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EFFICACY OF LIMBAL STEM CELL TRANSPLANTATION IN THE TREATMENT OF RECURRENT PTERYGIUM

Petra Kralj, Renata Iveković, Katia Novak-Lauš and Zdravko Mandić

University Department of Ophthalmology, Sestre milosrdnice University Hospital, Zagreb, Croatia

SUMMARY – The aim of the study was to assess the efficacy of limbal stem cell transplantation (LSCT) as a treatment for recurrent pterygium. Eighteen eyes with recurrent pterygium underwent LSCT. Twelve eyes had been previously operated by the 'bare-sclera' technique, 3 by conjunctival rotation and 3 by amnion membrane transplantation. No serious intraoperative complications occurred, except for reversible conjunctival graft edema in 2 eyes, Tenon's granuloma in one case, and hematoma under the graft in one case. In 16 eyes no pterygium recurrence was recorded during the follow up period. Two recurrences were recorded during 18 months after surgery. It is concluded that LSCT is a successful and safe yet time-consuming and technically demanding method in the management of recurrent pterygium.

Key words: *Recurrent pterygium; Limbal stem cell transplantation; Graft edema*

Introduction

Pterygium is a fibrovascular overgrowth of degenerative bulbar conjunctivae growing over the limbus into the cornea. It is a worldwide disease that causes chronic irritation and discomfort, restricted ocular motility and decreased vision secondary to growth over the pupillary axis or induced astigmatism, or disruption of the precorneal tear film[1]. When vision is affected or the symptoms become more bothersome, excision of the pterygium is indicated[2]. Pterygium can be easily removed, but has a strong tendency to recurrence. Recurrence rate after primary excision rises up to 50%, although various treatment approaches including surgical procedures, beta-irradiation, laser and medications have been proposed for the treatment of pterygium[2,3]. When surgical techniques proposed for primary pterygium are applied in recurrent cases, secondary recurrence is increased. Recently, limbal-conjunctival autograft transplantation has been used in the treatment of recurrent pterygium. The limbal zone is the rim of cornea approximately 0.5 mm wide that abuts against the sclera. It has been proposed that limbal stem cells play an important role in the pathogenesis of pterygium. In this theory, the pathogenesis of pterygium can be conceptualized as occurring in two stages: 1) initial and progressive disruption of the limbal corneal-conjunctival epithelial barrier; and 2) progressive active 'conjunctivalization' of the cornea by tissue characterized by extensive cellular proliferation, inflammation, connective tissue remodeling, and angiogenesis[4]. Based on this pathogenesis theory, the aim of this study was to assess the efficacy of limbal stem cell transplantation (LSCT) in the treatment of recurrent pterygium.

Correspondence to: *Petra Kralj, MD*, Augusta Šenoe 152, HR-10290 Zaprešić,Croatia

E-mail: pero80@gmail.com

Patients and Methods

From February 2005 until April 2006, 18 patients with recurrent pterygium underwent LSCT for the removal of recurrent pterygium. Patients were operated on by the same surgeon. All patients fulfilled the criteria for eligibility described by Güller *et al*.: pterygium growth over the cornea by more than 3 mm, no other surface pathology, and no infection of the ocular surface or systemic pathology that might be a contraindication to ocular surgery[5]. Primary pterygium was operated with other methods: twelve eyes were operated by the 'bare-

Table 1. Demographic characteristics of study patients

Number of patients	Mean age (yrs)	Age range (yrs)	Follow up (months)
18	37.1±12.4	35-63	20±1.6

sclera' technique, three by conjunctival rotation, and three by amniotic membrane transplantation.

Limbal stem cell transplantation was done in parabulbar anesthesia. The recurrent pterygium was filled with *2%* lidocaine/1:100 000 epinephrine mixture to separate it from the underlying sclera. Pterygium was completely resected from the cornea with a No. 64 Beaver blade and the body of pterygium was dissected and excised by Westcott conjunctival scissors. Minimal cautery was used to control bleeding. After resection of the pterygium, a limbal conjunctival autograft containing 0.5 mm of clear cornea from the superotemporal site of the same eye was dissected free from Tenon's capsule. The graft was sutured to the recipient bed with an interrupted 10.0 vycril and nylon sutures. After the operation, a soft contact lens was applied and steroids were administered four times a day for 4 weeks, when the sutures were removed. Patients were evaluated on postoperative days 1, 7, 14 and 30, and then every 3 months for at least 1 year. Recurrence was defined as the postoperative growth of fibrovascular tissue by more than 1 mm onto the cornea. The preoperative and postoperative data were analyzed by χ^2 and Fisher's test; the level of significance was set at $p<0.05$.

