

ABNORMAL QUIESCENT NEOVASCULARIZATION IN A PATIENT WITH LARGE COLLOID DRUSEN VISUALIZED BY OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY

Adriano Carnevali, MD,*† Riccardo Sacconi, MD,*‡ Lea Querques, MD,*
Eleonora Corbelli, MD,* Alessandro Rabiolo, MD,* Giuffrè Chiara, MD,*
Vincenzo Scordia, MD,† Francesco Bandello, MD, FEBO,*
Giuseppe Querques, MD, PhD*

Purpose: We report a case of large colloid drusen complicated by extensive quiescent choroidal neovascularization in both eyes.

Methods: Case report.

Results: A 46-year old woman was referred to our department with diagnosis of early-onset retinal drusen. Review of examinations performed 16 years before along with current multimodal imaging evaluation showed the presence of numerous large colloid drusen, subsequently replaced by quiescent choroidal neovascularization in both eyes, nicely visualized by optical coherence tomography angiography.

Conclusion: This case suggests progressive development of quiescent neovascularization beneath the drusen as a possible late evolution of degenerating large colloid drusen.

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*From the *Department of Ophthalmology, University Vita-Salute, IRCCS Ospedale San Raffaele, Milan, Italy; †Department of Ophthalmology, University of*

“Magna Graecia,” Catanzaro, Italy; and ‡Department of Ophthalmology, University of Verona, University Hospital of Verona, Verona, Italy.

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F. Bandello consultant for: Alcon (Fort Worth, TX), Alimera Sciences (Alpharetta, GA), Allergan Inc. (Irvine, CA), Farmila-Thea (Clermont-Ferrand, France), Bayer Schering Pharma (Berlin, Germany), Bausch and Lomb (Rochester, NY), Genentech (San Francisco, CA), Hoffmann-La Roche (Basel, Switzerland), Novagali Pharma (Évry, France), Novartis (Basel, Switzerland), Sanofi-Aventis (Paris, France), Thrombogenics (Heverlee, Belgium), Zeiss (Dublin), G. Querques consultant for Alimera Sciences (Alpharetta, GA), Allergan Inc (Irvine, CA), Bayer Shering-Pharma (Berlin, Germany), Heidelberg (Germany), Novartis (Basel, Switzerland), Sandoz (Berlin, Germany), and Zeiss (Dublin). The remaining authors have no conflicting interests to disclose.

A. Carnevali and G. Querques had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Reprint requests: Giuseppe Querques, MD, PhD, Department of Ophthalmology, University Vita-Salute, IRCCS Ospedale San Raffaele, Via Olgettina 60, Milan 20132, Italy; e-mail: giuseppe.querques@hotmail.it

Large colloid drusen (LCD) is a subgroup of early-onset retinal drusen and is considered as a benign condition.¹ Other forms of early-onset drusen have also been described: cuticular drusen and Malattia Leventinese (ML). Cuticular drusen were described in 1977 by Gass² as small, round yellow lesions randomly scattered in the macula and in the mid periphery of the retina; they are easily visualized by fluorescein angiography, harboring a typical “stars in the sky” appearance in early phases, and indocyanine green angiography shows mainly hyperfluorescent drusen with some hypofluorescent drusen.³ Malattia Leventinese, also called dominant drusen, is caused by a mutation in the endothelial growth factor containing fibrillin-like extracellular matrix protein 1 (*EFEMP1*) gene⁴; the diagnosis is based on fundus examination showing small radial drusen, a unique feature

