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Peripheral Findings and Retinal Vascular Leakage on Ultra-Widefield Fluorescein Angiography in Patients with Uveitis

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Purpose: To compare ultra-widefield fluorescein angiography (UWFFA) with simulated conventional fluorescein angiography (FA) to evaluate peripheral pathology and leakage and correlate with clinical activity in patients with uveitis.

Design: Retrospective chart review.

Participants: All uveitis patients initially evaluated with UWFFA (Optos 200Tx) between May 2012 and December 2013 were included in this study, including follow-up visits through August 2014.

Methods: Uveitis status was deemed as having active or inactive inflammation based on clinical examination. Changes to therapy, influence on management, and clinical diagnosis were also noted. UWFFA images were compared with simulated 50-degree FA images to evaluate for peripheral lesions, and leakage location was also graded. Imaging characteristics were then correlated with clinical information.

Main Outcome Measures: Correlation of leakage on UWFFA with clinical inflammation.

Results: An initial set of 243 uveitis patients and a total of 1008 eye images were reviewed. When UWFFA was compared with a simulated 50-degree FA image, UWFFA added additional information regarding the presence of peripheral vascular leakage in 25%, peripheral nonperfusion in 14%, peripheral lesions in 6.6%, and peripheral neovascularization in 3.9% of patients. A total of 600 eye images exhibited fluorescein leakage, of which 21% displayed central leakage only, 11% had central and peripheral leakage, 31% had peripheral leakage only, and 37% had diffuse vascular leakage. Based on peripheral findings on widefield angiography, the treatment was changed in 69 patients (28%). Corresponding eye examinations were reviewed for each imaging session, and of 600 eye images with vascular leakage, 567 eye images were also clinically active, which was 95% sensitive as a surrogate indicator of clinical inflammation. Anterior chamber cell and vitreous haze also significantly correlated with leakage on widefield angiography.

Conclusions: Retinal vascular leakage on UWFFA reveals increased pathology and leakage compared with conventional angiography, which can influence management, and accurately identifies and correlates with active inflammation in patients with uveitis. A more objective measure of inflammation in the form of leakage exhibited on UWFFA may help standardize treatment and care of patients with uveitis. *Ophthalmology Retina 2017;■:1–7 © 2017 Published by Elsevier Inc. on behalf of the American Academy of Ophthalmology*

Multiple imaging modalities are valuable to the diagnosis and management of uveitis patients, including fundus photography, fundus fluorescein angiography (FA), indocyanine green angiography, fundus autofluorescence, optical coherence tomography, and ultrasonography.[1] FA has become an essential tool in the evaluation, diagnosis, and monitoring of posterior uveitis.[2,3] Several uveitic syndromes can exhibit characteristic patterns of leakage on FA that often assist in diagnosis and can highlight inflammation that is not seen clinically.[4,5]

Conventional fundus FA has traditionally aided in the diagnosis and management of uveitis, but is limited by a 30- to 60-degree field of view per exposure. The Early Treatment of Diabetic Retinopathy Study Group developed a protocol with 7 overlapping 30-degree fields (conventional 7 standard field) to capture a greater extent of the retinal periphery to 75 degrees of retina.[6] Manual or automated photomontages of conventional images can provide excellent detail in small-field images; however, they lack the dynamic ability to capture angiography over time. Montaging can also miss areas of the periphery (especially anterior to the equator) and can have variability in contrast, brightness, magnification, and distortion in the periphery.[7,8] Peripheral sweeps using conventional fundus photography if no automated montaging is available also make it difficult to locate and compare peripheral lesions over time. In 2005, Staurenghi et al[9] described an integrated widefield contact lens system with confocal scanning laser ophthalmoscopy that could capture up to 150 degrees of the fundus with simultaneous fluorescein and indocyanine green angiography.

Noncontact, ultra-widefield FA (UWFFA) has been commercially available since 2000 and utilizes confocal scanning laser ophthalmoscopy to capture up to a

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200-degree field of view in a single FA image.[10] UWFFA has proven to be advantageous in imaging several chorioretinal diseases, including diabetic retinopathy,[11] retinal vein occlusion,[12] choroidal masses,[13] uveitis,[2,14,15] retinal vasculitis,[3,16] choroidal dystrophies (such as gyrate atrophy and choroideremia),[17] retinal detachment,[18] and pediatric retinal disease.[19] In a study of patients with diabetic retinopathy, compared with the Early Treatment of Diabetic Retinopathy Study 7 standard field, UWFFA can image 3.2 times more total retinal surface area, 3.9 times more nonperfusion, and 1.9 times more neovascularization.[11] Mudvari et al[20] found that ultra-widefield photography alone without angiography can image 48% more retinal area and 40% more cytomegalovirus retinitis area compared with conventional 9-field photography, and ultra-widefield photography also caught 2 of 12 eyes with peripheral cytomegalovirus lesions that were missed on conventional photography.

