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Ophthalmic Features of Spinocerebellar Ataxia Type 7: A Case Report

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Male, 32-year-old
Final Diagnosis: Spinocerebellar ataxia
Symptoms: Ataxia • decrease in the visual acuity
Medication: —
Clinical Procedure: —
Specialty: Ophthalmology

Objective: Rare co-existance of disease or pathology

Background: Spinocerebellar ataxia (SCA) is an inherited progressive neurodegenerative disorder characterized by late-onset cerebellar and brainstem dysfunction. It is an autosomal dominant condition with monoallelic pathogenic expansion in the ATXN7 gene. Patients have neurological deficits, including ataxia and dysarthria. Visual symptoms are the first presenting signs in patients with SCA type 7 (SCA7), including severely affected visual acuity and color vision, ocular motility impairment, and retinal macular degeneration. This is one of the first reports of the existence of keratoconus in a patient with SCA7. Few theories explain this coexistence, including vigorous rubbing of the eyes, and genetic and environmental etiologies.

Case Report: A 34-year-old man with SCA7 underwent genetic and ophthalmic investigations. Multiple family members of the patient had a positive history of ataxia. He had an abnormal posterior and anterior corneal elevation on Pentacam (Pentacam-Oculus, Optikgeräte GmbH, Wetzlar, Germany) and was eventually diagnosed with keratoconus in both eyes, which is not a known feature of SCA7. Later, he underwent a penetrating keratoplasty in the left eye with no subsequent improvement in vision. No further treatment was offered to the patient due to the guarded visual prognosis caused by the retinal pathology. He continues to have routine follow-ups in the Ophthalmology Clinic.

Conclusions: This case reinforces the importance of recognizing the guarded visual outcome in these patients due to the macular degeneration and progressive nature of the disease. Therefore, appropriate and adequate patient counseling about the visual prognosis is essential before proceeding with any ocular surgical interventions.

Keywords: Keratoconus • Keratoplasty, Penetrating • Spinocerebellar Ataxias

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/932279

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Background

Spinocerebellar ataxia (SCA) is an inherited progressive neurodegenerative disorder characterized by late-onset cerebellar and brainstem dysfunction [1]. There are approximately 50 genetically different types of SCAs reported in the literature and type 7 is 1 of the most common types [2]. SCA type 7 (SCA7) is an autosomal dominant entity that shares a common genetic mechanism with other autosomal dominant SCAs, which is an expansion of the glutamine chain due to an increase in the cytosine-adenine-guanine (CAG) repeats of the causal gene on chromosome 3p12-13. This gene controls the production of the protein ataxin-7 [3,4]. The age of onset for SCA7 is usually 30 years to 50 years and is inversely correlated with the length of the CAG repeat expansion [5].

The first neurological features of the disease are truncal or gait ataxia, which can progress to limb ataxia and dysarthria [6]. SCA7 is distinguished from other SCAs by the presence of visual dysfunction in the affected individuals. Visual symptoms can be the first presenting sign in a patient with SCA7 [7]; therefore, ophthalmologists should have a high index of suspicion for this diagnosis when a patient has a positive family history of visual loss and ataxia.

The reported ophthalmic features of SCA7 include severely affected visual acuity and color vision in the initial stages of the disease, which progress to complete blindness. In addition, ocular motility impairment can occur, including the slowing of saccades, ophthalmoplegia, and gaze-evoked nystagmus [6]. Retinal and macular degeneration is a hallmark of SCA7 that can be diagnosed prior to the appearance of abnormalities seen in the fundus examination by performing an electroretinogram (ERG) or ocular coherence tomography (OCT) [8]. Currently, curative therapy for the ophthalmic features of SCA7 is nonexistent; nonetheless, a study on animal models showed promising results with preservation of retinal function and no adverse effects of using RNA interference technology to reduce mutant and wild-type ataxin-7 expression in mouse retinas [9].

This case report is the first of its kind to document the coexistence of keratoconus along with SCA7 and could pose more questions than answers; however, it is important to discuss and investigate all the theories related to this coexistence.

