Drusen-like Deposits in Young Adults Diagnosed With Systemic Lupus Erythematosus

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• PURPOSE: To determine the prevalence of drusen-like deposits (DLDs) and choroidal changes in patients with systemic lupus erythematosus (SLE), with or without glomerulonephritis; and to correlate ocular findings with systemic features.

• DESIGN: Case-control study.

• METHODS: Sixty patients with SLE (age, 18–55 years; 30 with and 30 without SLE-related glomerulonephritis) and 60 age- and sex-matched healthy controls were enrolled. All patients underwent noninvasive multimodal imaging that included fundus photography, near-infrared reflectance, blue autofluorescence, blue reflectance, and spectral-domain optical coherence tomography (SDOCT). Images were analyzed for the prevalence of DLDs. Distribution, size, and number of DLDs were measured. Correlations between ocular findings and systemic features were analyzed. Subfoveal choroidal thickness (SCT) was measured using the SDOCT.

• RESULTS: Drusen-like deposits were detected in 40% of SLE subjects and 3.33% of controls ($P < .0001$). Compared with other techniques, SDOCT detected the largest number of affected subjects. In eyes with DLDs, small, medium, and large lesions were found in 75%, 50%, and 42% of cases, respectively. Drusen-like deposits were located in the nasal, temporal, inferior, superior, and central regions of the posterior pole in 83%, 75%, 67%, 54%, and 25% of eyes, respectively. The prevalence of DLDs in patients with SLE was similar regardless of renal involvement, but patients with glomerulonephritis had more DLDs per eye, larger deposits, and DLDs in >3 quadrants ($P < .001$, $P = .03$, $P = .009$, respectively). Subfoveal choroidal thickness was greater in patients with SLE ($P = .002$).

• CONCLUSIONS: Drusen-like deposits in patients with SLE were independent of renal disease and were best detected with SDOCT. Lupus-related glomerulonephritis was associated with more fundus abnormalities and a screening SDOCT should be considered in all patients with SLE. Drusen-like deposits in the absence of glomerulonephritis may support the recent proposal that complement alteration is the primary cause of these lesions. (Am J Ophthalmol 2017;175:68–76. © 2016 Elsevier Inc. All rights reserved.)

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SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) IS AN AUTOimmune disease characterized by loss of immune tolerance against nuclear antigens, polyclonal autoantibody production, immune complex deposition, multiorgan damage, and a relapsing/remitting clinical course.[1] As with most autoimmune diseases, there are no specific clinical or laboratory tests to confirm the diagnosis of SLE. Instead, the diagnosis of SLE is based on the presence of at least 4 of the 11 criteria described by the American Rheumatologists Association (ARA).[2] The ARA criteria consist of a number of SLE-related organ disorders such as skin rash, arthritis, nephritis, and immune dysfunction.

Although not mentioned in the ARA list, ophthalmologic involvement can occur in 2%–30% of patients with SLE. Several ocular tissues can be involved, but the retinal vessels are most commonly affected.[3] Early manifestations of retinopathy, such as small intraretinal hemorrhages and cotton-wool spots, usually occur prior to the onset of ocular symptoms.[4] Detecting these abnormalities on fundus examination can identify patients at high risk for more advanced disease.[5]

A number of asymptomatic funduscopic changes have been reported to be possible markers for disease activity. Baglio and associates found choroidal alterations and drusen-like deposits (DLDs) on indocyanine green angiography (ICGA) in a small cohort of patients affected by SLE glomerulonephritis. They suggested a possible correlation between these ocular findings and renal involvement.[6] The absence of large confirmatory studies, and the invasive nature and high costs of ICGA, may contribute to the rarity of these findings.

During the past few years, noninvasive imaging techniques, particularly fundus autofluorescence (FAF) and spectral-domain optical coherence tomography (SDOCT), have become the gold standards for the detection and characterization of drusen and DLDs in both ocular and systemic conditions.[7–10] The introduction of enhanced-depth imaging (EDI) has improved visualization of the choroid on SDOCT and enables noninvasive assessment of choroidal