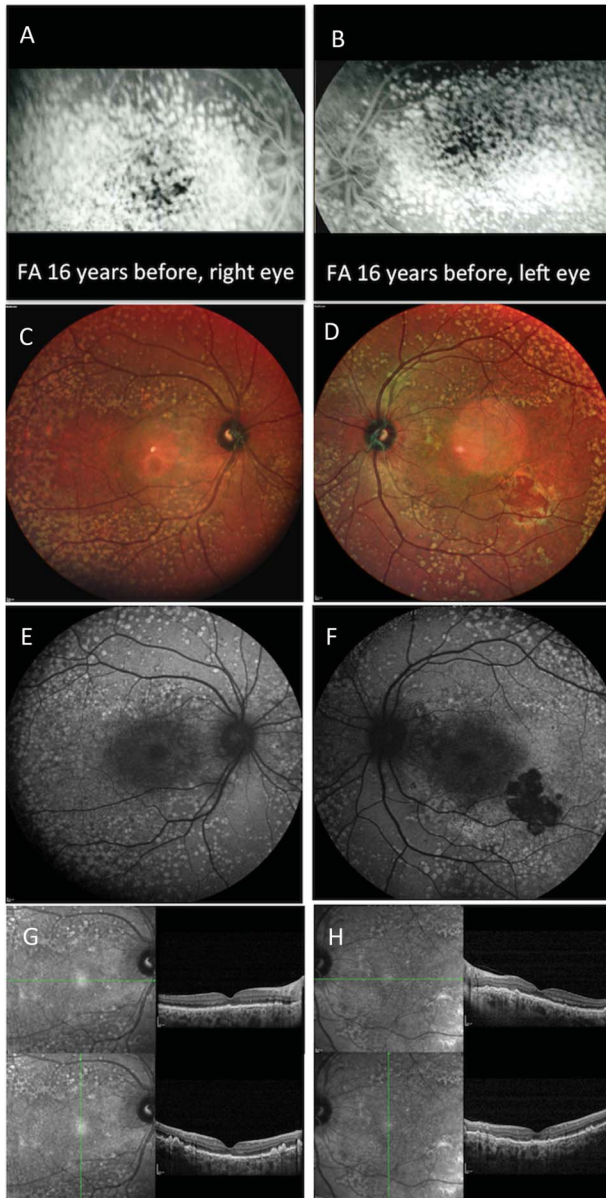


Fig. 1. Fluorescein angiography performed 16 years ago, multi-color image, fundus autofluorescence (FAF), structural spectral domain optical coherence tomography (SD-OCT) of the right and left eyes. **A** and **B.** FA shows the large colloid drusen as homogeneously hyperfluorescent lesions in the right and left eyes involving the posterior pole. **C–F.** Multi-color image and FAF of the right eye reveal the presence of large colloid drusen at the posterior pole (**G**) structural SD-OCT of the right eye shows an irregular flat elevation of the retinal pigment epithelium (RPE) with moderately reflective material in the sub-RPE space (horizontal scans) and presence of convex drusen with various internal reflectivity only (vertical scans) (**H**) structural SD-OCT of the left eye shows an irregular flat elevation of the RPE with moderately reflective material in the sub-RPE space in the absence of intra/subretinal fluid.

of ML. In ML, indocyanine green angiography shows large drusen as hyperfluorescent spots surrounded by halos of hypofluorescence.³ In LCD, in the intermediate and late phases of indocyanine green angiography, the drusen show a hypofluorescent center surrounded by

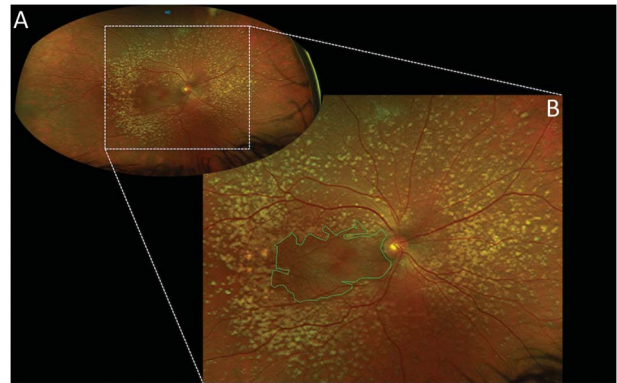


Fig. 2. Ultra-widefield image of the right eye. **A.** Ultra-widefield image shows the presence of large round drusen in correspondence with the vascular arcades, middle periphery, and far periphery. **B.** Note the posterior pole (demarcated area), that is not involved by large colloid drusen.