Case Report

A 34-year-old man presented with progressive ataxia from the age of 32 years and progressive binocular visual loss as the main ophthalmic symptoms. His mother and brother had cerebellar ataxia and they died aged 52 years and 15 years, respectively. Their family pedigree is shown in **Figure 1**. He underwent genetic examination that confirmed the diagnosis of SCA7, with the presence of a monoallelic pathogenic expansion in the ATXN7 gene. Since he was 20 years old, he had more vision deterioration in the left eye (OS) than the right eye (OD). He underwent a penetrating keratoplasty for keratoconus in the left eye at the age of 22, although he reported no improvement in vision after this surgical intervention. The preoperative data of the left eye, including visual acuity, refraction, and Pentacam (Pentacam-Oculus, Optikgeräte GmbH, Wetzlar, Germany) examination were not accessible as the surgery was performed in a remote institute.

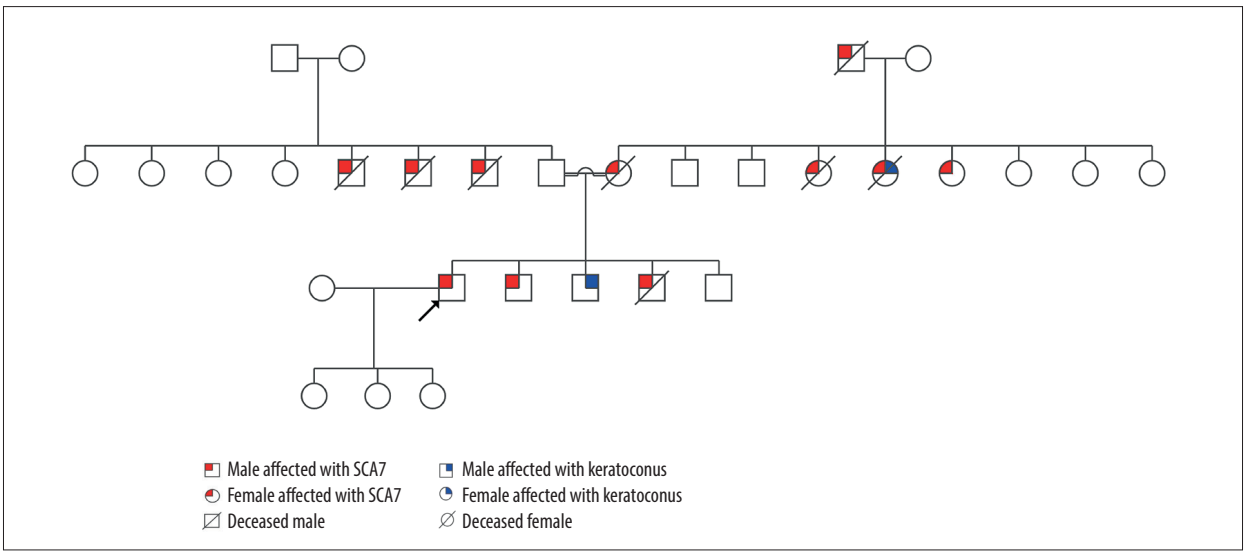

Figure 1. The family tree (pedigree) of spinocerebellar ataxia type 7 (SCA7)-affected individuals. Arrowhead shows the reported case; filled symbols indicate clinically affected individuals with SCA7 (red) and keratoconus (blue).

