with a power and duration around 2000–2500 mW and 2000–2800 ms, respectively. Therefore, we believe that the IOP needs to be checked immediately after TSCPC and managed properly if it is elevated.

Conflict of interest

The authors declare no conflict of interest.

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Sir,

Assessment of a three-generation pedigree with Fuchs endothelial corneal dystrophy with anticipation for expansion of the triplet repeat in the *TCF4* gene

Fuchs endothelial corneal dystrophy (FECD) has a significant genetic component to its pathogenesis and several genetic risk factors for FECD have been discovered. The first genetic risk factor for FECD, transcription factor 4 (*TCF4*), was detected by a genome-wide association study.[1] A trinucleotide repeat, $(CTG)_n$ also known as CTG18.1, is located within an intron of the *TCF4* gene.[2] Expansion of the *TCF4* trinucleotide repeat is associated with FECD and expansion to >40 repeats confers a hazards ratio of 1.64 for a corneal transplant.[3] Anticipation, earlier onset of disease with increasing severity in successive generations, occurs in diseases caused by trinucleotide repeat expansions (ie, Huntington's disease).[4]

Case report

We investigated the potential role of *TCF4* trinucleotide repeat expansion in a three-generation pedigree with a history suggestive of anticipation. FECD was diagnosed via slit lamp biomicroscopy by a board-certified ophthalmologist with cornea fellowship training, graded using a modified Krachmer scale of 0 (no disease)–6 (>5 mm of central confluent guttae with corneal edema),[5] and examined via confocal microscopy (ConfoScan 4, Nidek Technologies, Fremont, CA, USA) and corneal tomography (Pentacam HR, Oculus, Lynnwood, WA, USA).

Three family members were diagnosed with FECD[5] and displayed features of anticipation. The age at diagnosis occurred earlier in each successive generation, with the grandmother, mother, and daughter receiving the diagnosis of FECD at 63, 48, and 27 years of age, respectively (Figures 1 and 2). The severity of corneal endothelial disease was greater in each successive generation, with the grandmother, mother, and daughter displaying a modified Krachmer Grade of 2, 4, and 6, respectively, and central corneal thickness (right/left) of 535/537, 568/572, and 627/602 μm, respectively.

The size of the *TCF4* trinucleotide repeat was evaluated in members of the FECD pedigree to determine if an expansion of the repeat might be the source of anticipation. The *TCF4* trinucleotide repeat was amplified from family member DNA samples with the polymerase chain reaction, cloned, and sequenced using standard methods.[6] Each family member's genome has two copies of the *TCF4* gene. Analysis of these DNA sequences revealed the exact number of *TCF4* trinucleotide repeats in each family member's genome. The grandmother, mother, and

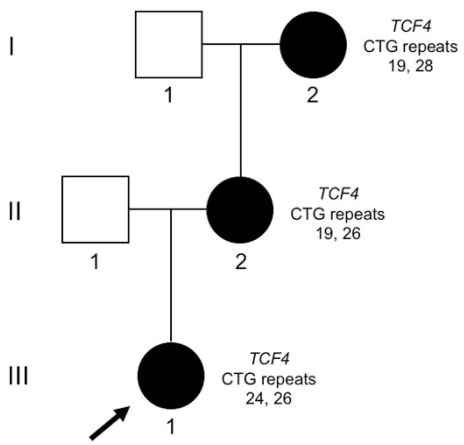

Figure 1 Three-generation FECD pedigree. The proband is indicated with an arrow and symbol III-1, while the proband's mother and grandmother are indicated by symbols II-2 and I-2, respectively. Family members diagnosed with FECD are indicated with symbols that are shaded black. The number of *TCF4* trinucleotide repeats in each family member's genome was determined by PCR amplification and DNA sequencing, and is indicated to the right of their pedigree symbol.

