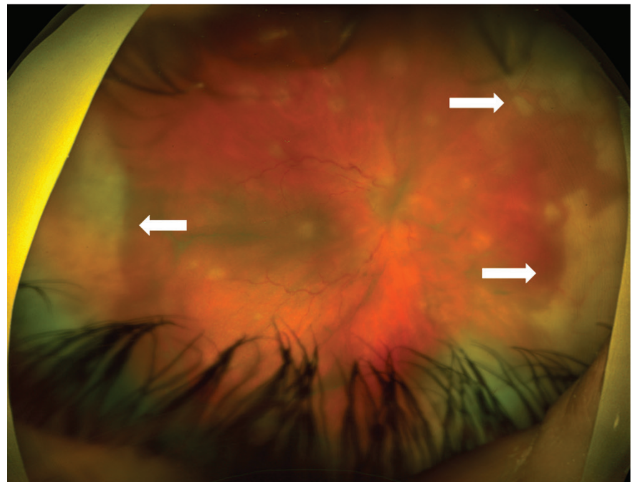

Figure 3. A 16-year-old male presented with redness in his right eye. Examination was limited due to history of developmental delay and cerebral palsy. A widefield fundus photo showed areas of peripheral retinal whitening and necrosis (arrows). Polymerase chain reaction of aqueous humor confirmed the presence of herpes simplex virus particles in the eye.

the disease, size of the lesions, appearance of new lesions, and response to treatment (Figure 1). As treatment progresses, color photos can be used to document the progress of lesion regression. In rare cases of diffuse unilateral subacute neuroretinitis, motile larvae are often found more easily on color fundus photography with good sweeps, leading to a definitive diagnosis (Figure 2).[6] We tend to prefer regular color photos with sweeps over widefield images that are in false color, as the larvae are seen more easily.

Ultra-Widefield Imaging

Standard fundus cameras capture 30° to 55° images, and peripheral sweeps and seven- or nine-field montage images are often used to increase the field of view.[7] However, it has been shown that conventional images may miss peripheral pathology 30% of the time, despite use of nine-field montages.[5] Ultra-widefield (UWF) imaging technology enables visualization of up to 200° of the fundus in one shot, 1.5 times the field of view of a conventional nine-field montage.[7,8]

UWF imaging is especially useful in managing pediatric patients. The Optos UWF imaging systems require less patient cooperation compared to regular fundus cameras and can be used to get an image in an otherwise uncooperative child, facilitating accurate diagnosis and treatment while decreasing the need for examination under anesthesia (Figure 3).[10]

Fluorescein Angiography

Sodium fluorescein is an orange-red dye with a molecular weight of 376 Da and is 80% bound to protein (mainly albumin). The unbound portion emits fluorescence.

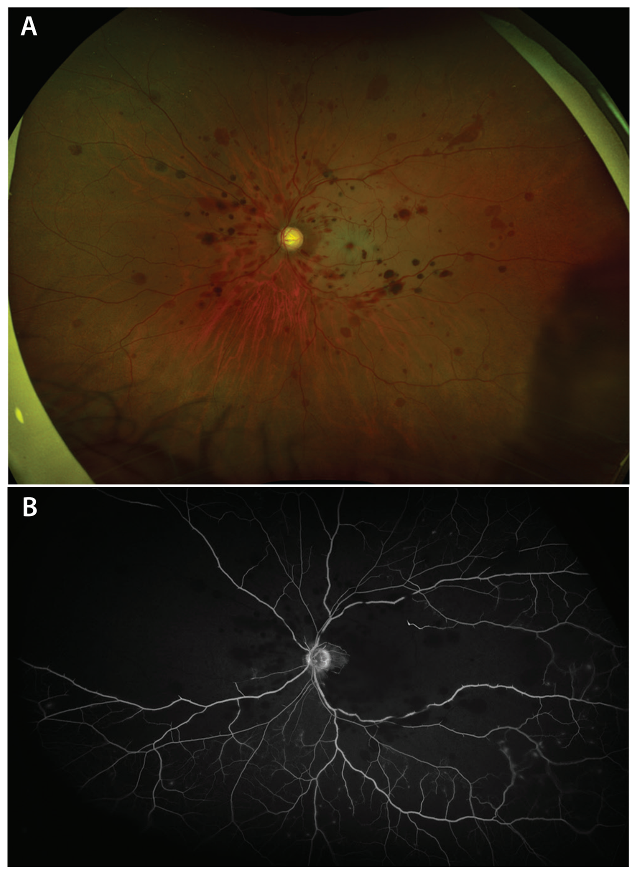

Figure 4. A 61-year-old black man presented with sudden onset vision loss to hand motion in his left eye. Fundus examination revealed multiple areas of intraretinal and subretinal hemorrhage and retinal edema (A). Widefield FA showed multiple branch retinal artery occlusions and retinal vasculitis, mainly involving arteries (B, arrows).

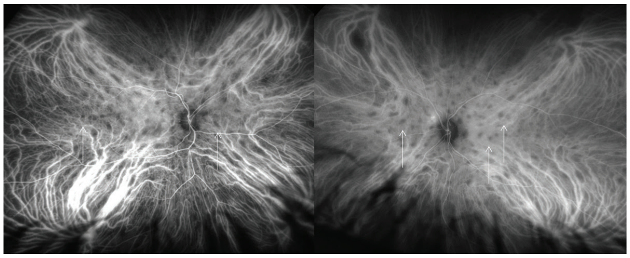

Figure 5. A 40-year-old white woman presented with decreased vision and photopsia in each eye. ICGA showed multiple subretinal hypofluorescent birdshot (vitiliginous) lesions in each eye (arrows). Lab workup revealed the presence of HLA-A29+.