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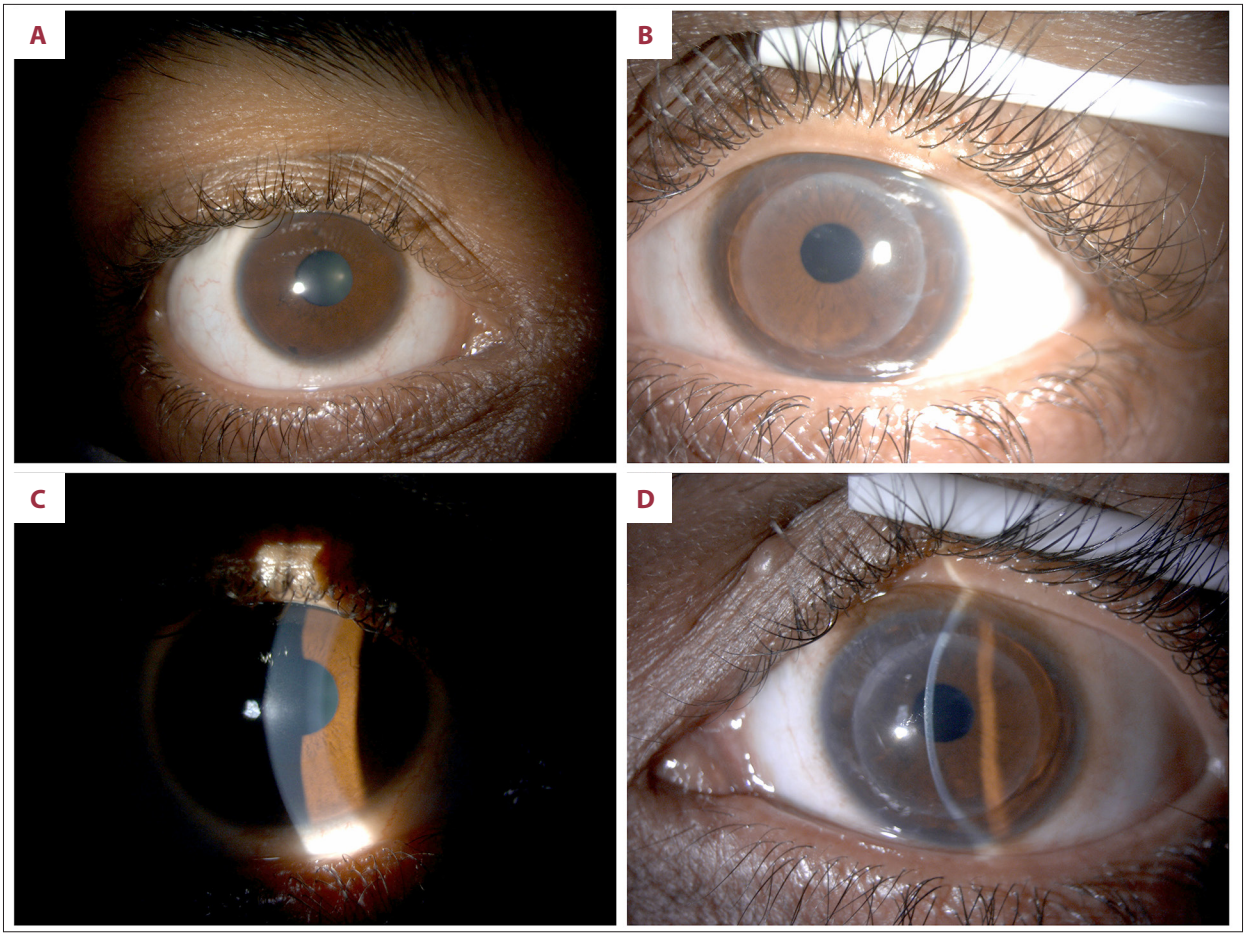

Figure 2. Biomicroscopic slit lamp photos: (**A**) Right eye with diffused illumination. (**B**) With the slit beam, the right eye showed advanced keratoconus with central corneal scarring. (**C**) Left eye with diffused illumination. (**D**) With the slit beam, the left eye showed a clear sutureless corneal graft with no signs of rejection.