a hyperfluorescent halo. This halo is bordered with a peripheral thin hypofluorescent ring, harboring a “donut shape.”³ On structural spectral domain optical coherence tomography angiography, most LCD appear convex with medium and homogeneous internal reflectivity.⁵

Finally, in age-related macular degeneration, an original autofluorescence pattern characterized by a central area of decreased autofluorescence surrounded by an annulus of increased autofluorescence has been described, suggesting changes in the retinal pigment epithelium.⁶ The difference in lipid composition between the core and the edge of the drusen could be responsible for these patterns of staining.

We report a case of a 46-year old patient affected by quiescent choroidal neovascularizations (CNVs) in LCD involving both eyes. In the literature, quiescent CNV has never been reported as possible complications of LCD.

Case Report

A 46-year old woman was referred to our department with diagnosis of early-onset retinal drusen. Review of examinations performed 16 years before, including fluorescein angiography, revealed LCD in the posterior pole and beyond the vascular arcades (Figure 1). The patient did not report a decrease in visual acuity in recent years.

Best-corrected visual acuity was 20/20 in the right eye and 20/25 in the left eye; intraocular pressure and anterior segment were unremarkable. Fundus examination revealed the presence of a large round drusen in correspondence with the vascular arcades, middle periphery, and far periphery in both eyes, with an area of retinal atrophy along the inferior temporal arcade in the LE (Figures 2 and 3). Fundus autofluorescence showed hyperautofluorescence from the large drusen and a hypoautofluorescence at the posterior pole in both eyes (Figure 1). Structural spectral domain optical coherence tomography (Spectralis HRA+SD-OCT; Heidelberg Engineering, Heidelberg, Germany) revealed an irregular flat elevation of the retinal pigment epithelium with moderately reflective material in

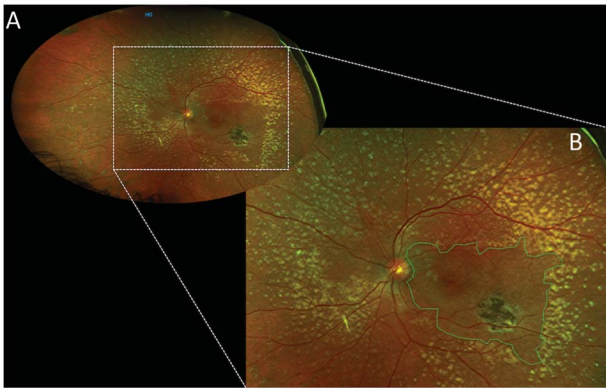


Fig. 3. Ultra-widefield image of the left eye. **A.** Ultra-widefield image shows the presence of large round drusen in correspondence with the vascular arcades, middle periphery, and far periphery. **B.** The posterior pole (demarcated area) shows the absence of large colloidal drusen (16 years after) and the presence of a pigmented area along the inferior temporal arcade.

the sub-retinal pigment epithelium space, absence of intra/sub-retinal hyporeflective fluid, and presence of convex drusen with various internal reflectivity (Figure 1). Swept-source optical coherence tomography angiography (OCT-A, PlexElite 9000 SS-OCT; Carl Zeiss Meditec, Inc, Dublin, OH) revealed an extensive neovascular network in the choroidal plexus that involved the whole posterior pole up to the arcades in both eyes. The CNVs appeared on optical coherence tomography (OCT-A) angiography as irregular, poorly defined, foveal-involving networks with visible core vessels (Figures 4 and 5).