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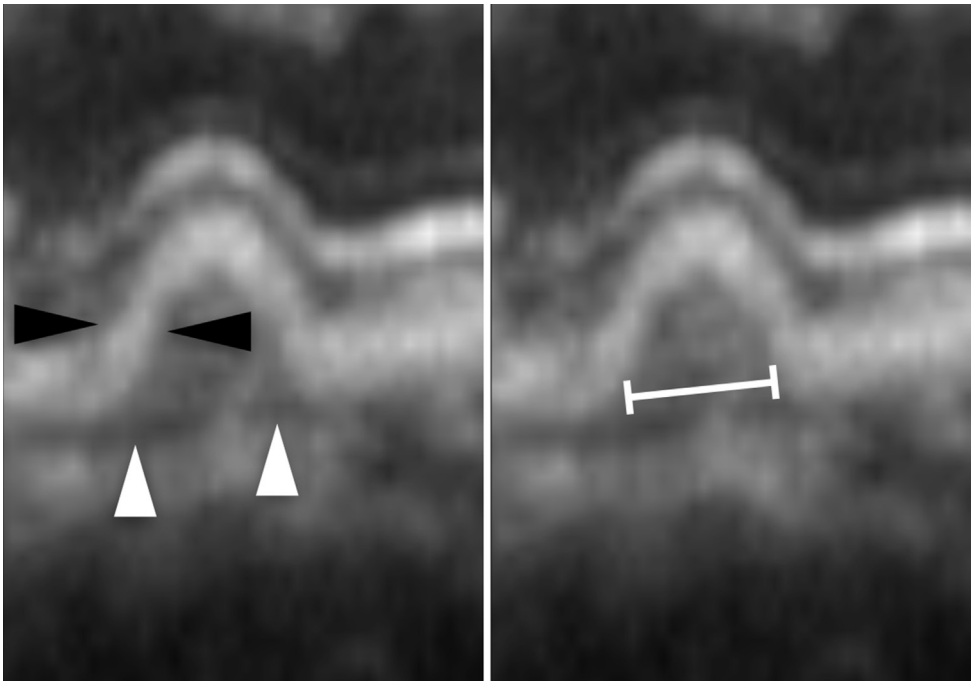

FIGURE 1. Drusen-like deposit (DLD) size assessment technique on spectral-domain optical coherence tomography (SDOCT) scan. Measurement of DLD size was divided into 2 steps. (Left) First, the borders of the retinal pigment epithelium (RPE) detachment (black arrowheads), representing the deposits' lateral boundaries, and Bruch membrane (white arrowheads) were identified. (Right) Following this, a linear segment parallel to the Bruch membrane was drawn between the previously identified RPE borders using the Heyex Eye Explorer linear caliper measurement tool.

structures and measurement of thickness in several diseases, including SLE.[11]

The aim of this index study was to assess the prevalence of DLDs and choroidal changes in patients with SLE (with or without renal involvement) using various noninvasive imaging techniques, and to compare them to age- and sex-matched healthy controls. Correlation between the ocular findings and the systemic status of the patients, including the ARA criteria, treatment, and the renal involvement, was also determined.

METHODS

IN THIS CROSS-SECTIONAL CASE-CONTROL STUDY, 60 PATIENTS with SLE that were being treated in the Immunology/Nephrology Unit of the IRCCS-Cà Granda Foundation – Ospedale Maggiore Policlinico, Milan, Italy, and 60 age- and sex-matched healthy controls were enrolled. Institutional Review Board approval was obtained and the study adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all the subjects prior to enrollment in the study.

• **INCLUSION CRITERIA:** The diagnosis of SLE was based on the presence of at least 4 of the 11 ARA criteria. Among the 60 patients with SLE (cases), 30 had biopsy-proven SLE-related glomerulonephritis and the remaining 30 had SLE without renal involvement. The American College of Rheumatology (ACR) criteria for glomerulonephritis—detection of persistent proteinuria >0.5 g/day or >3+ by dipstick, and/or cellular casts including red cells, hemoglobin, granular, tubular, or mixed[12]—were used to rule out renal disease.

Patients with refractive errors less than spherical equivalent of ±3 diopters were included in the study. Age-matched control subjects had no known ocular or systemic diseases.

• **EXCLUSION CRITERIA:** Patients with 1 or more of the following conditions were excluded: history of previous or ongoing ocular or systemic disease known to cause changes in the retina or the choroid other than SLE; history of previously diagnosed SLE-related retinopathy (ie, small intraretinal hemorrhages and cotton-wool spots); media opacities that prevent the acquisition of images that are adequate for analysis; and inability to understand or sign the informed consent. Patients older than 55 years were excluded to avoid the presence of age-related drusen.

• **STUDY PROCEDURES:** All patients enrolled into the study underwent complete ocular examinations, including best-corrected visual acuity, anterior segment slit-lamp