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Secondary Amyloidosis in a Corneal Graft

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Purpose: To describe a case of secondary amyloidosis that occurred in a corneal graft.

Methods: A 30-year-old Japanese woman had opacities in the corneal graft in her right eye. Slit-lamp microscopy examination demonstrated nodular, subepithelial opacities in the graft. Results of a physical examination and her past medical history were unremarkable, except for a history of a penetrating keratoplasty for keratoconus at the age of 17. Since then, the patient had worn a hard contact lens for over 10 years. The specimen obtained by keratectomy was examined histologically.

Results: The histologic examination revealed hyaline, and amorphous materials stained with Congo red, which were dichroic under polarized light. Transmission electron microscopy showed the characteristic fibrillar pattern of amyloid.

Conclusions: This appears to be the first reported case of secondary amyloidosis in a corneal graft. A long-standing history of hard contact lens wear may play a role in the pathogenesis of this rare condition. **Jpn J Ophthalmol 2002;46:305–307** © 2002 Japanese Ophthalmological Society

Key Words: Amyloidosis, cornea, keratoconus, keratoplasty.

Introduction

Secondary corneal amyloidosis has been reported to occur following ocular trauma, phlyctenular keratitis, trachoma, interstitial keratitis, trichiasis, and keratoconus.[1–4] Chronic inflammatory conditions are thought to be the contributing factors for this rare, degenerative change. We describe here a case of secondary amyloidosis that occurred in a corneal graft. This case, to the best of our knowledge, appears to be the first reported case of secondary amyloidosis in a corneal graft.

Case Report

A 30-year-old Japanese woman was referred to the Cornea Clinic of Keio University Medical Center in June 1999 because of contact lens intolerance in the right eye. Her best-corrected visual acuity was 20/25 in the right eye and 20/20 in the left eye. The patient had a history of an uncomplicated penetrating keratoplasty for keratoconus in the right eye at the age of 17, and subsequent hard contact lens wear for over 10 years. Slit-lamp microscopy examination demonstrated nodular, gray-white opacities in the subepithelial zone in the lower edge of the graft (Figure 1A). Refractile filamentary lines were also present in the anterior stroma. The lower edge of the graft overrode on the host cornea. Superficial, fine vessels were seen in the lower cornea adjacent to the limbus. The left eye was unremarkable and had no sign of keratoconus. A general physical examination revealed no other abnormalities. The patient's medical history and family history were unremarkable except for the above-mentioned keratoplasty in the right eye. She was in excellent health and had never been treated for any chronic diseases.

The patient underwent a superficial keratectomy in the right eye in September 1999. Although some opacities in the subepithelial lesion remained, the

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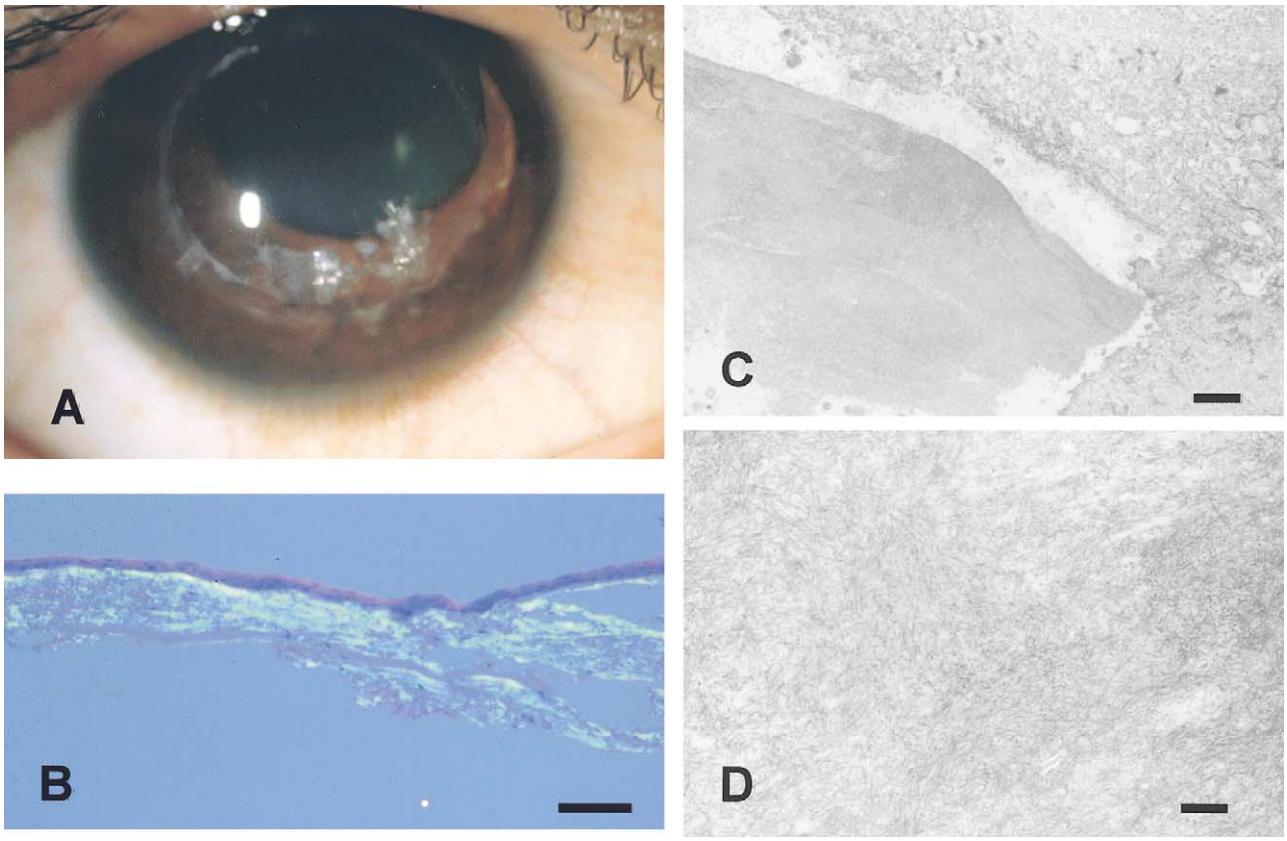

