Fluorescein Angiography and Optical Coherence Tomography Correlation in Various Retinal Diseases

It is important to know the strengths and weaknesses of imaging modalities and their unique uses for diagnosing different retinal diseases.

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Fluorescein angiography (FA) and optical coherence tomography (OCT) scans are important tools used in the examination and management of retinal diseases. These investigative modalities complement each other, and many situations require both imaging methods to make the correct diagnosis and treatment plan. This article compares the 2 technologies in various clinical situations.

Fluorescein angiography provides retinal circulation details, and OCT offers high-quality anatomic images. Fluorescein angiography is invasive, nonquantitative, and subjective, with limited use for patients with small pupils or insufficient media clarity. Optical coherence tomography is objective and is not so much affected by pupil size or media clarity. Registration of OCT scans helps clinicians properly assess patients during follow-up visits. Both diagnostic tools depend heavily upon patient cooperation. Both are useful, and often complimentary, in the diagnosis and management of a variety of retinal disorders, such as age-related macular degeneration (AMD), idiopathic juxtafoveolar retinal telangiectasis (IJRT), myopic choroidal neovascularization (CNV), uveitic cystoid macular edema (CME), diabetic macular edema (DME), central serous chorioretinopathy (CSC), and vitreomacular interface disorder.

Each modality has unique strengths and weaknesses. Kozak et al,[1] in analyzing discrepancy rates between intravenous FA and time-domain OCT (TD-OCT) for diagnosing macular edema, found that the sensitivity of FA and OCT was 98.7% and 96.1%, respectively. In 3.86% of eyes, they found that FA showed dye leakage in the macular area, but TD-OCT showed normal foveal contour. Similarly, TD-OCT detected both intraretinal and subretinal fluid in 1.17% eyes, while FA failed to detect any fluid. The largest number of discrepancies was found while scanning for DME, and FA was more sensitive than TD-OCT for this condition: 42.2% of eyes showed discrepancy. Fluorescein angiography and TD-OCT were equivalent when testing for AMD.

Barteselli et al[2] compared oral FA with spectral-domain OCT (SD-OCT) in diagnosing macular edema. Fluorescein angiography was as sensitive as SD-OCT for management of AMD; however, FA provided better details in cases of DME and macular edema associated with retinal vein occlusions. Spectral-domain OCT was

more sensitive in the diagnosis and management of purely anatomic disorders such as macular holes. The overall discrepancy between FA and SD-OCT was 4.56%. This discrepancy was greater in cases of diabetic retinopathy and uveitis. The highest agreement rate (0.95) and lowest rate of disagreement (0.83) was noted in AMD, particularly in wet AMD.

WET AGE-RELATED MACULAR DEGENERATION

Neovascular AMD is diagnosed based on leakage patterns found on FA. Optical coherence tomography, however, is more useful for following up with patients after they have been diagnosed. Fluorescein angiography is required to reassess the diagnosis in patients who do not respond to a given treatment. Optical coherence tomography provides quantitative evaluation of the disease and provides information about structural changes, particularly for outer retinal structures.

Barteselli et al[2] reported the highest agreement rate (0.95) and the highest sensitivity (0.99) for both techniques in eyes with AMD. They also reported the lowest discrepancy rate (0.83) in patients with AMD compared with those with other retinal pathologies. Physicians should consider simultaneous evaluation using FA and SD-OCT to detect all cases of new, persistent, or recurring macular edema in cases of wet AMD.

Giani et al[3] evaluated SD-OCT findings that predict angiographic leakage in CNV. They reported a statistically significant association between SD-OCT and FA findings for eyes that displayed fluid and neurosensory detachment, intraretinal flecks, and low reflectivity or undefined boundaries from subretinal material, but not for intraretinal cystic spaces or retinal pigment epithelium (RPE) detachment.

SUBRETINAL NEOVASCULARIZATION IN IDIOPATHIC JUXTAFOVEOLAR RETINAL TELANGIECTASIS

Diagnosis of subretinal neovascularization associated with IJRT is challenging due to presence of associated leakage from telangiectatic vessels on FA and presence of cystic changes on OCT (Figure 1). We reported an interobserver agreement (measured in kappa, k) for diagnosis of subretinal neovascularization on FA and SD-OCT. The k value for subretinal neovascularization on FA was 0.373; for subretinal neovascularization on SD-OCT, it was 0.775.[4] The sensitivity to make a diagnosis of subretinal neovascularization secondary to IJRT for FA was 52.3%; the specificity for diagnosing the same disease for FA was 70.0%. Regarding SD-OCT, the sensitivity and specificity was 72.7% and 64.1%, respectively, in reference to color fundus photography. The negative predictive value of SD-OCT (80.6%) was higher than that of FA (73.7%).