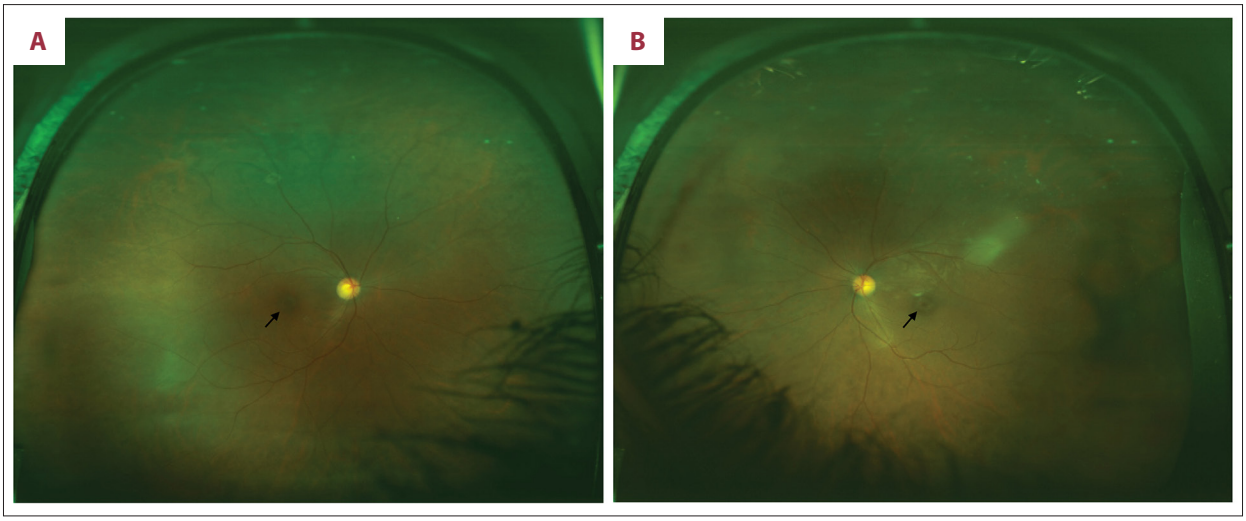

Figure 3. (**A**) Ultrawide-field (UWF) Optos (Optos California, Dunfermline, Scotland, United Kingdom) fundus photo of the right eye, with bull's eye maculopathy (arrowhead) and optic disc pallor. (**B**) Left eye showed bull's eye maculopathy (arrowhead) with optic disc pallor.

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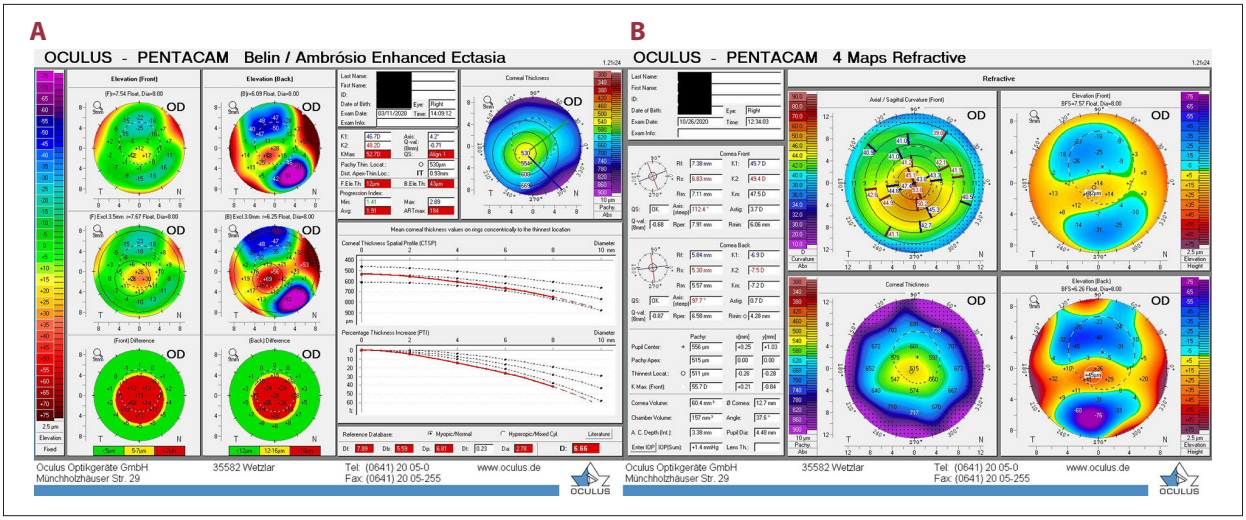

Figure 4. (**A**) Belin/Ambrosio Enhanced Ectasia Display of the right eye with elevation data on the left and pachymetric data on the right. (**B**) Keratometric values of the right eye on Pentacam (Pentacam-Oculus, Optikgeräte GmbH, Wetzlar, Germany) showed the displaced cone and inferior steepening on the axial curvature map, and a significant elevation suggestive of keratoconus in the posterior float.

