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Allogeneic corneoscleral limbus tissue transplantation for treatment of the necrosis in porphyria eye disease

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Abstract

• **Porphyria cutanea tarda (PCT) with ocular complications are rarely reported. To the best of our knowledge, no reports exist on allogeneic corneoscleral limbus tissue transplantation for treatment of these. Amniotic membrane grafting had been performed in their patient suffering from porphyria eye disease, but necrosis developed in the grafts. Nevertheless, in our patient, allogeneic corneoscleral limbus transplantation prevented necrosis from development at corneoscleral limbus. So we considered that the allogeneic corneoscleral limbus transplantation might be an option to repair the necrosis in porphyria eye disease with avoiding sunlight and using artificial tear drops.**

• **KEYWORDS:** porphyria; scleral necrosis; allogeneic; transplantation

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INTRODUCTION

Porphyria is a group of metabolic disorders caused by an inherited deficiency or acquired derangement of any of the eight key intracellular enzymes necessary to synthesize haem, which is an end-product of porphyrin metabolism in the body. Several types of porphyrias have been recognized, which are characterized by some specific patterns of overproduction and excretion of porphyrins and its precursors[1]. Distributing to the skin or other exposed regions of the body and absorbing light of certain wavelengths, the metabolite generates free radicals that give rise to photodynamic cell injury [2]. Ocular complications are rarely reported in porphyries [3]. Scleral necrosis, corneal and conjunctival scarring, are among the most common [4-12]. To the best of our knowledge, no reports exist on allogeneic corneoscleral limbus tissue transplantation for treatment of these. Therefore, we aim to introduce this effective therapy for the eye complications in the article.

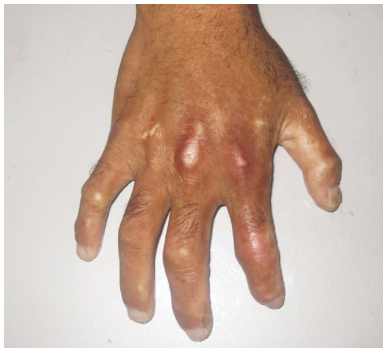

Figure 1 Systemic manifestations of porphyria cutanea tarda Scars and hyperpigmentation located on light exposed facial skin, the dorsa of the hands and fingers, mild resorption of terminal phalanges in the hand.

SUBJECTS AND METHODS

Subjects The study was performed according to the Declaration of Helsinki standards and was approved by the Institutional Review Board of Jinglin Hospital. A 27-year-old yellow male patient with porphyria cutanea tarda (PCT) was referred to the department of ophthalmology at Jinling Hospital in March 2009 for severe scleral necrosis. There was consanguinity between the parents. The young man had been apparently well excepting for 6 fingers of his left hand until the age of 17. He had then begun to develop blisters over the exposed regions of his body, predominantly on the face, neck and upper and lower limbs. These lesions would resolve spontaneously only to recur again. Each such episode left a varying degree of scarring and hyperpigmentation. His face and limbs had become disfigured over a period of a few years (Figure 1). Screening test for porphyria was reported as being positive in urine.

Visual acuity was 4/20 in the right eye and 12/20 in the left eye with an accurate projection of light in both eyes. The patient had scleral necrosis area approximately 3 mm in diameter at corneoscleral limbus in both eyes with longer eye lashes (the right eye is more serious than the left eye) (Figure 2A). Moderate corneal opacity without corneal vascularization was present on the right cornea, whereas the cornea was clear in the left cornea.