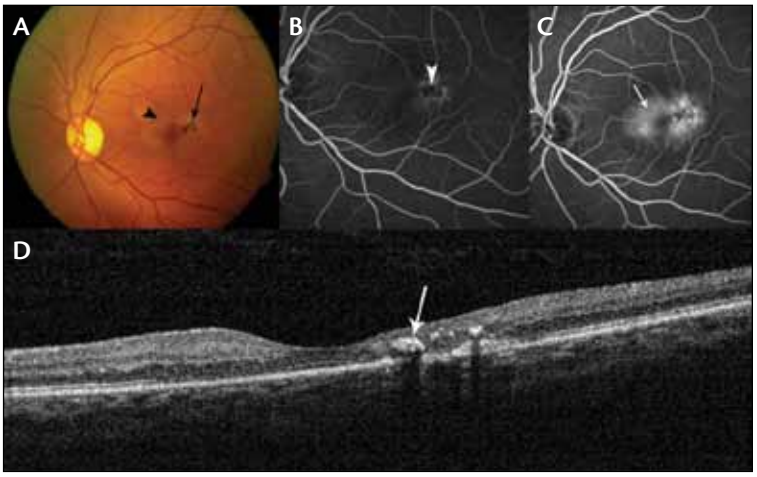

Figure 1. Type 2A idiopathic juxtafoveolar retinal telangiectasis. Color fundus photograph (A) shows graying of the parafoveal retina (arrow) with pigments (arrow) and telangiectatic vessels. Fluorescein angiography shows early hyperfluorescence from the telangiectatic vessels along with blocked fluorescence due to pigments (arrow; B) leading to diffuse hyperfluorescence in the late phase (arrow; C). Spectral-domain optical coherence tomography shows thinning of fovea with back-shadowing due to pigments (arrow; D) with no intraretinal or subretinal fluid.

Interobserver agreement was better for SD-OCT compared with FA in making the diagnosis of subretinal neovascularization. SD-OCT is better than FA for ruling out the presence of subretinal neovascularization. As with AMD patients, serial monitoring of response to treatment is best done with noninvasive imaging modalities such as OCT.

MYOPIC CHOROIDAL NEOVASCULARIZATION

Myopic CNV is difficult to diagnose clinically because of concomitant posterior pole chorioretinal atrophic changes, prominent choroidal vessels, subretinal hemorrhage associated with lacquer cracks, pigments, and scarring (Figure 2).[5,6]

Occasionally, FA and OCT both fail to make a diagnosis of myopic CNV. This can be for any number of reasons, including smaller areas of neovascularization, less exudation, eccentric fixation and poor focusing during testing, or the inability to obtain images due to long axial length. Fluorescein angiography and OCT frequently display substantial disagreement regarding the activity in eyes with

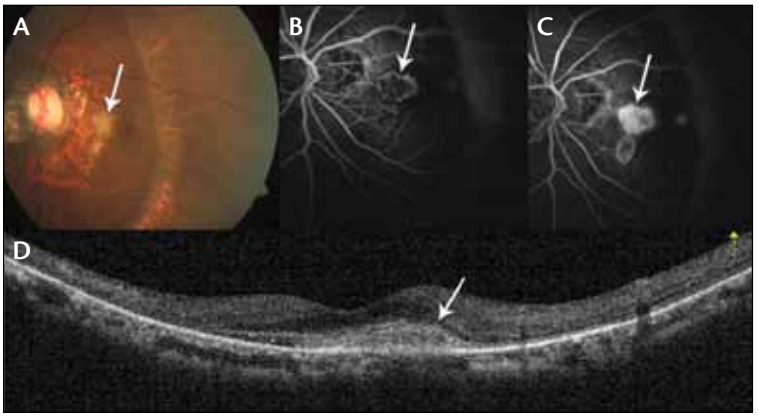

Figure 2. Myopic choroidal neovascular membrane. Color fundus photography (A) shows gray membrane (arrow) with high myopic fundus. Fluorescein angiography shows early hyperfluorescence with noticeable membrane (arrow; B) leading to hyperfluorescence in the late phase (arrow; C), suggestive of staining. Spectral-domain optical coherence tomography shows hyperreflective lesion above the retinal pigment epithelium (arrow; D) with no intraretinal or subretinal fluid suggestive of scarred choroidal neovascular membrane.

myopic CNV. Leveziel et al[5] reported that, although more than 80% of eyes with exudative myopic CNV displayed leakage on FA, less than half had corroborative evidence of exudation on OCT. When recently diagnosed cases of myopic CNV were included, they found that reliable and interpretable diagnosis of CNV was made by FA alone in 61.3% of cases (38 of 62), by SD-OCT alone in 22.6% of cases (14 of 62), and by both SD-OCT and FA in 16.1% of cases (10 of 62). There was no agreement about signs of active CNV between these 2 imaging methods (k 25.7 ±10%; *P* = .0044).