Utilizing UWFFA, we can now detect inflammatory activity and retinal vascular leakage in uveitis patients beyond a standard 30- to 60-degree field of view, as demonstrated in prior studies in noninfectious posterior uveitis[2] and noninfectious retinal vasculitis.[16] The purpose of this retrospective study is to compare UWFFA with simulated conventional FA to evaluate peripheral pathology and leakage in patients with uveitis, to correlate these findings with clinical activity based on examination, and to determine whether UWFFA influenced management.

Methods

Patient Population and Data Collection

In this institutional review board–approved retrospective, consecutive, observational case series, clinical and imaging data were collected from patients with a diagnosis of uveitis, initially imaged with the Optos 200Tx UWFFA platform (Optos PLC, Dunfermline, Scotland) between May 1, 2012, and December 31, 2013, including follow-up visits through August 31, 2014. All patients were treated by 2 clinicians (C.Y.L. and S.K.S.) at the Cleveland Clinic Cole Eye Institute in Cleveland, Ohio. This study was approved by the Cleveland Clinic Institutional Review Board, complied with the Health Insurance Portability and Accountability Act of 1996, and followed the tenets of the Declaration of Helsinki.

Baseline and follow-up clinical data were recorded in an electronic database. Clinical data included patient demographics; uveitis diagnosis; topical, periocular, and systemic therapies; documentation of uveitis activity; presence of anterior chamber cell (grade 0–4); presence of vitreous haze (grade 0–4); change in management; and whether UWFFA was used to rule out posterior segment inflammation. Clinically active or inactive uveitis was denoted by the treating physician based on the summation of patient-reported symptoms, the presence of anterior chamber cell or vitreous haze, and interpretation of all imaging acquired during the clinic visit.

Ultra-Widefield Fluorescein Angiography Acquisition and Analysis

All UWFFA images were acquired with the Optos 200Tx ultra-widefield retinal imaging system, which can image up to 200 degrees of the retina in a single image. All patients received a standard infusion of 5 ml of 10% sodium fluorescein through the antecubital vein. One mid-phase fully perfused image (at 60–90 seconds) and a second late-phase image (at 7–10 minutes), centered on the optic disc and macula, were chosen for analysis for each eye at each visit with available imaging.

The mid-phase and late-phase widefield FA images were used to compare with a 50-degree (high-magnification) image to simulate comparison with a conventional FA image (Fig 1). Peripheral findings were documented for both images and compared. Location of fluorescein leakage was also documented for all UWFFA images. Leakage was classified as central leakage (if it involved

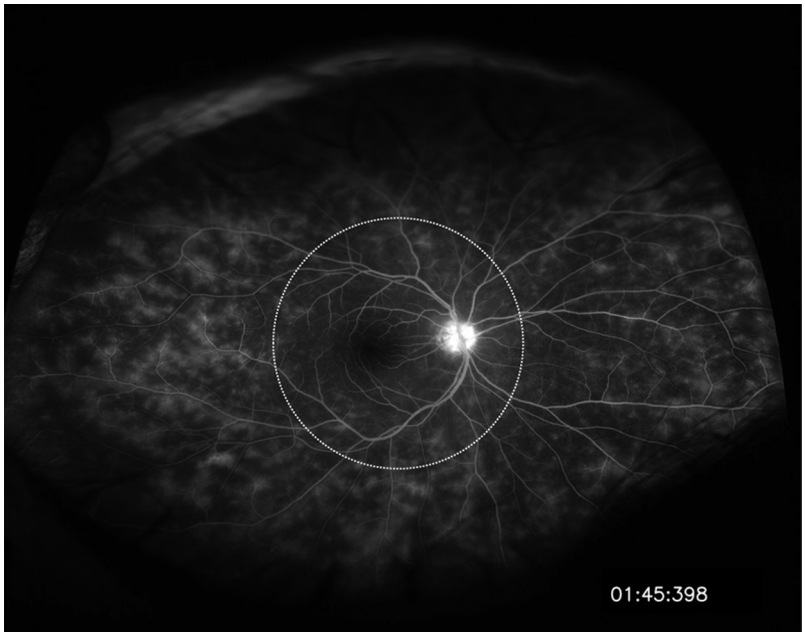

Figure 1. Example of an ultra-widefield fluorescein angiogram with diffuse peripheral vascular leakage and a simulated 50-degree standard field of view (outlined with *dashed white circle*).