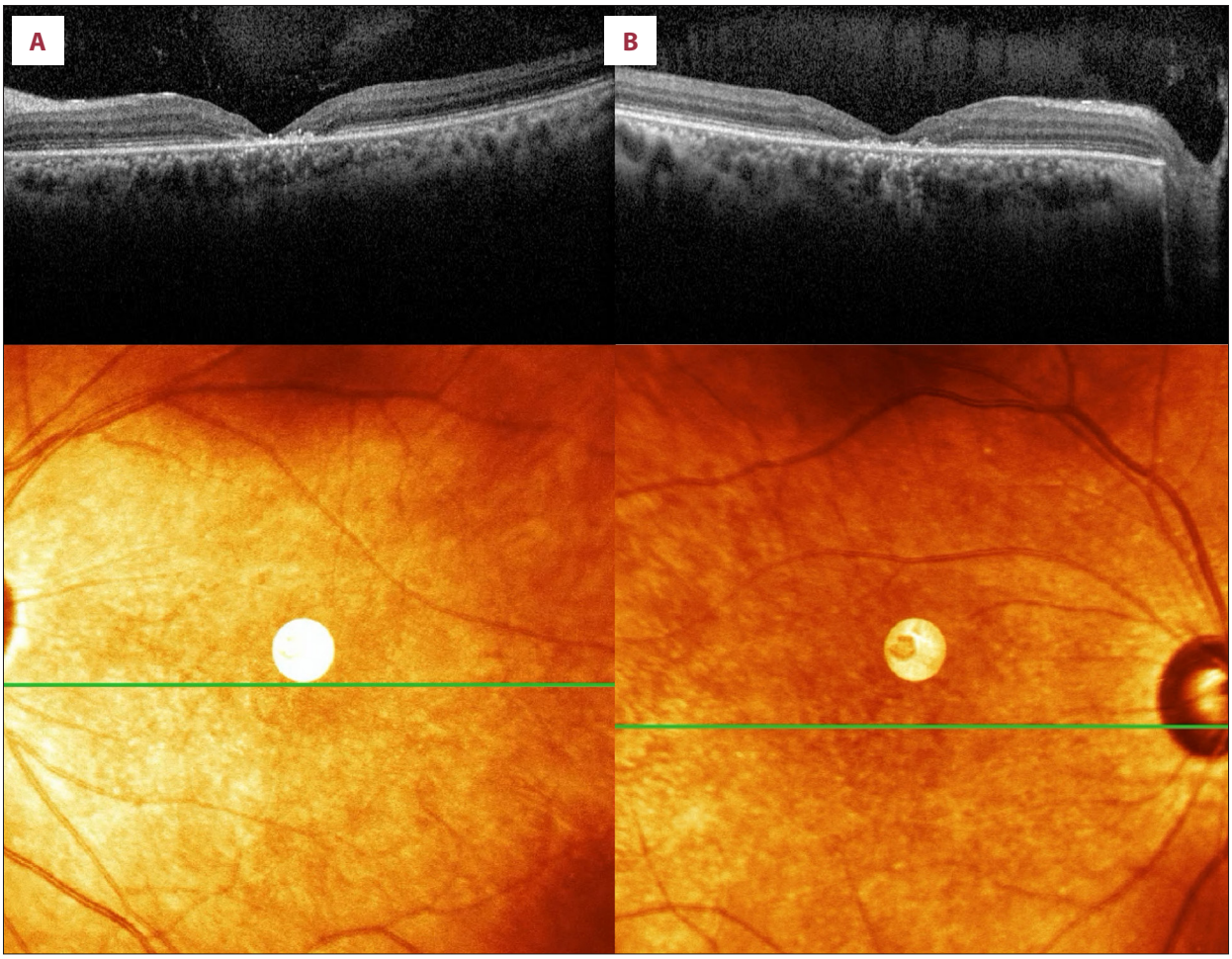

Figure 5. Ocular coherence tomography of the left eye (**A**) and right eye (**B**) with corresponding en face infrared images showed foveal hyperreflectivity with inverse shadowing indicating foveal atrophy in both eyes due to the loss of photoreceptors.