UVEITIC CYSTOID MACULAR EDEMA

Fluorescein angiography is usually not mandatory to make a diagnosis of uveitic CME, but is useful when one wants to look for vasculitic or ischemic changes, optic nerve leakage, or presence of CNV. Good quality FA images are difficult to obtain in the presence of small pupil, cataract, and vitreous haze. Optical coherence tomography may be beneficial in making diagnosis of CME in such situations. Additionally, OCT gives information about the presence of epiretinal membrane (ERM), outer retinal structure damage, and RPE atrophy. Recent developments in choroidal imaging have brought new management tactics to uveitis patients, especially those with Vogt-Koyanagi-Harada disease.[7]

Kempen et al[8] showed that macular thickening can be present with or without leakage on FA. Agreement in diagnosis of macular thickening on OCT and FA (k ¼ 0.44) was moderate. Macular leakage was present in 40% of cases free of macular thickening, whereas macular thickening was present in 34% of cases without macular leakage. Biomicroscopic evaluation for macular edema failed to detect 40% of cases of macular thickening and 45% of cases of macular leakage. Biomicroscopic evaluation diagnosed 17% of cases with macular edema that did not have macular thickening and diagnosed 17% of cases of macular edema that did not have macular leakage.

Overall, OCT is the best initial test for evaluation of suspected uveitic CME and is the best method to evaluate the response to treatment in cases of uveitis.

DIABETIC MACULAR EDEMA

In DME, FA is not required to make the diagnosis but is required to plan laser photocoagulation. Additionally, FA is required to diagnose clinically concealed neovascularization, particularly before cataract surgery. Fluorescein angiography also helps diagnose macular ischemia in eyes with unexplained vision loss. Optical coherence tomography helps quantify and classify macular edema, evaluate outer retinal structure damage, and perform adequate follow-up.

Discrepancy between FA and OCT is not uncommon in eyes of patients with diabetes. Barteselli et al[2] reported a high discrepancy rate (18.12%) and a low kappa agreement (0.52) between the 2 imaging modalities in eyes with DME. Fluorescein angiography appeared to be more sensitive than SD-OCT in detecting macular edema (1.00 vs 0.79). Spectral-domain OCT has a lower sensitivity in cases of low-grade leakage from vessels or microaneurysms. Mild leakage, either focal or diffuse, may not be sufficient to create an obvious pattern of intraretinal fluid, to create retinal structural changes, or to affect foveal thickness.

PSEUDOPHAKIC CYSTOID MACULAR EDEMA

In cases of pseudophakic CME, FA is usually not required for making the diagnosis. However, FA can help rule out any associated DME or inflammatory leakage. Optical coherence tomography is sufficient to make the diagnosis, to rule out presence of any tractional component or ERM, and for follow-up. Barteselli et al[2] reported that oral FA has better sensitivity compared with SD-OCT for postsurgical CME, with only 8.7% discrepancy.

CENTRAL SEROUS CHORIORETINOPATHY

Central serous chorioretinopathy, generally considered a self-limiting disease, can be diagnosed clinically. Most

cases improve spontaneously. A few cases, however, show persistent subretinal fluid; OCT helps quantify the subretinal fluid in cases that do not spontaneously improve. FA is required to find the leakage site for laser photocoagulation. Only OCT scans should be used for follow-up evaluations.

VITREOMACULAR INTERFACE DISORDERS

Cystic changes on OCT without leakage suggest tissue damage from long-standing edema or mechanical forces such as vitreomacular traction. Optical coherence tomography helps determine the area from which one might find a plane of dissection for removal of the ERM. Upon serial follow-up, many cases of successful ERM removal show anatomical recovery. In cases of vitreomacular traction, OCT can easily distinguish focal traction from diffuse traction. Optical coherence tomography also helps determine if there is a possibility of inner retinal layer deroofing during surgery that requires informed consent. Fluorescein angiography has a limited role in vitreomacular interface disorders unless clinical examination shows evidence of inflammatory pathology.

COMPLEMENTARY TECHNOLOGIES

Findings on FA and OCT are related but not interchangeable. Although OCT provides detailed imaging of retinal layers, allows detection of microstructural changes, and helps perform quantitative assessment during follow-up, it does not contribute to our understanding of circulatory changes in the ways FA does. Therefore, in our opinion, the use of either or both imaging technologies is advisable for the most accurate diagnosis and management of retinal diseases. ■

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