Discussion

Using structural spectral domain optical coherence tomography and OCT-A, we described a case of

a 46-year old patient affected by quiescent CNV in LCD involving both eyes. Active CNV is a well-known complication of other types of early-onset retinal drusen, which include ML and cuticular drusen.⁵ The age of diagnosis for quiescent CNV in our patient with LCD is in line with that reported for development of active CNV in ML and cuticular drusen.^{6,7} However, to the best of our knowledge, quiescent CNV has never been reported in the literature as possible complications of LCD. Recently, Mathis et al⁸ reported an association between LCD and polypoidal choroidal vasculopathy. In addition, our group reported a case of LCD complicated by active CNV and geographic atrophy, in which a single intravitreal anti-vascular endothelial growth factor injection resulted in the resolution of CNV activity.⁹

Quiescent CNV is a finding described in the setting of age-related macular degeneration (AMD) for nonexudative AMD eyes and in patients with pachychoroid neovascularopathy complicated by Type 1 neovascularization.^{10,11} The utility of OCT-A in CNV detection in different ocular conditions has been extensively described in the literature.¹⁰⁻¹³

Interestingly, a review of examinations performed 16 years before along with current multimodal imaging evaluation showed the presence of numerous LCD, subsequently replaced by quiescent CNV in both eyes, nicely visualized by optical coherence tomography angiography. This case suggests the progressive development of quiescent neovascularization beneath

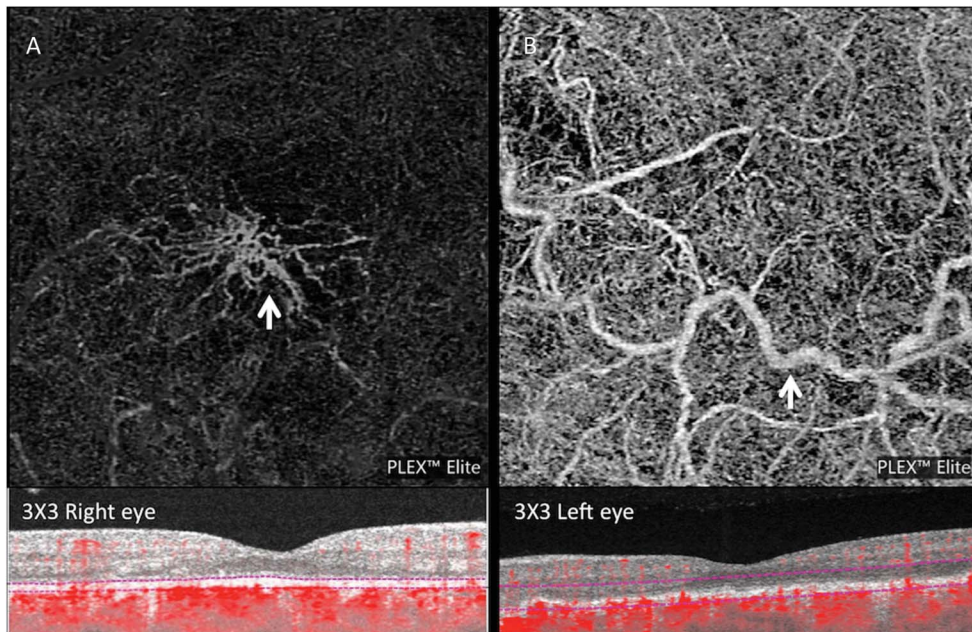
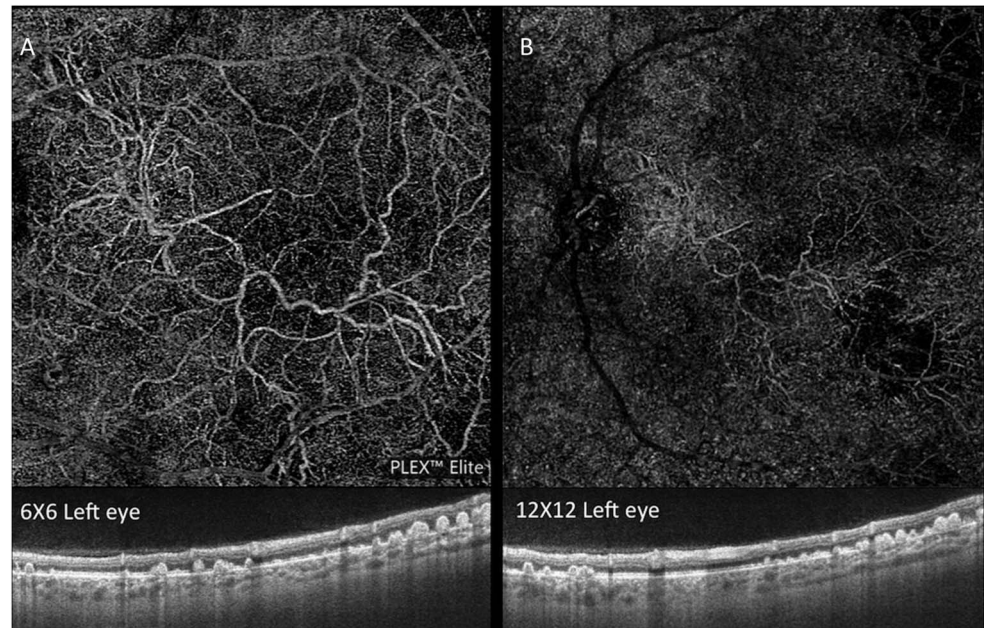