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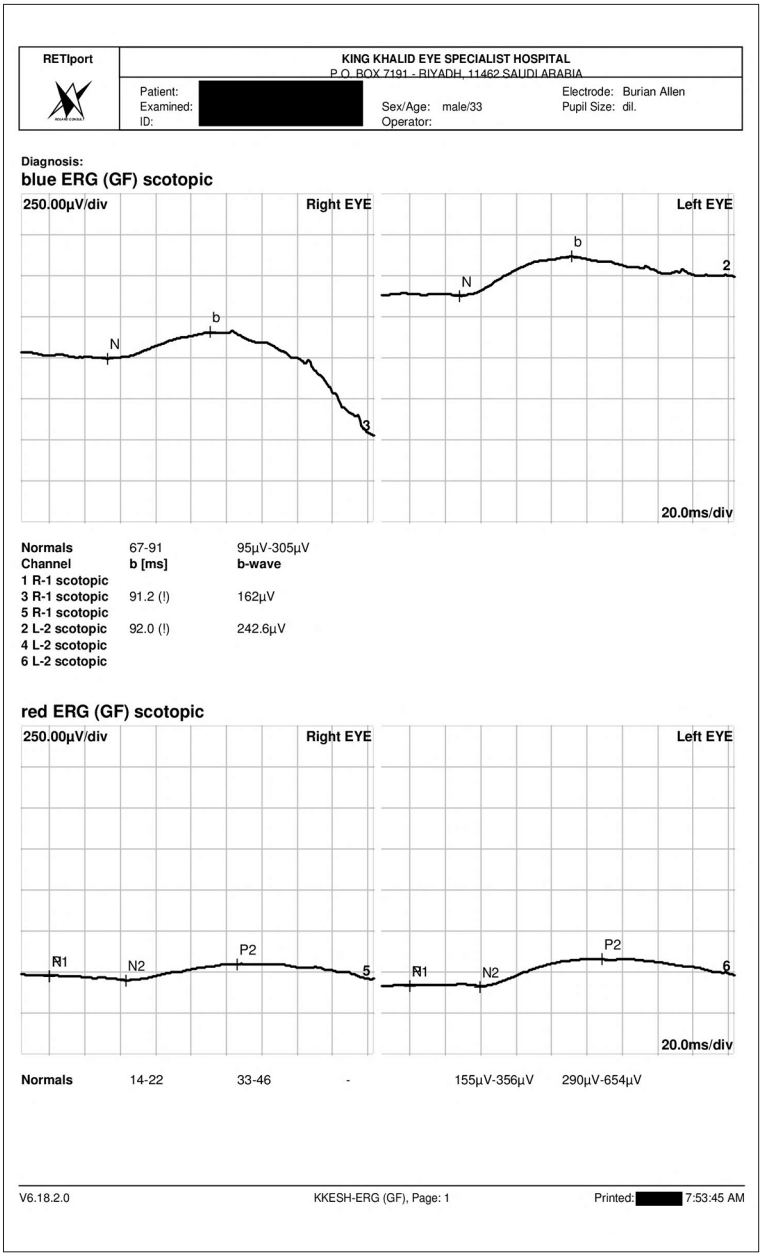

Figure 6. Electroretinogram showed a non-recordable cone response in both eyes.

At the current presentation, an ophthalmic examination revealed a visual acuity of 20/200 in both eyes. Color vision was evaluated using the Ishihara pseudoisochromatic color plates and he was not able to discriminate any of the plates in both eyes (0/11). He had normal intraocular pressure in both eyes, refraction was characterized by compound myopic astigmatism in the right eye, and simple myopic astigmatism in the left eye. The refraction of the OD showed -1.50 sph -3.50 cyl (35) and the OS showed -1.00 cyl (105). Extraocular motility was normal in both eyes and he was orthophoric. Slit lamp biomicroscopy of the anterior segment revealed superficial scarring of the cornea in the right eye, a normal iris, and a clear lens (**Figure 2A, 2B**). The examination of the left eye showed a clear corneal graft without sutures, a normal iris, and an intraocular lens in place (**Figure 2C, 2D**). A dilation examination of the retina and optic nerve revealed the loss of the normal foveal reflex, granular and atrophic appearance of the macula, sclerosing of the blood vessels, and a pale optic nerve head in both eyes. The fundus autofluorescence of the right eye is shown in **Figure 3A**; the left eye had a similar appearance (**Figure 3B**).

