Effectiveness of topical bevacizumab in bilateral primary lipid keratopathy

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ABSTRACT

Case report: A 75-year-old man with bilateral idiopathic lipid keratopathy underwent a penetrating keratoplasty in the left eye. One month later, there was deep corneal neovascularisation extending across the bed and the graft-host interface, with a whitish opacity surrounding the vessels. Topical bevacizumab (25 mg/mL) was administered 4 times daily for 2 months with partial regression of corneal neovascularization.

Discussion: Topical bevacizumab may be useful in preventing a recurrence of lipid deposition after penetrating keratoplasty in patients with bilateral primary lipid keratopathy, although its long-term efficacy needs to be assessed.

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Eficacia de bevacizumab tópico en queratopatía lipoidea bilateral primaria

RESUMEN

Caso clínico: Varón de 75 años con queratopatía lipoidea bilateral primaria. Es intervenido de queratoplastia penetrante en ojo izquierdo. Al mes se observa neovascularización corneal profunda extendiéndose sobre el lecho y la interfase injerto-huésped, con opacidad blanquecina alrededor de los neovasos. Se inicia tratamiento con bevacizumab tópico (25 mg/mL) 4 veces/día durante 2 meses, con regresión parcial de la neovascularización corneal.

Discusión: Bevacizumab tópico puede ser útil en la prevención de la recidiva de la queratopatía lipoidea tras queratoplastia penetrante en pacientes con queratopatía lipoidea bilateral primaria, aunque sería conveniente determinar su eficacia a largo plazo.

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Introduction

Primary bilateral lipid keratopathy is a rare disease,¹ characterized by fatty deposits in plates located in the corneal epithelium and stroma which bring about yellowish white opacification of the central, paracentral of peripheral cornea that course affecting the visual axis. There is no history of previous ocular disease and lipid levels in serum are normal. There is no effective treatment for this disease. Even penetrating keratoplasty fails due to the recurrence of said deposits in the graft.

Bevacizumab (Avastin®, Genentech, South San Francisco, CA, USA) is a humanized monoclonal antibody that competitively inhibits the vascular endothelial growth factor (VEGF).³ ⁴ VEGF plays a crucial role in the pathogenesis of corneal neovascularization because it is a powerful and highly selective myogen of the vascular endothelial cells as well as a modulator of the vascular potency. In a murine chemical burn experimental model, Manzano et al.² observed that topical bevacizumab limits corneal neovascularization. A range of subsequence studies have reported the efficacy of topical and conjunctival bevacizumab on corneal neovascularization in humans.

This paper presents a case of primary bilateral lipid keratopathy with transparent graft after penetrating keratoplasty and adjuvanting treatment with topical bevacizumab.

Clinic case

Male, aged 75, diagnosed with primary bilateral lipid keratopathy, was referred for progressive visual acuity (VA) loss.

An ophthalmological exploration of the patient revealed a VA of 20/60 in the right eye (RE) and hand movement in the left eye (LE). Biomicroscopy revealed a white yellowish corneal opacity throughout the thickness of the stroma in an incomplete ring shape, respecting the visual axis in the RE and involving the central corneal in the LE (Fig. 1A). In addition, it also revealed superficial and deep neovascularization extending towards the center of the cornea. The lipid levels in serum were normal. The patient was submitted to penetrating keratoplasty surgery with extracapsular removal of cataract and intraocular lens implant in the LE. The post surgery treatment included topical steroids and antibiotics 4 times a day (Tobradex®, Alcon-Cusí, Barcelona, Spain), 2% topical cyclosporine 4 times a day and oral prednisone 50 mg/day, in descending regime during 2 weeks.

One month later, biomicroscopy revealed deep corneal neovascularization extending over the substrate and the graft-host interface at 3 and 6 o’clock, with a whitish capacity around the vessels (Fig. 1B). After obtaining the informed consent for providing compassionate use medication, topical treatment was initiated with bevacizumab (25 mg/mL): 4 times/day/2 months, in a descending regime during 6 months. At month 8, patient was maintained with topical bevacizumab: 1 time/day. Fig. 1C illustrates a partial regression of corneal neovascularization with transparent graft. VA was of 20/40.

Discussion

Previous clinical and histopathological studies have reported the presence of corneal neovascularization in idiopathic lipid keratopathy. The role of said neovessels in the pathogenesis of the disease is unknown. However, the presence of these corneal neovessels increases the risk of rejection after penetrating keratoplasty and facilitates the recurrence of lipid deposits in the graft. Various methods have been utilized to treat said neovascularization including steroids, argon laser photocoagulation,³ photodynamic therapy and diathermia with fine needles. The success of these therapies was limited due to the thermal damage suffered by the cornea and the high rate of vascular recanalization after the treatment.

It has been demonstrated that the inhibition of VEGF reduces corneal neovascularization in the iris and the choroids. Topical and subconjunctival application thereof has been utilized for treating ocular surface neovascularization in the Stevens-Johnson syndrome, in chemical cornea burns, graft against host disease, herpetic stromal keratitis, corneal graft reject, filament keratopathy and recurring pterygium. Recently it has been reported that both subconjunctival bevacizumab and intracorneal bevacizumab are efficient to obliterate corneal neovascularization in lipid keratopathy.⁴ As far as we know this is the first time the efficacy of topical bevacizumab is reported to maintain the transparency of the graft after penetrating keratoplasty in idiopathic lipid keratopathy.

Fig. 1 – (A) Biomicroscopic image, showing the whitish opacification of the cornea involved in the visual axis in LE. (B) One month after penetrating keratoplasty, deep corneal neovascularization can be seen extending through the substrate and the graft-host interface, with whitish opacity around the vessels. (C) Eight months after treatment a partial regression of corneal neovascularization can be seen, with the diminished size and thickness of the vessels.
keratopathy. Bevacizumab restricts neovascularization with a partial regression of neovessels.\textsuperscript{5} However, more studies would be required to establish the optimum dosage and duration of said treatment to regulate the neovascular process as well as to determine the ocular and systemic safety thereof.

In conclusion, treatment with topical bevacizumab could be useful to prevent lipoid keratopathy relapse after penetrating keratoplasty, although it would be convenient to determine its long-term efficacy. Although this report presents a single clinic case, we recommend the use of topical bevacizumab in the management of this pathology.

Conflict of interests

The authors have no conflict of interests to declare.

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