2813 - Multimodal imaging highlights novel phenotypic changes in late-onset retinal macular degeneration prior to loss of visual acuity

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Introduction

•Late-onset retinal macular degeneration (LORMD) is a rare blinding eye disease with autosomal inheritance resulting from a single point mutation.

•LORMD is an clinically important condition as it shares key clinical and pathological characteristics with age-related macular degeneration (AMD).

•LORMD has been proposed as a good inherited model for AMD.

•Early clinical diagnosis and monitoring of LORMD has proven difficult requiring specialised equipment.

•Recent developments in retinal imaging have enabled the improved investigation of the neuro-retina and sub-retina in early LORMD patients to assist both diagnosis and monitoring of the disease..

Aims

1) To investigate whether choroidal thickness is affected choroid is affected in LORMD when compared to age-sex matched controls.

2) To investigate the rate of progression of patients with stage 2 disease using scanning laser ophthalmoscopy (SLO).

Methods

OCT study

•7 LORMD patients and 8 controls were recruited and matched for refractive power in a case-controlled observational study.

•All patients were in stage 2 disease with a mean LogMAR BCVA -0.1. Controls also had a mean BCVA of -0.1.

•Patients had an average age of 56.7 years with 5:2 male:female ratio whilst controls had a mean age of 57.9 years with a 5:3 male:female ratio

•We investigated all the patients using Spectralis SD-OCT (Heidelberg Engineering, Heidelberg, Germany) Figures were analysed using a semi automated analysis of choroid depth using figures gained for the fovea.

SLO study

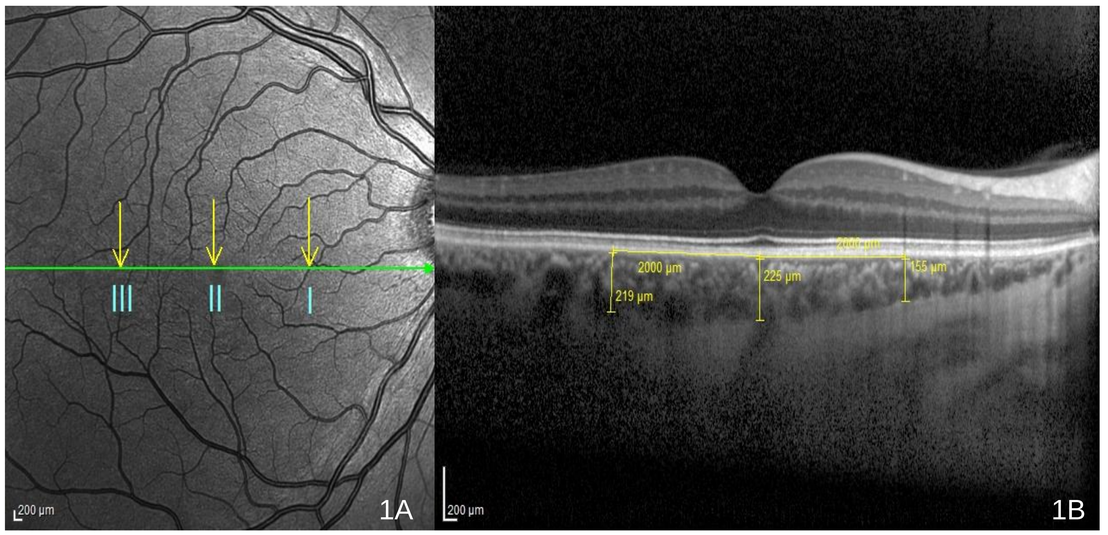
•Longitudinal cohort study measuring autofluorescence.

•The same 7 LORMD patients were analysed on Heidelberg SLO at baseline and after approximately annually for 3 years to monitor atrophy..

•The areas of reduced autofluorescence were measured at these time points using Heidelberg Region finder software.

•This method of measuring in LORMD was initially validated with two masked retinal specialists using 20 test images.