Results

No serious intraoperative complications occurred. Two (11.11%) eyes showed temporary graft edema in the first 3 postoperative days, but finally disappeared without excessive scar formation. Tenon's granuloma and hematoma under the graft were observed in one case each. Donor area healed without any complications. In 16 (88.89%) eyes no pterygium recurrence was recorded during the follow up period. In two cases, pterygium recurrence was recorded: in one patient after 18 months and in the other after 11 months. In one eye with recurrent pterygium and symblepharon formation, normal ocular motility was achieved. Visual acuity (VA) improvement was noted in 12 eyes, while in 6 eyes it remained unchanged. Best-corrected VA improved by three Snellen lines in 4 eyes (from 0.6 to 0.9 and from 0.4 to 0.7 in two patients each); by two Snellen lines in 6 eyes (from 0.5 to 0.7 and from 0.7 to 0.9 in three patients each); and by one Snellen line in 2 eyes (from 0.5 to 0.6).

Table 2. Results of the study

Age (yrs)	Recurrence n (%)	Recurrent time (months)	No recurrence n (%)
<40	1 (16.66)	18	5 (83.34)
>40	1 (8.33)	11	11 (91.67)
Total	2 (11.11)		16 (88.89)

Discussion

Pterygium is a worldwide degenerative corneal disease with a multifactor etiology, and its incidence is higher in tropical and subtropical countries where prolonged exposure to UV radiation is common[1]. Although many surgical approaches have been developed, pterygium recurrence after surgical excision is still a main problem[3]. Recurrent pterygium is more difficult to control, and various treatment modalities have been proposed. In 1990, Tseng *et al.* showed the limbus to be a distinct cellular structure lying between the corneal and conjunctival epithelium, containing stem cells that are vital for normal corneal epithelial regeneration and preventing the growth of conjunctival epithelium onto the cornea through contact inhibition[7]. Although the pathogenesis of pterygium has not yet been fully clarified, the concepts on the pathogenesis of pterygium and importance of the limbus and its stem cells have resulted in the development of new techniques such as LSCT[5]. Several authors recommend the use of LSCT for the prevention of recurrences in either primary or recurrent pterygium surgery. LSCT has also been used in treating corneal diseases with stem cell deficiency, such as chemical or thermal burns, aniridia, Stevens-Johnson syndrome, ocular pemphigoid, conjunctival squamous cell carcinoma and contact lens associated ocular surface abnormality[3]. This operative technique is associated with intraoperative and postoperative complications. Graft edema due to desiccation, handling with forceps or distortion of the graft were the most frequent complications of LSCT in our study; however, they were not sight threatening and disappeared in the first few postoperative days. Tenon's granuloma and hematoma under the graft were as also observed in our study. Other complications that are reported in the literature include graft retraction, epithelial inclusion cysts, necrosis of the

graft, and pseudopterygium formation at the donor site[3]. Although we did not observe any complications from retrobulbar anesthesia, the potential for these complications including retrobulbar hemorrhage, optic nerve damage, penetration of the globe, and death should be mentioned[5]. As the procedure can be performed with subconjunctival or sub-Tenon anesthesia, the main disadvantages of LSCT are the need for healthy conjunctival donor tissue and the time and expertise required.

Recurrence of pterygium, or in our study recurrent pterygium is a postoperative complication that should be separately analyzed. According to some literature data, the use of LSCT reduces the recurrence rate but still does not completely eliminate it. There is a large variability of recurrence rates in different studies. Our study included 18 patients with recurrent pterygium. During the follow up period, pterygium recurrence was recorded in two eyes, i.e. after 11 and 18 months in one eye each. In younger men, pterygium recurrence was recorded at a longer time than in older ones.

In conclusion, LSCT is a time-consuming and technically demanding method, but with a relatively low rate of recurrence, and can be recommended in the treatment of recurrent pterygium.

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Sažetak

Učinkovitost transplantacije limbalnih stanica kod recidivirajućih pterigija

P. Kralj, R. Iveković, K. Novak-Lauš i *Z. Mandić*

Cilj rada je prikazati učinkovitost transplantacije limbalnih stanica (LSCT) kao načina liječenja recidivirajućih pterigija. Ukupno je 18 očiju s recidivirajućim pterigijem operirano tehnikom LSCT; 12 bolesnika je primarno bilo operirano tehnikom *'bare sclera'*, 3 rotacijom konjunktive i 3 transplantacijom amnijske membrane. Nije bilo značajnijih intraoperacijskih komplikacija osim reverzibilnog edema konjunktivnog grafta kod 2 bolesnika, Tenonovog granuloma kod jednog bolesnika te hematoma također kod jednog bolesnika. Kod 16 bolesnika nije bilo recidiva pterigija tijekom vremena praćenja, dok se kod 2 bolesnika recidiv javio unutar 18 mjeseci. Zaključak rada je da je LSCT uspješna i sigurna metoda u liječenju recidivirajućih pterigija, iako je tehnički i vremenski dosta zahtjevna.

Ključne riječi: *Recidivirajući pterigij; Transplantacija limbalnih stanica; Edem grafta*