Specular microscopy revealed a low endothelial cell count in both eyes (1538 cells/mm^2 OD and 1040 cells/mm^2 OS). The Belin/Ambrosio Enhanced Ectasia map showed a significantly high D value suggestive of keratoconus (**Figure 4A**). Furthermore,

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the corneal Pentacam (Pentacam-Oculus, Optikgeräte GmbH, Wetzlar, Germany) examination of the right eye demonstrated high keratometry readings in the curvature map with a displaced cone and inferior steepening and the posterior float showed a significant elevation (**Figure 4B**). His maternal aunt has SCA7 and keratoconus; however, his brother had only keratoconus (**Figure 1**). The results of the OCT (Spectralis, Heidelberg Engineering, Inc., Heidelberg, Germany) of the macula showed a loss of the photoreceptor layer and foveal atrophy as shown in **Figure 5A** (left eye) and **Figure 5B** (right eye). An ERG revealed a non-recordable cone response (**Figure 6**). He continues to have routine follow-ups at the Ophthalmology Clinic for the monitoring of ophthalmic signs and no further treatment was offered to the patient due to the guarded visual prognosis. The study was approved by the institutional review board and informed consent was obtained from the patient.

Discussion

SCA7 is an autosomal dominant disease due to the expansion of the protein ataxin-7, characterized by the progressive onset of ataxia, dysarthria, and macular degeneration [10]. The clinical severity of SCA7 depends on the number of CAG repetitions [7]. The underlying pathophysiology of this disorder includes the atrophy of the spinocerebellar pathways, pyramidal tracts, and motor nuclei in the brainstem and spinal cord [1].

Patients diagnosed with SCA7 develop progressive retinal atrophy that eventually leads to blindness. Initially it affects the cone function, although later it can affect the function of the rods as seen in the present case. The macular OCT of our patient revealed the loss of photoreceptors and foveal atrophy, which coincides with previous reports of other patients with SCA7 [1]. The corneal endothelial cells are often affected in patients with SCA7 [1]. Similarly, the examination by specular microscopy demonstrated decreased cell density and abnormal morphology of the endothelial cells in our patient's right eye. It has been suggested that there is an inverse relation between the endothelial cell density and the number of CAG repeats [1].

This is the first reported case in the literature about keratoconus associated with SCA7. The corneal tomography of our patient showed clear diagnostic evidence of keratoconus in the right eye with a high keratometry reading, abnormal posterior and anterior elevation maps, and irregular astigmatism with inferior steepening in the curvature map. There is 1 report of congenital corneal astigmatism with spinocerebellar ataxia; however, genetic testing did not confirm the diagnosis of SCA [11].

The incidence of keratoconus was last reported in 2005 to be 20 cases/10 000 people in the Asir region of Saudi Arabia [12], which is significantly higher than the reported worldwide incidence (annual rate of 2/100 000 people) [13].

The presence of keratoconus in the setting of SCA7 in the present patient could be attributed to genetic factors affecting the corneal structure or accidental coexistence. However, the fact that the patient's brother was diagnosed with keratoconus without SCA7 hints at the likelihood that the coexistence of those 2 conditions in our patient is a mere coincidence. It is important to point out that patients with SCA7 are considered to have a guarded visual prognosis due to the progressive nature of the disease and the involvement of the macula, as evident in our patient who underwent keratoplasty in the left eye and yet his visual acuity is the same as that of the other (unoperated) eye. Therefore, it is critical to highlight the importance of extensive preoperative diagnostic workups for any young patients with unexplained bilateral visual loss. Before proceeding with any surgical intervention, a contact lens fitting is an important modality to utilize for illustrating the visual potential of patients with keratoconus.

Conclusions

There are varieties of ocular manifestations that can lead to visual loss in patients diagnosed with SCA7. To the best of our knowledge, this is the first reported case of advanced keratoconus managed by keratoplasty in a patient diagnosed with SCA7. It is crucial that ophthalmologists recognize the guarded visual prognosis in these patients before proceeding with any surgical intervention.

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Department and Institution Where Work Was Done

Anterior Segment Division, King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia.

Conflicts of Interest

None.

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