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Case Presentation

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Systemic Bevacizumab Side Effect on Penetrating Keratoplasty in a Pediatric Patient

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Abstract

Purpose: To evaluate the effect of bevacizumab on corneal epithelial cell healing after penetrating keratoplasty.

Methods: A 14-year-old boy treated with systemic bevacizumab for Ewing Sarcoma underwent penetrating keratoplasty (PK) because of a corneal neurotrophic perforated ulcer.

Results: The patient was treated with systemic bevacizumab (10 mg/kg, cycles repeated every 21 days, according to the Italian Association of Pediatric Hematology and Oncology protocol), which significantly decreased the corneal epithelial cell migration and viability. Several corneal interventions were performed; however, a dramatic reduction in corneal thickening, associated with progressive stromal melting, was observed over time. Anterior segment optical coherence tomography showed stromal colliquation at the donor-recipient junction. After detachment of colliquated graft, bulb evisceration with prosthesis implantation was planned.

Conclusions This case report suggests that bevacizumab should be carefully used for treating corneal neovascularization in cases of epithelial cell defects, and that PK is not recommended in patients treated with systemic bevacizumab at a concentration ≥ 5.00 mg/ml.

Keywords: Bevacizumab; Penetrating keratoplasty; Ewing sarcoma

Introduction

Bevacizumab, a full length recombinant humanized monoclonal antibody against Vascular Endothelial Growth Factor (VEGF), is widely used as a topical agent for the treatment of corneal neovascularization [1]. However, some authors have reported that bevacizumab affects corneal epithelial cell wound healing, decreases integrin expression, downregulates nerve growth factor, and

increases stromal response [2]. Neurotrophic keratopathy is related to alterations in corneal nerves, leading to impairment of sensory and trophic function with consequent breakdown of the corneal epithelium, affecting the health and integrity of the tear film, epithelium, and stroma [3]. In patients with Ewing Sarcoma [4] that present radionecrosis secondary to chemotherapy, systemic bevacizumab is prescribed for its anti-inflammatory and anti VEGF action. We describe a case of a 14-year-old boy treated with systemic bevacizumab for Ewing Sarcoma, which underwent Penetrating Keratoplasty (PK) because of a corneal neurotrophic perforated ulcer. To our knowledge, this is the first report of side effects induced by bevacizumab during corneal surgery.

Case Presentation

A 14-year-old male with facial Ewing sarcoma with hypoesthesia and complete right hemiface paralysis, was treated with systemic bevacizumab (10 mg/kg, cycles repeated every 21 days, according to the Italian Association of Pediatric Hematology and Oncology protocol). Few days after corneal neurotrophic ulcer diagnosis an amniotic membrane transplantation was performed. However, one week after surgery a corneal central wide perforation was observed. The patient then underwent PK, but the slit lamp examination showed the progressive decreasing of Anterior Chamber Depth (ACD), with corneal melting and final complete atalamia. After suture revision, a second PK combined with amniotic membrane transplantation was performed, suturing cornea with 27 single stitches. The graft colture examination resulted negative. Twelve days after PK, ACD quickly decreased because of stitches loosening and progressive corneal thinning at donor-recipient junction. We then revised again corneal suture, and another amniotic membrane transplantation combined with conjunctival flap and tarsorrhaphy were performed. Nevertheless, these procedures, ACD decreased, and anterior segment optical coherence tomography (iVue SD-OCT, Optovue, Fremont, CA) showed a stromal colliquation in the area corresponding to donor-recipient junction **(Figure 1)**. A complete donor melting with graft detachment finally occurred. Evisceration with bulb prosthesis implantation was then planned.