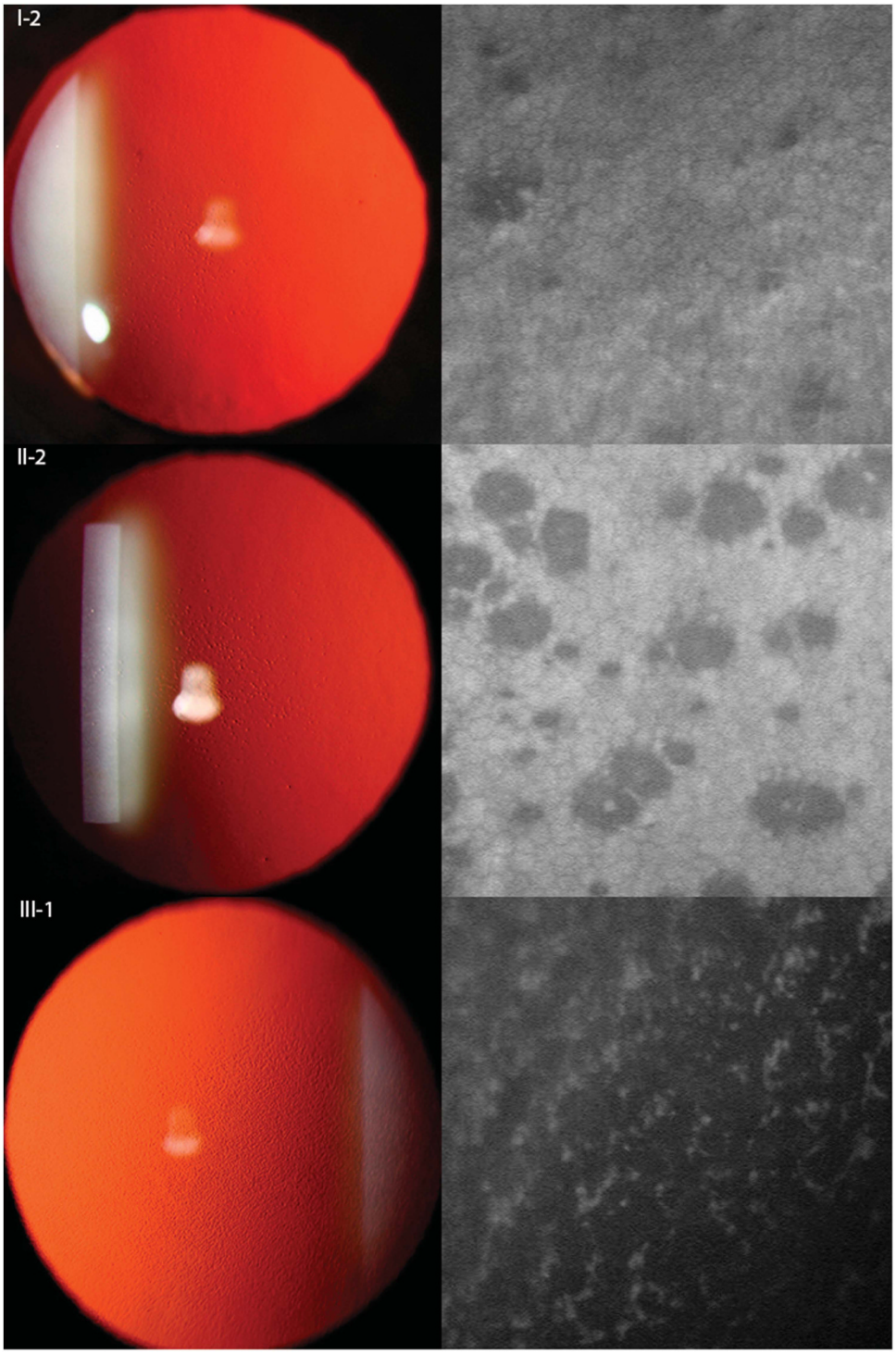

Figure 2 Clinical features of FECD pedigree. Confocal microscopy (right column) and slit lamp biomicroscopy (left column) images of affected family members. Patient I-2 (top row) demonstrated mild corneal guttae (modified Krachmer Grade 2) with endothelial cell density of 1976 cells per mm^2 and rare polymegathism. Patient II-2 (middle row) demonstrated moderate corneal guttae (modified Krachmer Grade 4) with endothelial cell density of 1693 cells per mm^2 and mild polymegathism. Patient III-1 (bottom row) demonstrated confluent corneal guttae (modified Krachmer Grade 6) with diffuse endothelial cell dropout.

daughter had 19 and 28, 19 and 26, and 24 and 26 CTG repeats in *TCF4* genes, respectively (Figure 1).

Comment

All three family members with FECD had <40 *TCF4* trinucleotide repeats. While larger numbers of *TCF4* trinucleotide repeats confer higher risk for FECD, 20% of patients with FECD have fewer than 40 repeats as in this pedigree.[2] Moreover, there is no expansion of *TCF4* trinucleotide repeats in successive generations of the pedigree (Figure 1). These data demonstrate that anticipation of FECD in this pedigree is not due to trinucleotide repeat expansion in the *TCF4* gene. The earlier age at diagnosis and severity of FECD in offspring of this pedigree may be due in part to ascertainment bias and/or other genetic and environmental factors. However, the *TCF4* trinucleotide repeat may underlie anticipation in other FECD pedigrees with patients that have larger numbers of repeats than were observed in this study.

Conflict of interest

The authors declare no conflict of interest.

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