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Ultra-Widefield Imaging in Patients with Angioid Streaks Secondary to Pseudoxanthoma Elasticum

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Purpose: To investigate the application of noninvasive ultra-widefield (UWF) imaging in patients with angioid streaks secondary to pseudoxanthoma elasticum (PXE) and to compare detected findings with those obtainable with 7 standard 30° fields (7SF) imaging.

Design: Cross-sectional, observational study.

Participants: Forty eyes of 20 consecutive patients with angioid streaks secondary to PXE (8 women and 12 men; mean age, 56.9 ± 12.3 years).

Methods: Consecutive patients with angioid streaks secondary to PXE seeking treatment between January and June 2016 at the Medical Retina & Imaging Unit of the Department of Ophthalmology, University Vita-Salute San Raffaele, underwent UWF imaging (California; Optos PLC, Dunfermline, UK). Ultra-widefield color images and fundus autofluorescence (FAF) were evaluated. Ultra-widefield findings then were compared with those obtainable with 7SF.

Main Outcome Measures: Types and location of retinal lesions secondary to PXE.

Results: Peripheral lesions not entirely visible with 7SF were identified in 29 of 40 eyes (72.5%; $P < 0.0001$). These peripheral lesions included peau d'orange (52.5% of the eyes), coquille d'oeuf (52.5%), cracked eggshell (5.0%), comet lesions (27.5%), peripheral retinal degenerations (17.5%), parastreak atrophies (10.0%), and peripheral hemorrhage (5.0%). Furthermore, chorioretinal atrophies, drusen of the optic disc, cracked eggshell, pattern-like dystrophies, and retinal hemorrhages associated with angioid streaks were observed on digital color or FAF images, or both, and described.

Conclusions: Ultra-widefield imaging showed valuable usefulness in patients with angioid streaks by providing in a single image the entire spectrum of retinal alterations associated with PXE. Peripheral lesions often are present in patients with angioid streaks and may be missed with 7SF imaging. A careful examination of fundus periphery should be performed during screening and follow-up visits. *Ophthalmology Retina 2016;■:1–8 © 2016 by the American Academy of Ophthalmology*

Angioid streaks are breaks in Bruch's membrane typically (although not always) visible at fundus examinations as irregular dark red-brown-gray lines radiating from the optic nerve. Angioid streaks are associated with a number of pathologic characteristics, including pseudoxanthoma elasticum (PXE; responsible for nearly 50%–80% of angioid streaks), Paget's disease of bone, and hemoglobinopathies.[1] Adjunctive retinal findings in patients with angioid streaks are essential at the beginning to orientate the diagnosis, monitor the progression of the disease, and guide the treatment. These include areas of chorioretinal atrophies, comet lesions, coquille d'oeuf, peau d'orange, drusen of the optic disc, and retinal hemorrhages.

Because patients with angioid streaks should undergo ophthalmologic evaluations on a regular basis because of the increased risk of ocular complications (eg, choroidal neovascularization and retinal hemorrhages), it is essential to choose the appropriate imaging techniques for their follow-up. In recent years, new instruments have become available that incorporate ultra-widefield (UWF) imaging. Ultra-widefield imaging refers to noncontact technologies providing panoramic images of the retina above 100° in the field of view.[2] This technology has shown clinical usefulness in different disorders, like diabetic retinopathy, vascular occlusions, uveitis, and age-related macular degeneration.[2–4] In addition, the ability to obtain multimodal images nearly simultaneously with the same platform makes UWF imaging ideal to study progressive and complex diseases involving the retina, such as PXE.

Pseudoxanthoma elasticum is an autosomal recessive disorder secondary to mutations in the *ABCC6* gene.[5] It is a rare disease with a prevalence between 1:25 000 and 1:100 000[6] that leads to dystrophy of extracellular matrix resulting from increase mineralization.[7] A variety of ocular alterations may develop in patients with PXE, including peau d'orange, angioid streaks, chorioretinal atrophies, comet lesions, and

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Figure 1. Margins of the 30° captures were overlaid on ultra-widefield images to show how this imaging method may detect more peripheral lesions than 7 standard 30° fields (7SF) imaging. Peripheral comet lesions (white arrows) are outside the area of 7SF imaging.

choroidal neovascularization.[8] The aim of the present study was to investigate the application of noninvasive UWF imaging in patients with angioid streaks secondary to PXE by analyzing the fundus features on color images and green fundus autofluorescence (FAF) imaging and to compare detected findings with those obtainable with 7 standard 30° fields (7SF) imaging.

Methods

In this cross-sectional, observational study, consecutive patients with angioid streaks secondary to PXE seeking treatment between January and June 2016 at the Medical Retina & Imaging Unit of the Department of Ophthalmology, University Vita-Salute, San Raffaele Hospital, who underwent UWF imaging with the Optomap California fundus camera (Optos PLC, Dunfermline, UK) were reviewed retrospectively. Inclusion criteria were 18 years of age or older, angioid streaks secondary to PXE diagnosed by skin biopsy or genetic analysis and UWF fundus color and green FAF images. Exclusion criteria were previous intraocular surgeries except for uneventful cataract extraction more than 6 months before UWF image acquisition; insufficient image quality resulting from media opacities; contraindication to mydriasis (ie, narrow angle); eye diseases other than angioid streaks, including age-related macular degeneration, retinal vasculopathies, vitreoretinal diseases, central serous retinopathy, or previous retinal detachment. This study adhered to the tenets of the Declaration of Helsinki. All patients signed a written general consent to participate in observational studies, which was approved by the ethics committee of San Raffaele Hospital.

All patients underwent a complete ophthalmic examination and multimodal imaging analysis, including best-corrected visual acuity, indirect ophthalmoscopy, spectral-domain optical coherence

Table 1. Main Demographic Characteristics and 7 Standard 30° Fields Sensitivity for Retinal Alterations in Patients with Pseudoxanthoma Elasticum

Characteristics	Data
Gender (no.)	
Male	12
Female	8
Mean age ± SD (yrs)	56.9 ± 12.3
Total no. of eyes/patients	40/20
7 standard 30° fields sensitivity*	
Comet lesions	59.3%
Peau d'orange and coquille d'oeuf	55.1%
Cracked eggshell	50.0%
Peripheral hemorrhages	75.0%
Peripheral retinal degenerations	50.0%
Parastreak atrophies and angioid streaks	81.6%
Macular atrophy	100.0%
Optic disc drusen	100.0%
Macular pattern-like dystrophy	100.0%

SD = standard deviation.
*Calculated taking ultra-widefield imaging results as reference and evaluating the ability of 7 standard 30° fields to capture completely the different types of lesions associated with pxeudoxanthoma elasticum.