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Multimodal imaging of late-onset retinal degeneration complicated by bilateral choroidal neovascularization

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We report on the management of a case of bilateral macular choroidal neovascular membranes (CNVMs) associated with late-onset retinal degeneration (LORD).

AQ1

A 54-year old woman presented with a 6-year history of nyctalopia. Both her father and paternal grandfather had a history of night blindness. Snellen visual acuities were 6/6 OD and 6/5 OS. Fundal examination revealed bilateral macular atrophy and drusen-like deposits, with well-defined scalloped areas of RPE atrophy in the mid-periphery. Cone mediated electroretinography (ERG) was normal, however rod and mixed photoreceptor responses were significantly below normal levels in both eyes. Furthermore, pattern ERG and occipital pattern visual evoked potentials to the smallest 10’ checks were degraded, indicative of reduced bilateral macular function.

AQ2

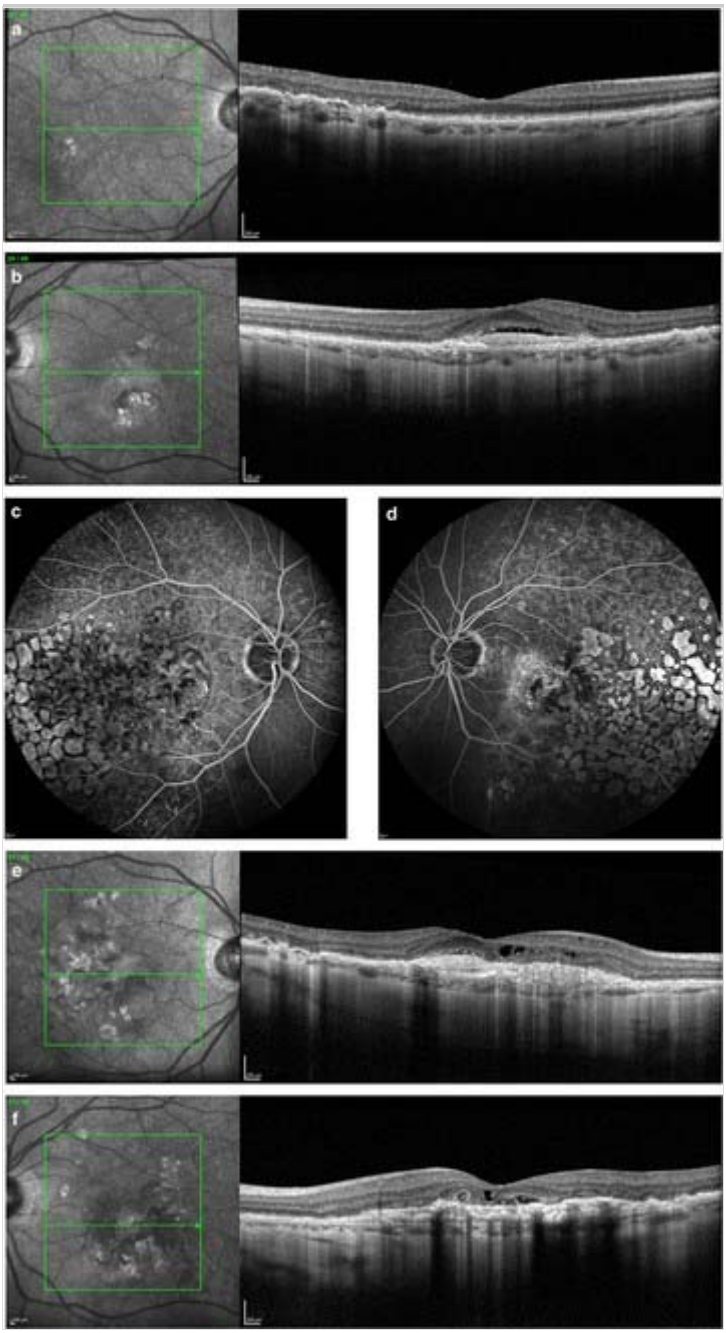
AQ3

AQ4

At the planned 6-month follow-up no change in the vision had been noticed by the patient though visual acuities were found to be 6/7.5 OD and 6/24 OS. Examination revealed a left CNVM with subretinal fluid and a course of three ranibizumab (Lucentis) intravitreal injections at monthly interval were initiated (Fig. 1a, b). Subsequent DNA analysis identified a heterozygous C1QTNF5 change c.489C>G p.(Ser163Arg), confirming the diagnosis of LORD.

