Deep lamellar keratoplasty for corneal perforation due to chronic graft-versus-host disease following allogeneic hematopoietic stem-cell transplantation

Chronic graft-versus-host disease (GVHD) is a common complication following allogeneic hematopoietic stem-cell transplantation (allo-HSCT), frequently involving the ocular system.[1-3] Topical or systemic use of corticosteroid is occasionally beneficial;[4] however, there has been cases to progress to corneal perforation.[5-7] We will report a case of a patient who developed corneal perforation in the course of chronic GVHD following allo-HSCT, which was successfully treated by deep lamellar keratoplasty.[8]

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A 55-year-old woman with acute myeloblastic leukemia received allo-HSCT from an HLA-identical sibling in July 2002. Her clinical course had been uneventful until day 171, when she developed extensive chronic GVHD involving the skin, lung, liver, and eyes. She presented dry eye with discharge. Ophthalmologic examination revealed reduced tear function. Schirmer test was 3 mm in both eyes. We resumed prednisolone 1 mg/kg. However the response to corticosteroid was minimal. Ocular sicca was treated with tear substitutes and topical corticosteroids. Decreased visual acuity with severe ocular pain occurred in the right eye on day 269.

Visual acuity was 20/500 (20/250) in the right eye and 20/30 (20/25) in the left. Ophthalmologic examination revealed a right para-central corneal perforation (1×2 mm) without infectious signs, which was plugged by the iris tissue, with almost complete disappearance of anterior chamber (Figure 1). She was diagnosed with a corneal perforation due to severe dry eye, requiring emergent surgical interventions. She was given an antibiotics-ointment. Covering the perforated cornea with collagen shield or amniotic membrane was considered difficult because of the hole size and round shape; however, there was no fresh donor cornea for penetrating keratoplasty. She was offered the option of deep lamellar keratoplasty using preserved donor corneas.[8] After having the patient's consent, we proceeded to the operation on day 270. After repositioning of incarcerated iris using viscoelastic materials into anterior chamber, recipient cornea was trephined in 7.5 mm diameter including both perforation area and pupillary area, and the stroma was removed to expose the Descemet's membrane. A preserved donor cornea stripped of the Descemet's membrane was then sutured in place. She received tear substitutes, autologous serum eye drops, and antibiotics-ointments. Double chamber, the existence of the space between the host Descemet's membrane and graft, was initially observed, but it disappeared two months later with the closure of Descemet's hole by fibrous tissue. The surface of transplanted graft was completely covered by the recipient's epithelium to form clear corneas with pigmented keratic precipitate and focal fibrosis of Descemet's membrane. Eighteen months after corneal transplantation, she is in good condition without evidence of leukemia recurrence, and her visual acuity recovered to 20/300 (20/100) (Figure 2). The pathogenesis of chronic GVHD is not well understood. In experimental and clinical studies of chronic GVHD, thymic atrophy, lymphocyte depletion, and autoantibody formation have been described.[9] Disruption of thymic apoptosis and failure to eliminate the majority of self-reactive lymphocytes may lead to impairment of lymphocyte homeostasis and self tolerance. Expansion and effector functions of autoreactive T-cells will then promote autoreactive B-cell activation and production of autoantibodies with target-organ damage including eyes. The most common manifestation of ocular involvement is a keratoconjunctivitis sicca with dry eyes. Severe forms of ocular chronic GVHD results in corneal perforation.

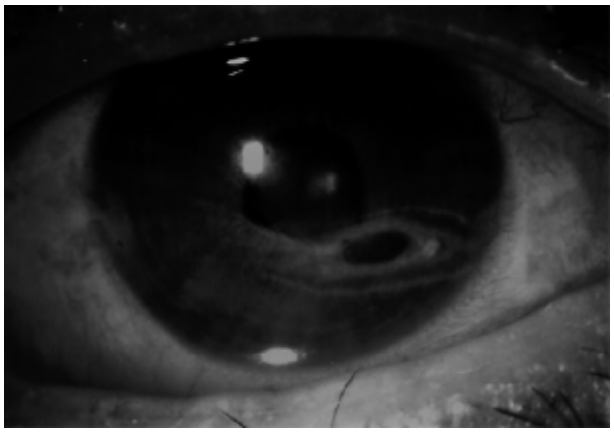

Figure 1. Photograph of her right eye showing the corneal perforation plugged by the iris tissue.

Figure 2. Transplanted cornea 3 months after corneal transplant. The lamellar graft remains clear, and the patient keeps visual acuity. Visual acuity in the right eye recovered to 20/300 (20/100).

Infection and graft rejection are major problems associated with keratoplasty. Most allo-HSCT recipients are immunocompromized, and keratoconjunctivitis sicca, a common manifestation of ocular GVHD, is an identified risk factor of infections following corneal transplantation.[10] These findings indicate that keratoplasty for corneal perforation associated with GVHD involves a significant risk of infections. Management of infections is important for successful keratoplasty in allo-HSCT recipients.

Concerning graft rejection, deep lamellar keratoplasty theoretically decreases the risk of rejection over penetrating keratoplasty because transplanted endothelium is a major target for rejection. Most patients with chronic GVHD are immunosuppressed by GVHD per se and treatment with immunosuppressive agents, which might be beneficial to prevent graft rejection. However, since patients with chronic GVHD receive long-term systemic corticosteroid and the corneal tissues have a hypovascularity, the wound healing of corneal grafts might be

delayed, leading to graft rejection. Optimal immunosuppression following deep lamellar keratoplasty in allo-HSCT recipients remains unknown.

In conclusion, this case shows that emergent corneal transplantation prevents ocular infection and preserves visual acuity in patients with corneal perforation associated with chronic GVHD. However, follow-up of this patient is too short to make a definite conclusion on corneal transplant after allo-HSCT. Further studies are required to investigate the long-term safety and usefulness of deep lamellar keratoplasty in allo-HSCT recipients.

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