Figure 1. Findings in a 30-year-old Japanese woman with opacities in the corneal graft in her right eye. (**A**) Photograph of the right eye. Nodular, gray-white opacities and refractile filamentary lines in the anterior stroma are present in the lower edge of the graft. (**B**) Photomicrograph of a section illuminated with polarized light. The deposits beneath the epithelium show yellowish-green birefringence typical of amyloid. Bar = 100 μm. (**C**) The electron-dense amyloid deposits appear fusiform and homogeneous. Bar = 1 μm. (**D**) The deposits are composed of delicate filaments measuring approximately 10 nm in diameter. Bar = 200 nm.

patient was able to wear a hard contact lens in the right eye without any discomfort. The visual acuity in the right eye corrected with a hard contact lens remained at 20/25. The patient's condition has remained stable throughout more than 2 years of follow-up.

The corneal specimen obtained by keratectomy was fixed in 10% neutral buffered formalin, then prepared for routine paraffin embedding, sectioning, and staining with hematoxylin-eosin and Congo red. The remaining small pieces of specimen were fixed in a buffered solution of 2% glutaraldehyde, post-fixed with 2% osmium tetroxide, and embedded in epoxy resin according to standard procedures. Thin sections were stained with uranyl acetate and lead citrate and examined by electron microscopy.

The corneal epithelium was intact but irregular in thickness. Nodular deposits of eosinophilic hyaline material were beneath the epithelium, replacing Bowman's layer and the anterior stroma. Occasional mononuclear cells were seen associated with the deposits. The deposits stained positively with Congo red dye, and showed a yellowish-green birefringence typical of amyloid when viewed under polarized light (Figure 1B). Transmission electron microscopy revealed that the amyloid deposits beneath the epithelial cells appeared homogeneous (Figure 1C). Epithelial basal cells were unremarkable except for the decrease in number of hemidesmosomes. The amyloid deposits were composed of delicate filaments measuring approximately 10 nm in diameter (Figure 1D).

Discussion

The clinical findings in our patient are similar to those seen in secondary amyloidosis or Saltzmann's nodular degeneration. Histological findings including Congo red-stained specimens and electron microscopic observation led us to the diagnosis of amyloidosis. Saltzmann's nodular degeneration, in which

collagen matrix and degenerated fibroblasts are seen by electron microscopy,[5] could be ruled out as the cause of the corneal lesion in our patient.

The various forms of amyloidosis may be localized or systemic, primary or secondary.[1] In our patient, systemic amyloidosis can be excluded, because she had been in excellent health and had never suffered from any chronic diseases. Familial forms of localized primary amyloidosis such as lattice dystrophy and gelatinous drop-like dystrophy, were excluded by her family history and the normal appearance of the other eye. Polymorphic amyloid degeneration is usually bilateral, and the deposits are located in the deepest level of the stroma.[6] Trichiasis, which is known to cause localized amyloidosis in the cornea,[7] was not seen in this patient.

Therefore, we believe that the patient is most likely to have had a secondary, localized amyloidosis that occurred in the corneal graft. Secondary corneal amyloidosis occurs following chronic inflammatory conditions such as ocular trauma, phlyctenular keratitis, trachoma, interstitial keratitis, and trichiasis.[1–3] In our patient, improper adaptation of the graft in the lower edge and a long-standing history of hard contact lens wear may have played a role in the pathogenesis of this rare condition. Superficial, fine vessels present in the lower cornea adjacent to the limbus are thought to be a sequelae of chronic inflammation. Stern et al reported a similar case of secondary corneal amyloidosis associated with keratoconus and hard contact lens wear.[4] To our knowledge, secondary amyloidosis has not been recognized as a complication of penetrating keratoplasty. Proper adaptation between the graft and the host cornea seems to be important to avoid this rare complication.

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