mm Hg in the right eye and 22 mm Hg in the left eye. Although the fundus view was blurry the optic disc did not have any glaucomatous appearance with the normal peripapillary retinal nerve fiber layer thickness. There was no family history of corneal disorders, in both parents and siblings (1 sister and 1 brother). After obtaining an informed consent, genomic DNA was isolated from the peripheral blood leukocytes. Direct DNA sequencing of the *SLC4A11* gene was performed. All 19 exons were amplified using the primers previously described.[3] For all amplicons, the genomic DNA was denatured at 95°C for 5 minutes, followed by 35 cycles of denaturation at 95°C for 30 seconds, annealing at 60°C for 30 seconds, extension at 72°C for 1 minute, and final extension at 72°C for 5 minutes. The polymerase chain reaction products were examined by 1.5% agarose gel electrophoresis, followed by staining of the gel in ethidium bromide (0.5 μg/mL), which then was visualized under an ultraviolet light in a Gel Doc 1000 gel documentation system (Biorad, Hercules, CA). Polymerase chain reaction amplicons were bidirectionally sequenced with the Big Dye terminator v3.1 cycle sequencing kit (Applied Biosystems, Foster City, CA), using the ABI PRISM 3100 Genetic Analyzer (Applied Biosystems). RefSeq ID: NM_032034.2 was used for complementary DNA nucleotide numbering.

We detected a novel homozygous mutation of c.1239C>A, which induced stop codon at 413 amino acid (p.C413*) and produced a truncated NaBC1 protein (Fig. 1B). This mutation has not been previously reported and was not found in ethnically matched controls.[5] Sequence of this region is conserved among eukaryotic species.[6] Nonsense mutation involving amino acid residues in the region with high interspecies conservation would be deleterious. p.C413* nonsense mutation resulted in premature truncation of the NaBC1 transcript without the entire cotransporter domain. Unstable messenger RNA (mRNA), resulting from the p.C413* nonsense mutation, might be vulnerable to nonsense-mediated mRNA decay, which is the process in which mRNAs containing premature termination codons are degraded before they produce large amounts of truncated proteins. Various mutations in *SLC4A11* have been identified in patients with CHED2 in a homozygotic or compound heterozygotic form. Mutations in *SLC4A11* gene were identified in 55% to 83% of CHED2 patients with high degree of genetic heterogeneity.[3,7–9]

In conclusion, to the best of our knowledge, this is the first Korean case of CHED2, confirmed by the c.1239C>A (p.C413*) mutation in the *SLC4A11* gene, which has not been previously reported. This study expands the mutational spectrum of autosomal recessive CHED.

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Impact of Collagen Cross-Linking for Keratoconus on Corneal Sensitivity

To the Editor:

Wasilewski et al[1] recently published a study investigating the impact of corneal collagen cross-linking (CXL) with riboflavin and ultraviolet A (UV-A) on corneal sensitivity in keratoconus patients. The authors performed a standard epithelium-off (epi-off) CXL procedure according to the Dresden protocol[2] in patients with progressive keratoconus and reported a significant decrease in corneal sensitivity, which was prominent at 1 week after the procedure, and recovered gradually over the following months. Based on these findings, the authors suggest that CXL induces a marked reduction of corneal sensitivity, probably because of damage in the nerve fibers of the corneal nerve plexus in the anterior stroma.

There are some points, which, in our opinion, merit further consideration. Whereas several studies have shown that epi-off CXL affects the morphology of the corneal subbasal nerve plexus,[3–5] the threshold for clinical manifestation of corneal nerve density variations is high. Alterations of corneal nerve density do not translate into clinically evident corneal hyposensitivity unless they reach absolute values below 835 micrometer per frame.[6] This was not the case in any study with a quantitative analysis of corneal nerve density after epi-off CXL published up-to-date. Whether the morphological alteration of the corneal nerve plexus after epi-off CXL could lead to functional impairment is yet to be investigated.

Moreover, Xia et al[7] have shown that intraepithelial nerve damage is rather caused by the mechanical removal of

the corneal epithelium, and the potential deeper corneal nerve damage is induced by the UV-A treatment. Deepithelialization alone significantly decreases corneal sensitivity, which gradually recovers and is fully restored in the presence of normal corneal homeostasis.[7,8] However, keratoconus is characterized by impaired corneal innervation and sensitivity, as a result of the underlying disturbance in corneal homeostasis.[9,10] Therefore, deepithelialization alone has a more drastic impact on corneal sensitivity in keratoconus because of both the "inherited" disease-associated neuropathy and the subsequent abnormal corneal regeneration.

In our opinion, corneal nerve injury due to deepithelialization alone and the increased vulnerability of the corneal nerve plexus in keratoconus may predominantly account for the observed decrease in corneal sensitivity after epi-off CXL. Potential direct functional corneal nerve damage by the UV-A irradiation requires further investigation.

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