•Ethics approval for the trial was provided by Newcastle Upon Tyne NHS Foundation Trust's ethics committee. The data analysis for this paper was generated using the Real Statistics Resource Pack software (Release 3.5).



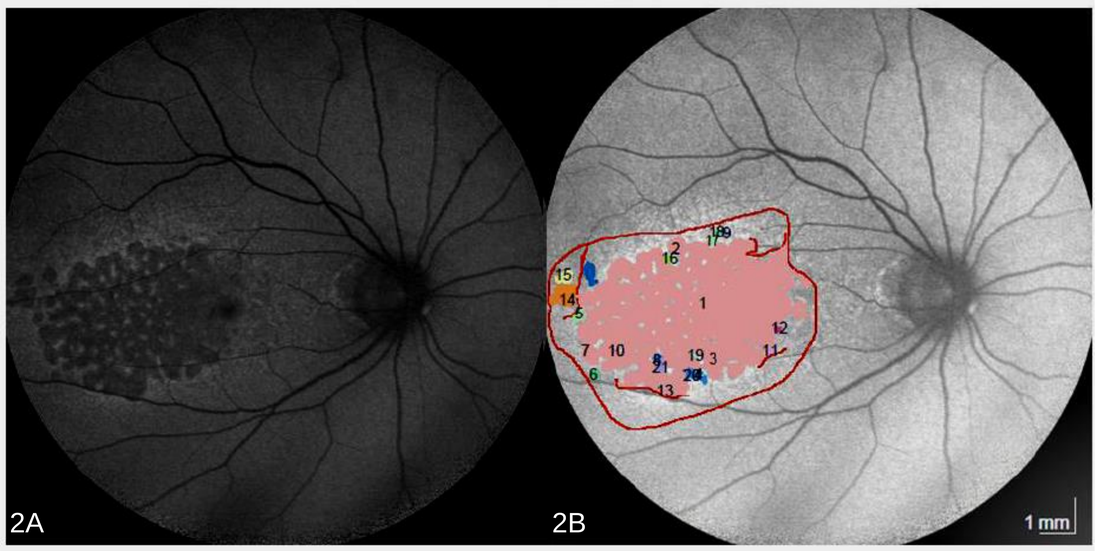


Figure 1A Scanning laser ophthalmoscope image highlights the points of choroidal thickness measured in a control eye using the fovea as a landmark

Figure 1B Heidelberg Spectralis software was used to measure choroidal depth using callipers measured in uM.

Figure 2A An example of a SLO image from a LORMD patient. Note the areas of marked reduced autofluorescence temporal to the macula.

Figure 2B The areas of reduced autofluorescence were mapped using a semi automated software and the figures for area were noted to calculate a rate of progression

Results

OCT study

•The choroid was significantly thinner in LORMD patients (mean=218.8uM, SD=72.5) when compared to controls (mean=278.8um, SD=73.7) ($P<0.05$) when measured at the fovea.

•No significant difference was found in the neuro-retinal thickness between cases and controls

•To confirm these findings neuro-retinal volume also showed no significant difference in loss in cases when compared to controls.

SLO study

•Measuring the areas of atrophy in LORMD with Heidelberg Region finder software was showed good agreement Cronbach's $\alpha=0.98$ using 2 masked observers.

•The average size of hypofluorescent areas at baselines was 3.6 mm^2

•There was poor correlation between age and size of areas at baseline ($R=0.12$)

•The rate of progression was 2.5mm^2/year (SD=2.1mm^2)

Conclusions

•We have previously described a staging system for L-ORMD and refined the phenotype using ICG, FFA, microperimetry and multifocal ERG

•In this research we further refine the phenotype further using OCT and show that autofluorescence can be used as a tool to monitor progression.

•The key findings of this study include:

1. Validation of the use of Region finder to measure the area of atrophy in LORMD
2. Marked variability in stage 2 disease area of atrophy and progression.
3. Greater rate of progression of atrophy when compared to geographic atrophy from papers in the literature.
4. Choroidal thinning in patients measurements at the fovea prior to foveal neuro-retinal loss

References

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