Recurrence of macular corneal dystrophy after keratoplasty is rare. We report light microscopic, immunohistochemical, electron microscopic, and serologic findings in a 78-year-old woman who underwent regrafting 49 years following the first penetrating keratoplasty. Examination of the corneal button revealed deposits of glycosaminoglycans in the graft beneath the Bowman layer, throughout the stroma, and in the endothelium with positive staining for antigenic keratan sulfate. By transmission electron microscopy, intracellular and extracellular deposits of a fibrillogranular material were detected in the stroma, Descemet membrane, and endothelium. The serum level of antigenic keratan sulfate was normal. Our findings indicate that macular corneal dystrophy type II may show late recurrence after penetrating keratoplasty with intense deposition of antigenic keratan sulfate in all corneal layers.

Macular corneal dystrophy (MCD) is an autosomal recessive disease characterized by deposition of glycosaminoglycans in the stroma, keratocytes, Descemet membrane, and endothelium of the cornea. It represents about one third of all stromal corneal dystrophies requiring keratoplasty in Europe (Germany). Macular corneal dystrophy has been shown to be a systemic disorder of keratan sulfate metabolism and has been subdivided into type I, type IA, and type II. Both immunophenotypes seem to be localized on chromosome 16q22. Recurrence of MCD within corneal grafts is relatively rare in comparison with other corneal stromal dystrophies but has been reported in a number of case reports and small series. To our knowledge, exact classification of the type of MCD in recurrences has not yet been described. We report herein the light microscopic, immunohistochemical, transmission electron microscopic, and serologic findings from a patient with recurrent MCD type II 49 years after initial penetrating keratoplasty.

A 78-year-old German woman with a family history of MCD (one sister affected) was first seen at our department for gradual decrease of vision in her right eye. Her right eye had undergone penetrating keratoplasty in 1943. Her left eye had a history of persistent angle-closure glaucoma and advanced glaucomatous optic atrophy. Best-corrected visual acuity was 20/200 OD and hand movements OS. Intraocular pressure was 15 mm Hg OU. Slitlamp examination findings of the right eye revealed a 3.5-mm, slightly temporally decentered corneal graft with superficial and moderate diffuse stromal opacification (Figure 1A). The peripheral (host) cornea was densely opaque (Figure 1B). A brown nuclear cataract was also present. The left eye showed a dense, diffuse opacification of the corneal stroma. The right eye underwent uneventful penetrating keratoplasty (7.5/7.8 mm) combined with extracapsular cataract extraction and posterior chamber intraocular lens implantation in April 1992. During follow-up which was until December 1997, the graft remained clear, and best-corrected visual acuity improved to 20/40 (Figure 1C).
PATHOLOGICAL FINDINGS

Macroscopically, the corneal button consisted of a central, 3.5-mm, mildly opaque round graft surrounded by a densely opaque rim of host cornea (Figure 2, A). The button was bisected. One half was processed for light microscopy and stained with hematoxylin-eosin, periodic acid–Schiff, alcian blue, Congo red, and Masson trichrome. For immunohistochemistry, paraffin-embedded 5-µm corneal sections were stained with a monoclonal antibody against antigenic keratan sulfate (AgKS). The other half of the corneal button was processed for transmission electron microscopy. The serum concentration of AgKS was determined using the...
Figure 3. Transmission electron microscopy reveals intracellular and extracellular deposits of a fibrillogranular material in the stroma, Descemet membrane, and endothelium in the donor and in the host cornea. A, Donor corneal stroma (bar = 8 µm); B, host corneal stroma (bar = 10 µm); C, donor cornea: slender keratocytes and fibrillogranular material (asterisk) (bar = 1 µm); D, host cornea: swollen keratocyte filled with intracellular material (asterisk) (bar = 5 µm); E, donor cornea: Descemet membrane (between thick arrowheads) and endothelium (bar = 4 µm); and F, host cornea: Descemet membrane (between thick arrowheads) and endothelium (bar = 4 µm). Note that the banded portion of Descemet membrane (small arrowheads in parts E and F) is unaffected in host and donor cornea. Both host and donor endothelial cells appear to be equally involved by deposits of fibrillogranular material; this could be owing to replacement of donor endothelium by diseased host endothelium.
monoclonal antibody 5-D-4 in a serum antigen-inhibition assay.6,7

Light microscopy revealed a corneal button with a well-adapted central 400-µm thick corneal graft with full-thickness scars on both sides (Figure 2, B, C). The epithelium showed mild edema and occasional bullous separation from the underlying Bowman layer. The Descemet membrane appeared slightly thicker peripherally than centrally. The central endothelium was mildly attenuated with 9 endothelial cells per high-power field (×400). Extensive deposits of glycosaminoglycans were present in all stromal layers and in the endothelium of the peripheral host cornea (Figure 2, D, E). In the central graft, glycosaminoglycans were localized as dense circumscribed deposits in the superficial stroma beneath the Bowman layer adjacent to the host cornea, and as fine diffuse deposits throughout all stromal layers and in the endothelium (Figure 2, D, E).

Immunohistochemistry for AgKS revealed an intense homogeneous staining of host and donor stroma and keratocytes, Descemet membrane, and endothelium (Figure 2, F). No positive staining was seen using isotypic control. The serum level of AgKS was normal (1380 nmol/L).

By transmission electron microscopic examination, intracellular and extracellular deposits of a fibrillogranular material were detected in the stroma, Descemet membrane, and endothelium in the donor and the host cornea. Additionally, numerous electron-lucent lacunae and vacuoles could be observed in the stroma and posterior nonbanded portion of Descemet membrane. In the host cornea, a marked loss of keratocytes with occasional large, swollen keratocytes completely filled with fibrillogranular inclusions was observed, whereas in the donor cornea, a normal number of keratocytes with signs of increased secretory activity was present (Figure 3, A through F). There was evidence of invasion of some large, diseased host keratocytes into the donor button in the pre–Descemet membrane stroma near the interface. Alterations of posterior Descemet membrane, including fibrillogranular deposits, electron-lucent lacunae, abnormal collagen fibers, and guttae formation, were more prominent in the host cornea.

Recurrence of MCD is comparatively rare.1,4,5 In this case of a patient with late recurrence of MCD 49 years after initial keratoplasty, we found a type II macular dystrophy with normal serum levels of AgKS and immunohistochemical evidence of AgKS in corneal stroma, keratocytes, Descemet membrane, and endothelium. Type II MCD is less common than type I, but both types may be allelic and represent the end points of a broad spectrum of MCD immunophenotypes.2,3 Immunohistochemical characterization of recurrences of MCD has so far not been performed. Whether MCD type II with normal serum levels of AgKS carries an increased risk for recurrence awaits further studies.

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