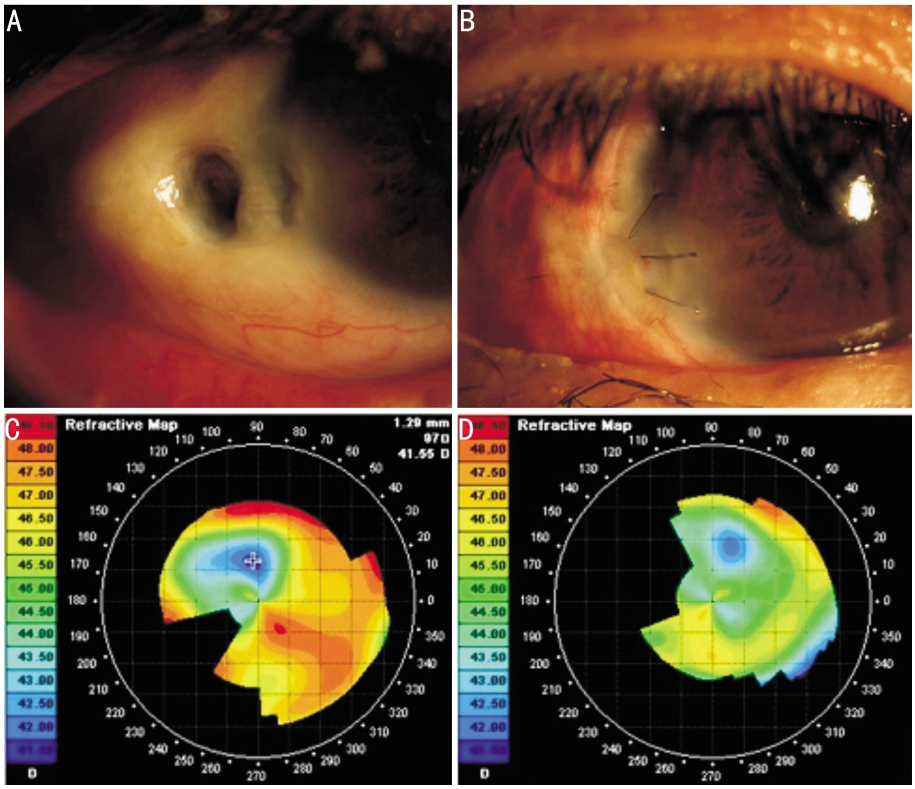

Figure 2 Comparison between before and after treatment of right eye A: A scleral necrosis area at corneoscleral limbus in right eye, the underlying uveal tract was seen on the floor of the crater; B: Three-month post transplantation, the graft resolution did not happened and the conjunctiva was migrated to cover the graft; C: Corneal topography was evaluated with the iTrace Visual Function. Corneal component contributed the major portion of the astigmatism in right eye; D: Corneal topography was evaluated with the iTrace Visual Function Analyzer. Three-month after treatment, corneal astigmatism seems relief (right eye).

Methods Corneal topography was evaluated by iTrace Visual Function Analyzer (Tracey Technologies, Houston, TX, USA). The patient was advised to avoid sunlight, wear UV-protective glasses and hat, and apply sunscreen for the areas exposed to the sunlight. Besides, artificial tear drops (Tears Naturale Free; Alcon, TX, USA) were used. The patient underwent allogeneic corneoscleral limbus transplantation closure for the scleral defects in the right eye. Then the removal corneal necrosis tissue was analyzed by immunohistochemical staining and transmission electron microscope.

RESULTS

Corneal topography was evaluated with the iTrace Visual Function Analyzer (Tracey Technologies, Houston, TX, USA). The results revealed that Sim K values of corneal topography were 45.11 D and 43. 20 D in right eye, 47.33 D and 44.27 D in left eye. Corneal curvature of the central corneal is 41.5 D, anterior corneal radius of curvature of the points located 1.5 mm to 2.5 mm away from the corneal apex on certain meridians is almost 47.5 D to 48.5 D in right eye. After analyzing the contribution of the anterior ocular components to retinal image quality, we found that a corneal component contributed the major portion of the astigmatism (Figure 2C, 2D).

There is mild epidermal hyperplasia in the margin of the necrosis which is characterized by interstitial fibrosis and collagen degeneration, with a small number of inflammatory cells infiltrating. The infiltrating cells in the necrosis showed positive immunostaining for CD4, CD68 and CD1a, but negative staining for CD8, and CD21/CD35. Those infiltrating cells are derived from histiocytes (Figure 3).

Three months after an allogeneic corneoscleral limbus transplantation, avoiding sunlight and using artificial tear drops, the cornea returned to be clear in the right eye and the visual acuity was increased to 0.6. There was no immunological rejection happened after allografting and an autologous conjunctiva piece was migrated to cover the graft (Figure 2B).

