

Case Report

Corneal allograft reaction associated with nonocular inflammation

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Summary

Corneal allograft rejection is known to have many risk factors, including ocular infection and inflammation. Although not reported in the literature, local nonocular inflammation may also have the ability to incite a graft reaction. We report 2 cases, one with dental inflammation and the other with a facial abscess, with simultaneous corneal transplant rejection. Possible pathophysiology and a review of the literature are given.

Introduction

Corneal allograft rejection is an important condition, requiring astute clinical judgment and quick intervention. Of the approximately 35,000 corneal transplants performed annually in the United States, allograft rejection is a leading cause of graft failure.¹ A 5-year follow-up of the Corneal Transplant Epidemiological Study reported that allograft rejection caused graft failure in 17.8% of the 107 failed cornea transplants.² Thirty years earlier, Arentsen noted that 42.2% of graft failures were caused by allograft rejection, followed secondly by factors related to uncontrolled glaucoma (19.5%).³

Localized nonocular infections have been anecdotally known to be associated with corneal graft reactions. Given their proximity to the eye, dental and facial infections pose a likely factor in inciting a graft reaction through immunologic stimulation, although, to our knowledge, no such cases have been previously reported.

It has been recommended that infections of the face, especially in vicinity of the eyes, should be treated prior to corneal transplantation, not only to prevent ocular infection during surgery but to also ensure success of the corneal graft by possibly preventing corneal rejection.⁴ Castroviejo⁵ recommended treating ocular infections immediately to prevent graft rejection. We report 2 cases of corneal transplant rejection associated with an extraocular source of inflammation.

Case 1

A 56-year-old woman with a history of keratoconus presented with acute corneal allograft rejection 2 years after having undergone corneal transplant surgery in her left eye. She was initially placed on prednisolone acetate 1% eyedrops daily. Despite treatment of the rejection episode with increased topical steroids, the graft eventually failed, and she required a second corneal transplant. Her postoperative course was initially unremarkable. Three months later, she developed dental pain and was found to have a dental infection that required extraction. Immediately after her tooth extraction, she developed left eye irritation and decreased visual acuity of 20/300. On slit-lamp examination, her corneal graft was found to be edematous, with Descemet's folds, a Khoudadoust line, and keratic precipitates on the endothelial surface. Due to the extent of the graft edema, ultrasound pachymetry could not accurately measure the central cornea thickness. She was diagnosed with acute graft rejection and treated with a sub-Tenon's injection of triamcinolone acetonide 40 mg/ml and started on hourly prednisolone acetate 1% as well as an oral prednisone taper, and topical sodium chloride (5%) solution. Within a month of treatment, the keratic precipitates resolved, the central cornea thickness decreased to 506 μ m, and her visual acuity returned to her baseline of 20/150. Six months later, she was scheduled to undergo two dental implants along her left upper jaw and a maxillary sinus floor aug-

Published May 7, 2014.

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doi:10.5693/djo.02.2013.12.001

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mentation procedure. Therefore, she was started on prophylactic topical prednisolone pulse therapy. Following her procedure, the topical steroids were tapered, and she experienced no additional episodes of rejection.

Case 2

A 55-year-old man with history of keratoconus and ocular hypertension underwent corneal transplantation in both eyes. Twenty years after transplant surgery, while on long-term daily prednisolone acetate 1% eyedrops, he was diagnosed with acute graft rejection. This complication was initially treated with prednisolone acetate 1% eyedrops hourly followed by a taper. Despite continued therapy, his graft became more edematous and his visual acuity decreased to 20/300. The graft eventually failed. He underwent repeat penetrating keratoplasty with cataract extraction 2 months later. He was doing well but then presented 8 months after transplant with complaint of decreased visual acuity, which was again tested at 20/300. On slit-lamp examination, his right cornea was edematous (central cornea thickness of 790 μm), with Descemet's folds and keratic precipitates. His right lower cheek was noted to be erythematous, edematous, and tender to touch. He reported that the facial swelling began a few days prior to his decreased visual acuity and appeared to originate from an inflamed inspissated sebaceous gland. The acute cornea graft rejection was treated with hourly 1% prednisolone acetate followed by a slow taper. A local hospital's emergency room diagnosed him with a cellulitis associated with a methicillin-resistant *Staphylococcus aureus* facial abscess. He underwent incision and drainage and was treated with a course of oral sulfamethoxazole and trimethoprim. Six months after the treatment of the facial abscess and the acute graft rejection, his visual acuity returned to baseline (20/30), and the central cornea thickness decreased to 596 μm .

Discussion

Over the last 50 years, many risk factors have been identified for allograft rejection.^{1,3,6-9} Given the relative immune privilege to the cornea from anterior chamber-associated immune deviation (ACAID), corneal transplants are less prone to rejection than other organ transplants. However, a disturbance in the ACAID by a variety of mechanisms increases the risk of rejection.⁸

Contact with the vascular system can incite rejection by providing a pathway for host immune cells to recognize a foreign graft. Host corneal neovascularization either pre- or postoperatively have been associated with rejection

episodes.^{1,3,8,9} Iris synechiae, which provide another connection with the vascular system, have also been noted to incite rejection.^{1,3} Increasing graft diameter size, typically larger than 8.0 mm, has a higher incidence of reaction.^{1,8,9} Although it was once believed that the close proximity between limbal vasculature and the donor tissue increased the probability of immune reaction, it is now known that immunocompetent cells, such as Langerhans cells, in the host peripheral cornea likely incite the response.¹

Prior surgical intervention or inflammatory disease, including prior rejection and failure, also poses a higher risk for graft rejection.^{1-3,9} Inflammatory diseases such as herpetic, interstitial, or traumatic keratitis carry a high risk for endothelial rejection.⁹ It is thought that these previous inflammatory episodes may alter the distribution of immune competent cells, which then may be present post-transplantation.¹

Nonspecific stimulation by any inflammatory process could release cells that activate the rejection process.³ This process has classically been considered a type 1 helper (Th1) cellular response.⁶ Other systemic immune competent cells are able to contact endothelial antigens circulating in the anterior chamber through Schlemm's canal.³ Proximal inflammation, as occurred in our patients as a result of localized nonocular infections, is likely to increase the amount of circulating acute inflammatory mediators, which may incite corneal graft rejection.

The risk of corneal allograft rejection from nonocular inflammation is likely underreported because patients are not usually asked about nonocular inflammation or infections in the clinical setting. Hence the association may not be made. When caring for a cornea transplant patient, the treating ophthalmologist should educate the patient about the signs and symptoms of graft rejection. In addition, the physician may consider broadening the conversation with patients to include a review of systems that includes dental and facial infections or other inflammatory conditions. Patients could also be informed of a potential association between these conditions and graft rejection. As always, any acute changes in visual acuity should be brought to the attention of the treating ophthalmologist immediately. Moreover, the prophylactic use of local or systemic steroids when facial or dental inflammation is present may reduce the risk of allogenic corneal graft rejection.

Further study of extraocular facial inflammation and corneal graft rejection in animal models is warranted to better understand the pathophysiology of this associa-

tion. In addition, a registry for the reporting of corneal graft rejection associated with nonocular inflammation would provide researchers with a larger patient cohort to help stratify the risk of rejection associated with various nonocular infections and procedures and clarify the benefit of prophylactic steroid treatment.

Literature Search

PubMed was searched last on December 10, 2013, for English-language articles using the following terms: *corneal graft reaction, transplant rejection, inflammation, AND/OR nonocular infection*. All 155 articles retrieved were analyzed to determine whether a case of graft rejection associated with nonocular inflammation was reported.

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