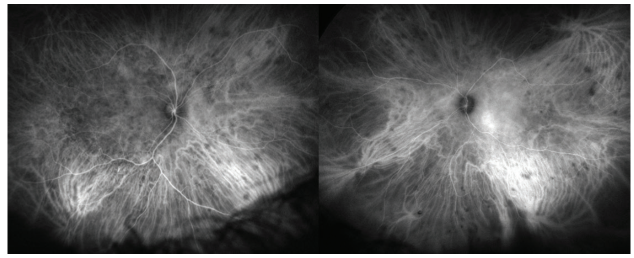

Figure 6. A 34-year-old black man presented with a 5-week history of blurry vision and photosensitivity in each eye. The presence of subretinal hypofluorescent lesions was noted in each eye with ICGA. Chest x-ray confirmed the presence of hilar lymphadenopathy and a diagnosis of sarcoidosis.

Sodium fluorescein is excited by blue light (465-490 nm) and fluoresces green light (520-530 nm). The free dye readily diffuses through the choriocapillaris. In a normal retina, the tight junctions of retinal endothelial cells and the zonula occludens of adjacent retinal pigment epithelial cells prevent leakage of dye to the retina. In uveitis this barrier is compromised.[11,12]

Fundus fluorescein angiography (FA) is widely used in the diagnosis and follow-up of patients with uveitis and retinal vasculitis. Abnormal patterns on FA can present as hypo- or hyperfluorescence. Hypofluorescence can be secondary to vascular filling defects and ischemia or blockage of fluorescein (by blood, vitreous opacities, pigment, etc.). Hyperfluorescence is caused by transmission (window) defects, staining, leakage, or pooling of fluorescein.

In uveitis, FA is helpful in diagnosing retinal vasculitis, differentiating active versus inactive disease by change in leakage pattern, differentiating occlusive versus nonocclusive vasculitis, evaluating optic nerve inflammation, and detecting retinal ischemia and the presence of CME or neovascularization.[4,5,9,11] UWF FA detects pathology in the periphery that is not visualized by conventional FA, potentially altering the approach to management (Figure 4).[5]

Indocyanine Green Angiography

Indocyanine green is a larger molecule (775 Da) than fluorescein, with peak light absorption at 795 nm and emission at 830 nm. Indocyanine green is also mostly protein-bound (98%). These properties result in less dye leakage through choroidal vessels and better visualization of the choroidal vasculature.[13]

Indocyanine green angiography (ICGA) is used to evaluate choroidal inflammation and lesions that are not visible or are subtle on clinical examination in patients with uveitis. Active choroidal inflammation presents as hypocyanescent spots on ICGA that can disappear with treatment.[14] The appearance and distribution of these spots may also help with diagnosis: They are more uniform in size in birdshot chorioretinopathy, sympathetic ophthalmia, and Vogt-Koyanagi-Harada syndrome and, by comparison, are variously sized and irregular in sarcoidosis and tuberculosis (Figures 5 and 6).[15]

In acute posterior multifocal placoid pigmentary epitheliopathy, or APMPPE, inflammation and involvement of the choriocapillaris results in choroidal ischemia, which presents as hypocyanescent patches on ICGA whether the disease is active or inactive, but the lesions decrease in size as the disease becomes inactive. In contrast, FA of APMPPE shows early blockage and late hyperfluorescent staining of the edges of the lesion in active disease, which turn into transmission defects as the disease becomes inactive.[12]

OCT

OCT is one of the most widely used imaging modalities in ophthalmology. This noncontact, noninvasive technology provides high-resolution cross-sectional images of the retina, choroid, and anterior segment. In uveitic eyes, OCT is helpful in determining ideal management protocol and predicting visual outcomes. CME, neurosensory detachment, and epiretinal membrane can be visualized on OCT more readily than with clinical examination. OCT is helpful in evaluating the integrity of the photoreceptor ellipsoid zone (EZ) and inner retina. It has been shown that in eyes with uveitic CME, loss of EZ is associated with poor visual outcomes.[18] A more recent study showed that the integrity of not only the outer retina, but also the inner retina, is important in visual function in eyes with uveitic macular edema. In that study, disorganization of retinal inner layers, presence of intraretinal cysts, and disruption of the EZ was associated with a poorer visual outcome.[19]

Ultrasound

Posterior segment B-scan ultrasonography provides noninvasive evaluation of the vitreous cavity, optic nerve, retina, and choroid. If media opacity precludes visualization of the retina on clinical examination, B-scan can be used to evaluate the status of the posterior segment. In eyes with clear media, B-scan can be used to evaluate posterior pathologies including diffuse thickening of the choroid, focal retinochoroidal lesions (granuloma, mass lesions, etc.), and presence of fluid in Tenon space (the T-sign in posterior scleritis).[14]

(Continued on page 81)

(Continued from page 61)

IMAGING CAPABILITIES ARE ONLY GETTING BETTER

Novel imaging methods have been used to better visualize or quantify ocular inflammation in uveitic eyes. Anterior segment OCT has been used to visualize and grade anterior segment cells with high correlation between slit-lamp grading and anterior segment OCT grading.[20] Additionally, newer methods using UWF FA have been developed to quantify peripheral leakage.[21] Further research is needed to automate quantification of posterior and anterior segment inflammation. ■

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