DISCUSSION

PCT is the most common form of all porphyries due to the deficiency of uroporphyrinogen decarboxylase have 3 types. Type Ⅰ PCT is sporadic and the enzyme deficiency is only in liver; type Ⅱ is hereditary and the deficiency is in all cells, hence the erythrocytes; and type Ⅲ is hereditary but the enzyme activity is normal in erythrocytes[4,13,14]. Sporadic PCT is frequently observed in adulthood as in our case. Excessive amounts of uroporphyrin and other porphyrin metabolites deposited in skin induce phototoxic, oxygen dependent damage characterized by subepidermal blistering with severe inflammation and subsequent ulceration and scarring due to exposure to a light. Skin fragility and vesiculobullous skin lesions are typical and have characters with

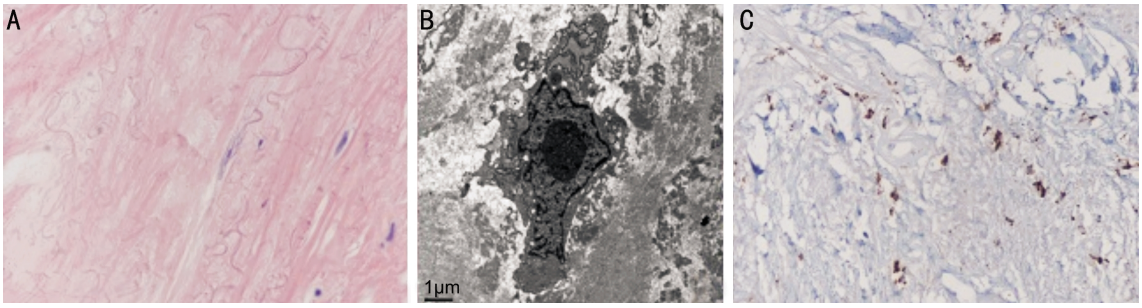

Figure 3 Representative histopathological micrographs of the scleral necrosis A: The necrosis is characterized by interstitial fibrosis and collagen degeneration (original magnifications, ×400, haematoxylin and eosin stain); B: Transmission electron micrographs shows fibroblast proliferative; C: Macrophages (CD68) shows positive staining (immunohistochemical staining, ×400).

hyperpigmentation, depigmentation, and melanosis in sunlight-exposed areas.

Ocular involvement is uncommon in porphyries. In an earlier study, Kurihara *et al*[7] showed the presence of porphyrins in the teardrop 4. Porphyrins have been suggested to cause vesication in the exposed parts of the lids, conjunctiva, cornea and sclera. The conjunctiva shows blisters and scarring and then it becomes atrophic and adheres firmly to the underlying sclera. As a result, the sclera becomes dehydrated because of the fibrotic reaction, and the underlying uveal tract is therefore seen on the floor of the crater. The cornea then demonstrates the formation of ulcers, perforation and scarring. As we can see in the case, anterior corneal radius of curvature of the points located 1.5 mm to 2.5 mm away from the corneal apex was flatter than normal cornea and the corneal morphological changes contributed the major portion of the whole astigmatism.

These eye lesions were therefore considered to be induced by photosensitivity. Differences in the ratio of eye lesions seen with the different types of porphyria may therefore depend on the liquid solubility of the various porphyrins, which would thus determine the severity of phototoxicity. Besides wearing UV-protective glasses and hat, frequent applying of artificial teardrops produces a mechanical effect of washing out the accumulating porphyrins on the ocular surface and may improve healing of scleral necrosis[15].

In the Altiparmak *et al* 's [4] work, amniotic membrane grafting had been performed in their patient suffering from porphyria eye disease, but necrosis developed in the grafts. The surgical treatment failed in their patient. Nevertheless, in our patient, allogeneic corneoscleral limbus transplantation was tried to prevent from necrosis development at corneoscleral limbus where is the thinnest region of anterior segment of eyeball. And, after the 3mo of follow-up, there were no signs of graft resolution and scleral necrosis development. So we considered that the corneoscleral limbus contains stem cells which can promote proliferation and migration and have immunosuppressive mechanisms to protect them from immunological reactions. The allogeneic corneoscleral limbus transplantation might be an option to repair the scleral necrosis in porphyria eye disease.

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