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CORRESPONDENCE

Association of unilateral lattice corneal dystrophy on slit lamp and bilateral confocal microscopy features with H572R mutation in the TGFBI gene

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Lattice corneal dystrophy (LCD) type 1 is a progressive dystrophy characterised by accumulation of amyloid in the corneal stroma, which has the appearance of thin branching reflective lights, leading to deterioration of visual acuity [1]. Lattice dystrophy can be identified by histology with Congo red, green birefringence with polarising filter and by confocal microscopy (IVCM) [1]. Unilateral lattice dystrophy (ULD) cases have been reported in the literature [2–5] associated with different pathogenic variances [3, 5], including the p.(His572del), which was suggested to cause unilateral presentation [3].

We previously reported one case of seemingly ULD, where a 24-year-old patient (patient 1) had clinical signs only in the left eye (Fig. 1a, b) but displayed evidence of LCD bilaterally with IVCM (Fig. 2a, b). Similarly, a 41-year-old patient (patient 2) was referred with slit lamp signs in the right eye only (Fig. 1c, d) but had bilateral lattice evidence with IVCM (Fig. 2c, d). This patient developed early lattice changes in the previously asymptomatic eye 5 years after first seen (Fig. 1e, f). A 31-year-old patient (patient 3) presented with unilateral dystrophy on slit lamp biomicroscopy (Fig. 1g, h) but was found to have bilateral lattice deposits with confocal microscopy (Fig. 2e, f). Genetic testing was performed in two patients (patients 1 and 2), who were both found to have a heterozygous mutation in exon 13c.1715 A>G p.(His572Arg), changing histidine to arginine at codon 572 (H572R). The third patient did not consent to have genetic testing.

Our findings provide further evidence that asymptomatic eyes in ULD may have sub-clinical disease, and that in early stages ULD can only be identified by IVCM, which is necessary for correct diagnosis. We also show that sub-clinical disease may develop into symptomatic disease in the long term and advise that patients need to be counselled that their unaffected eye may develop disease.

This rare asymmetric presentation was associated with H572R mutation in the two patients who agreed to have genetic testing. A mutation at this amino acid was previously reported with late unilateral presentation (at 63 years old) but IVCM was not performed and sub-clinical presentation was not excluded [3]. This mutation has also been linked with bilateral disease in patients where presentation was in the 3rd and 4th decades [5]. The three patients in this study are older than the classical 1st decade presentation for LCD. Our findings, taken together with those in literature, suggest that mutations affecting this amino acid may lead to a less aggressive phenotype, including asymmetric and asynchronous presentation, and that onset may be later than with classic LCD. We suggest that restraint should be exercised with diagnosing unilateral corneal lattice until changes have been excluded in IVCM. We also suggest that unless proven otherwise, unilateral LCD should be called asymmetrical LCD. This may have significant implications on patient's expectations and advice given.

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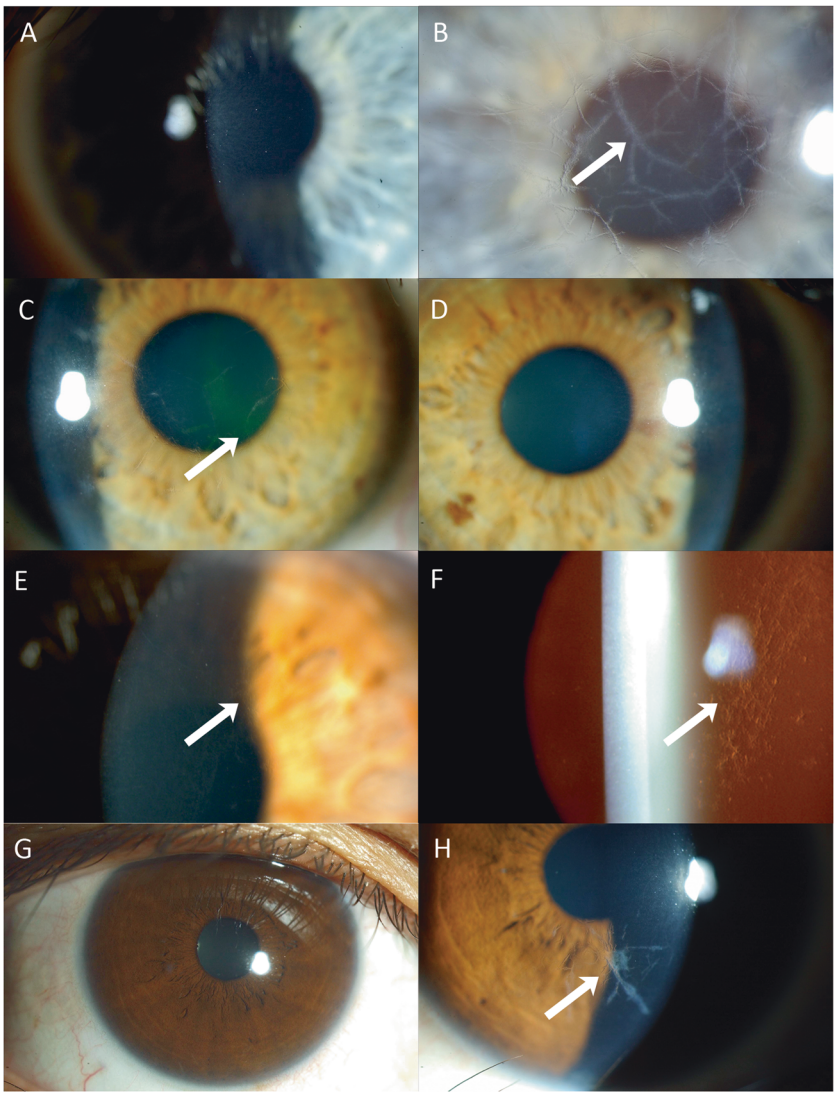