Fig. 4. 3 mm × 3 mm optical coherence tomography angiography (OCT-A) and corresponding structural spectral domain OCT (SD-OCT) of the right and left eyes. **A** and **B.** 3 mm × 3 mm OCT angiogram of the choriocapillaris plexus and the corresponding structural OCT B-scan of the right and left eyes showing an irregular, poorly defined neovascular network, foveal involving with a visible core (white arrow). Note in the corresponding SD-OCT of the left eye, the slab between the outer retinal layer and choriocapillaris contains the most important information about choroidal neovascularization.

Fig. 5. 6 mm × 6 mm and 12 mm × 12 mm optical coherence tomography angiography (OCT-A) and corresponding structural spectral domain OCT (SD-OCT) of the left eye. **A** and **B.** 6 mm × 6 mm and 12 mm × 12 mm OCT angiograms of the choriocapillaris plexus and the corresponding structural OCT B-scans of the left eye showing an irregular, poorly defined neovascular network, foveal involving with a visible core. Note in the 12 mm × 12 mm OCT angiogram, the extension of neovessels involving the whole posterior pole.



the drusen as a possible late evolution of degenerating LCDs. Of note, after the detailed description of this patient, we faced a second case showing similar features (data not shown), which gives further evidence of such possible evolution for LCD.

It is generally accepted in clinical practice that asymptomatic CNV does not have associated intra/subretinal exudation on optical coherence tomography and does not meet the criteria for anti-vascular endothelial growth factor therapy. Recently, our group was the first to demonstrate that OCT-A has a high sensibility and specificity for quiescent CNV detection in AMD and in pachychoroid neovasculopathy.^{8,9} It is noteworthy that different from the most frequent appearance of quiescent CNV in AMD, in this case CNVs appeared on OCT-A as irregular, poorly defined, foveal-involving networks with visible core vessels.¹⁰ Moreover, OCT-A showed a morphology with large straight dilated vessel, particularly evident in the left eye.¹⁴

In conclusion, we reported a case of LCD complicated by quiescent CNV bilaterally.

Since the original description, LCD has been considered as a benign condition. This report demonstrates that at least in some cases, LCD may present complications commonly observed in other chorioretinal diseases (both acquired and inherited) and thus should not be considered as a benign condition. Finally, the OCT-A may possibly be considered as a useful tool in the diagnosis, follow-up, and treatment decisions in patients affected by early-onset retinal drusen.

Key words: fluorescein angiography, quiescent choroidal neovascularization, large colloid drusen, optical coherence tomography angiography.

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