Fig. 1

LORD with secondary CNVM imaged by Heidelberg Spectralis optical coherence tomography (**a**, **b**, **e**, **f**), MultiColor (**g**, **h**), and fluorescein angiography (**c**, **d**)


a
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c
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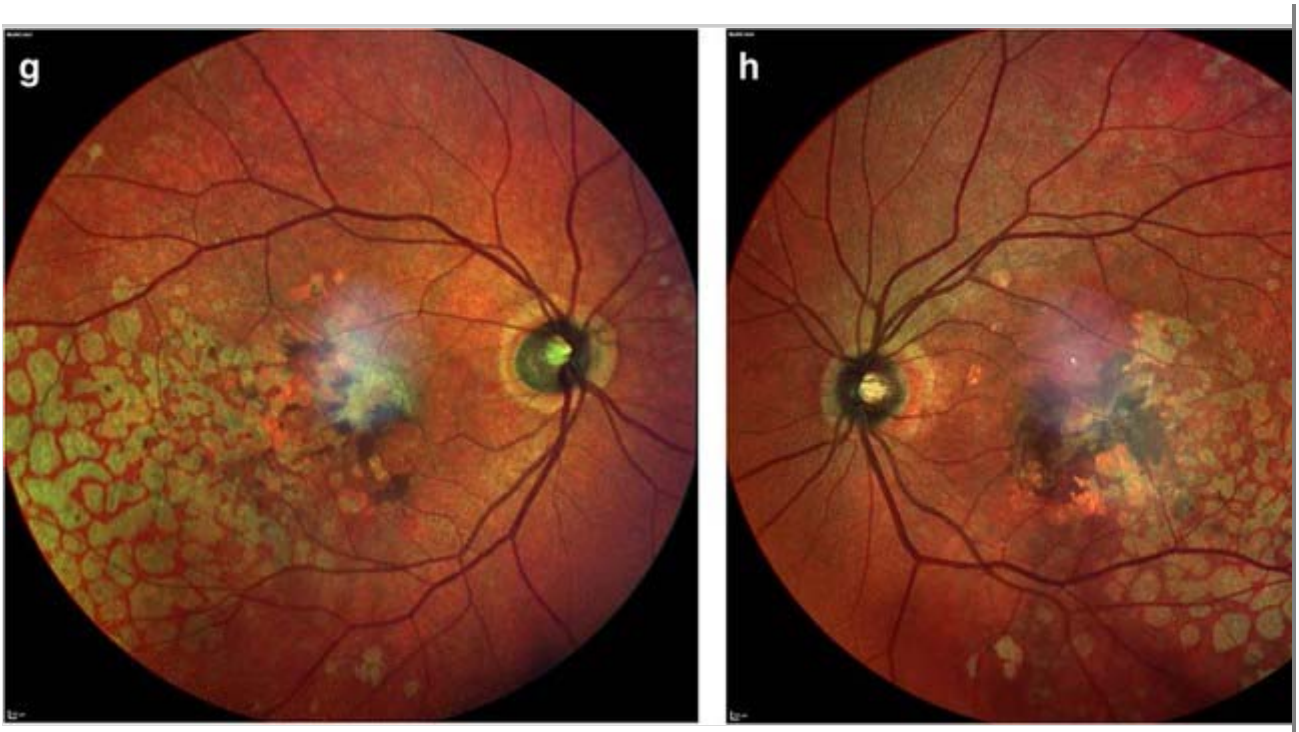


Visual acuity was 6/7.5 OD and 6/15 OS at 1 month following the third ranibizumab injection. Examination revealed no fluid in the left macula, however, an extrafoveal CNVM with mild subretinal fluid had now developed in the right macula. A course of three bevacizumab (Avastin) intravitreal injections at one-month interval was commenced in the right eye. At 6 week follow up visual acuity was 6/7.5 OD and 6/24 OS with examination showing no macular fluid bilaterally, which remained the case over the following months (Fig. 1c, d). After a further 17 months, visual acuities were 6/38 OD and 6/24 OS with OCT examination revealing intra- and subretinal fluid bilaterally (Fig. 1e–h). A further course of three intravitreal bevacizumab injections at monthly interval were initiated in both eyes, with plan for continued close monitoring and treatment.