Fig. 1 Slit lamp photographs. Arrows indicate presence of lattice lines. **a**, **b** belong to patient 1, who has the H572R mutation. **a** belongs to right eye (asymptomatic) and **b** belongs to left eye (symptomatic). **c**, **d**, **e** and **f** belong to patient 2, who has the H572R mutation. **c**, **d** were taken at referral. **c** shows right eye (symptomatic) and **d** shows left eye (asymptomatic). **e**, **f** show left eye 5 years after referral. **e** indicates an area of mild lattice lines, which are more distinguishable on retroillumination, as shown in **f**. **g**, **h** belong to patient 3, who declined genetic analysis. **g** belongs to the right eye (asymptomatic) and **h** to the symptomatic left eye

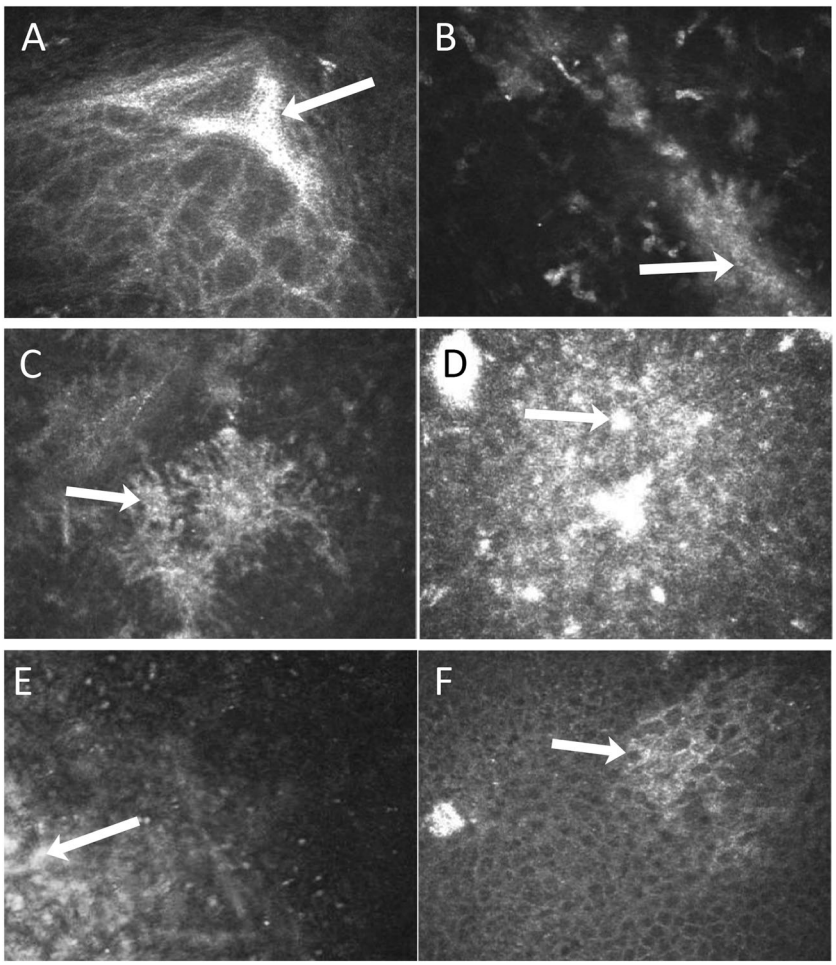

Fig. 2 IVCM photographs. Arrows indicate presence of amyloid deposits. **a**, **b** belong to patient 1. **a** corneal stroma (65 µm depth) of the unaffected right eye. **b** corneal stromal section (75 µm depth) of the affected left eye. **c**, **d** belong to patient 2 at referral. **c** corneal stroma (100 µm depth) of the affected right eye. **d** corneal stroma (106 µm depth) of the unaffected left eye. **e**, **f** belong to patient 3. **e** corneal stroma (201 µm depth) of the unaffected right eye. **f** corneal stroma (47 µm depth) of the affected left eye

Compliance with ethical standards

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

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