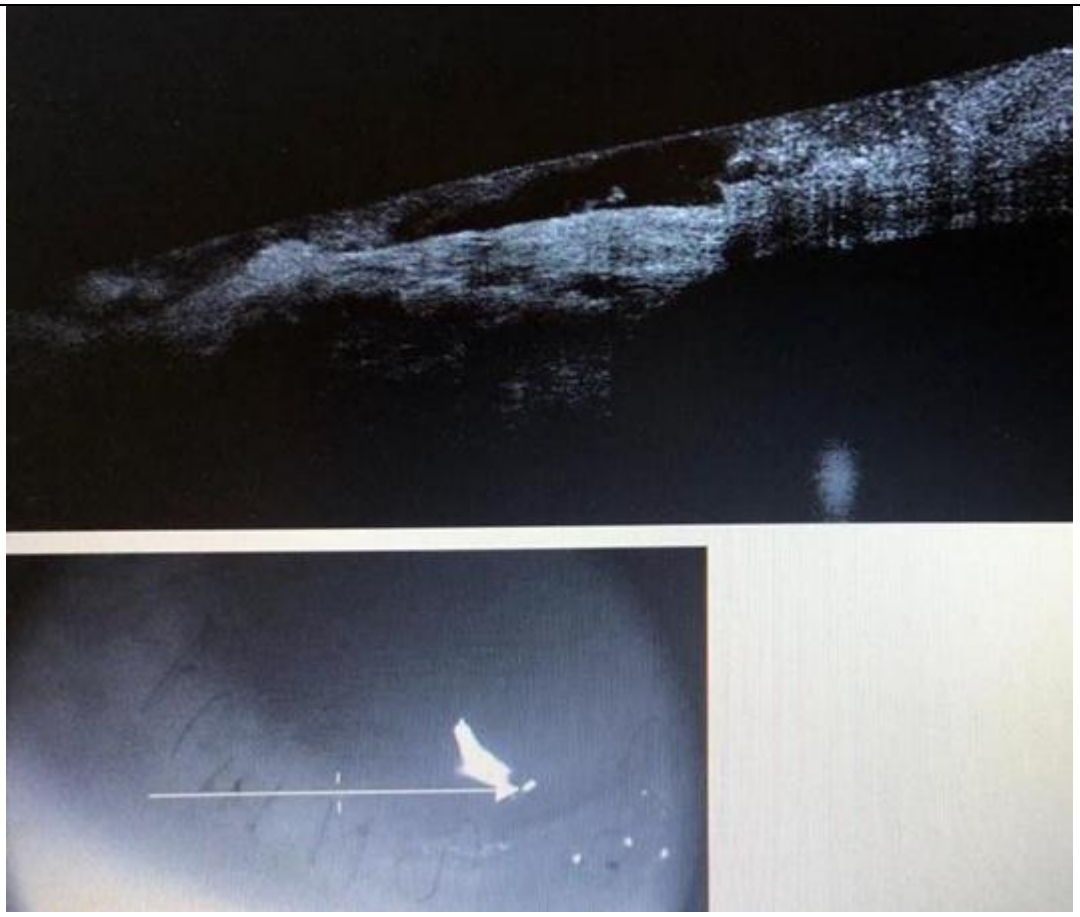

Figure 1: The anterior segment optical coherence tomography (iVue SD-OCT, Optovue, 117Fremont, CA) shows the stromal colliquation in the area corresponding to donor-118 recipient junction.

All interventions were performed under general anesthesia at the Bambino Gesù Children's Hospital in Rome, Italy. Informed consent was obtained for each intervention, and all experimental investigations followed the guidelines required by the institution. The study adhered to the Tenets of the Declaration of Helsinki.

Discussion

Anti VEGF agents are usually adopted for treating corneal neovascularization **[5]**, and up to now no side effect has been reported. Some authors however observed in vitro adverse effects of bevacizumab on the wound healing of corneal epithelial cell. Kang et al. **[2]** reported that bevacizumab significantly decreased corneal epithelial cell migration and viability compared with other anti VEGF agents, while Shokoohi et al. **[1]** that corneal epithelial and endothelial cells decrease in viability and undergo primary necrosis when exposed to bevacizumab at a concentration ≥ 5.00 mg/ml.

In conclusion, this case report suggests that bevacizumab should be carefully used for treating corneal neovascularization in cases of epithelial cell defects, and that PK is not recommended in patients treated with systemic bevacizumab at a concentration ≥ 5.00 mg/ml.

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