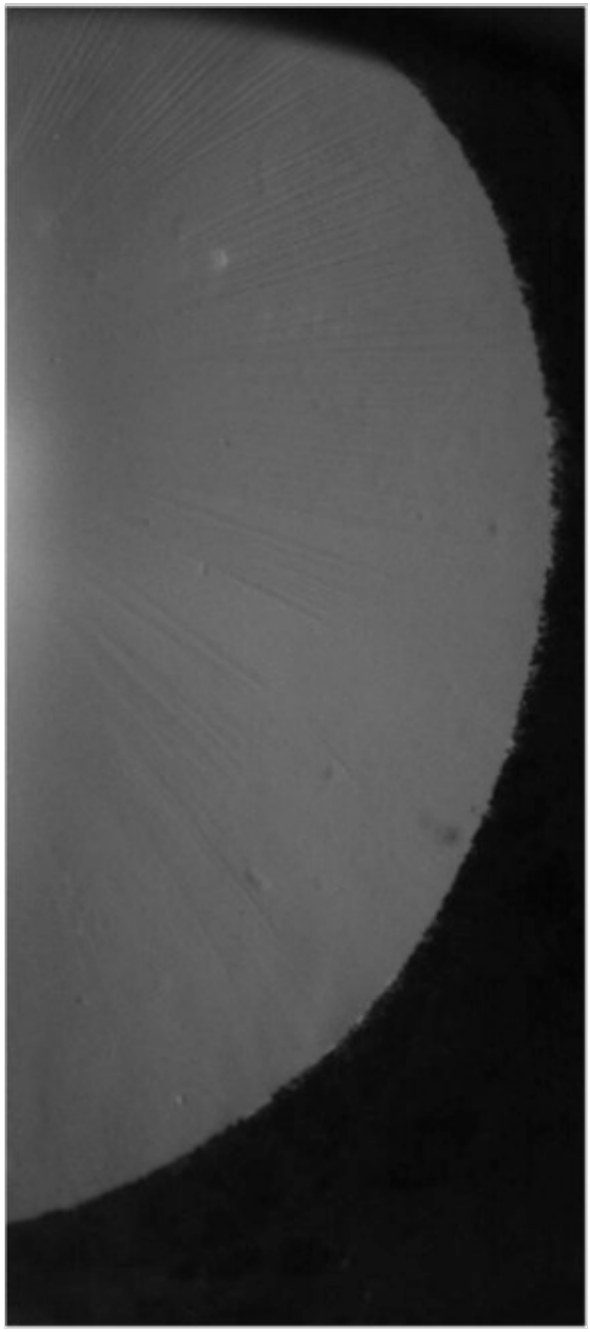
Discussion

LORD is an autosomal dominant ocular disease involving a mutation in the C1QTNF5 gene on chromosome 11, encoding Complement Component 1q and Tumor Necrosis Factor Related Protein 5. This rare condition is characterized by the onset of nyctalopia in midlife with progressive decline in central and peripheral vision. Fundus features include drusenoid deposits, pigmentary retinopathy, chorioretinal atrophy, CNVM, and retina-wide thick extracellular deposition between the retinal pigment epithelium and Bruch's membrane [1, 2]. Indeed, LORD may be mistaken for a number of conditions such as Sorsby fundus dystrophy, choroideraemia, retinitis pigmentosa, and

age-related macular degeneration. Our patient also showed the typical features of peripupillary iris atrophy and long anteriorly inserted lens zonules, which if present may aid diagnosis prior to genetic testing (Fig. 2).

Fig. 2

Anterior segment photo showing peripupillary iris atrophy and long anteriorly inserted lens zonules



Some studies have shown a positive effect of vitamin A supplementation in slowing the progression of LORD, whilst laser photocoagulation of associated CNVM has not been promising [3]. We have demonstrated that such CNV

lesions are responsive to anti-vascular endothelial growth factor therapy.

Within the eye, C1QTNF5 is significantly expressed in the RPE, ciliary process and lens epithelium, with studies showing an important role in adhesion between the RPE and Bruch's membrane [2, 3]. Continued research is necessary to further elucidate the function of C1QTNF5 and the pathogenesis of LORD, which could lead to the development of novel treatment strategies, possibly including retinal gene (CRISPR/Cas9) and cell based therapies [4, 5, 6].

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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