Pulse corticosteroid therapy in post-keratoplasty graft rejection: A strategy to restore vision

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SUMMARY

A case of corneal graft rejection following penetrating keratoplasty (PK) successfully managed with pulse corticosteroid therapy, leading to the reversal of graft rejection and restoration of vision. We present a case of a 35-year-old female with bilateral keratoconus who underwent PK for the left eye. The patient developed early graft rejection within two weeks postoperatively, presenting with conjunctival injection, corneal infiltrates and limbal vascularisation. Intensive topical and systemic therapy, including intravenous methylprednisolone pulse therapy (500 mg daily for three days), was administered, followed by oral corticosteroids and adjunctive treatments. Following pulse corticosteroid therapy, the patient exhibited significant improvement, with resolution of graft rejection signs and visual acuity recovery to 6/12 (pinhole 6/9) four months post-PK. Early recognition and aggressive management of graft rejection are critical for corneal graft survival. Pulse corticosteroid therapy offers a rapid and effective approach in reversing severe rejection while minimising prolonged systemic corticosteroid exposure.

INTRODUCTION

Corneal graft rejection is a sight-threatening complication that can occur after penetrating keratoplasty, potentially resulting in substantial endothelial cell loss and corneal decompensation.[1-2] Factors that increase the risk of corneal graft rejection include donor age, graft size, multiple graft procedures, a history of graft rejection and corneal vascularisation, as all these factors compromise innate immunological privilege.[1] Corneal transplant may be indicated in various conditions such as corneal ectasia, bullous keratopathy, stromal dystrophies, Fuchs' endothelial dystrophy, scarring, perforation or failure of a previous graft.[3] Early diagnosis of corneal rejection and timely treatment are essential to reduce visual morbidity and preserve the corneal transplant. We report this case in view of limited evidence regarding the use of systemic pulse corticosteroid in managing graft rejection following penetrating keratoplasty.

CASE PRESENTATION

A 35-year-old lady with history of allergic rhinitis, bronchial asthma, and hypertension presented with acute hydrops in the left eye in December 2023. She had been diagnosed with bilateral keratoconus in Glasgow in 2014 but had defaulted on follow-up. Her younger sister also has keratoconus, indicating a possible familial predisposition. Upon presentation, her best-corrected visual acuity (BCVA) was 6/24 in the right eye (RE) and counting fingers in the left eye (LE). Examination revealed signs of advanced keratoconus in both eyes. Munson's sign, prominent corneal nerves, Rizzuti sign and Vogt's striae were noted in the RE, while the LE showed central corneal oedema with bullae. Initial treatment included topical corticosteroids, antibiotic, hypertonic saline and atropine.

On August 7, 2024, she underwent penetrating keratoplasty (PK) for the left eye. Intraoperatively, the donor cornea exhibited a total epithelial defect and oedema. Postoperatively, her vision improved to 6/18 by the third day. However, complications arose on the twelfth postoperative day, including early graft rejection characterised by conjunctival injection, corneal infiltrates, epithelial defect and limbal vascularisation. These were managed with intensive antibiotics, topical corticosteroids and systemic doxycycline. Corneal re-suturing was performed two weeks later due to loose sutures, improving her vision to 6/60 (pinhole 6/12).

The patient was closely monitored for progressive corneal infiltrates by means of weekly review. On subsequent review, the condition worsened significantly. Corneal infiltrates were noted at 5 o'clock position at two points, involving the graft-host junction (GHJ) and the recipient tissue, corneal oedema extending from 4-7 o'clock at the GHJ. Superficial limbal vascularisation was present between 11 to 1 o'clock without compromising the GHJ. These findings warranted hospital admission for intravenous methylprednisolone pulse therapy (500mg daily for 3 days).

The patient was discharged on oral prednisolone 60 mg daily and topical corticosteroids and topical lubricant hourly together with hypertonic saline 3% every four hours to manage corneal oedema. Antibiotic coverage included topical levofloxacin and oral doxycycline. Additional supportive treatments included oral vitamin C to aid corneal wound healing and topical olopatadine 0.1% twice daily for allergic symptom control.

Two months post-PK, the patient developed steroid-induced ocular hypertension, with intraocular pressures (IOP) of 22 mmHg in the RE and 28 mmHg in the LE. This was addressed by rapidly tapering topical corticosteroid, switching from prednisolone acetate to fluorometholone (FML) and initiating dorzolamide eye drops.

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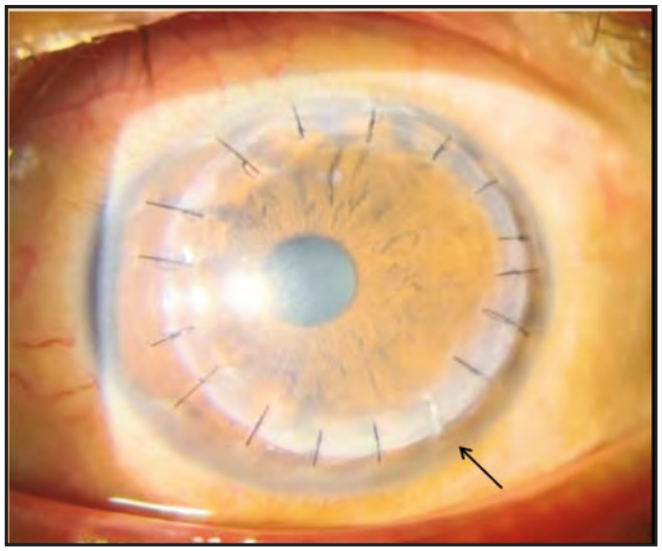

Fig. 1: The left eye of the patient demonstrates a corneal infiltrate (indicated by the arrow)

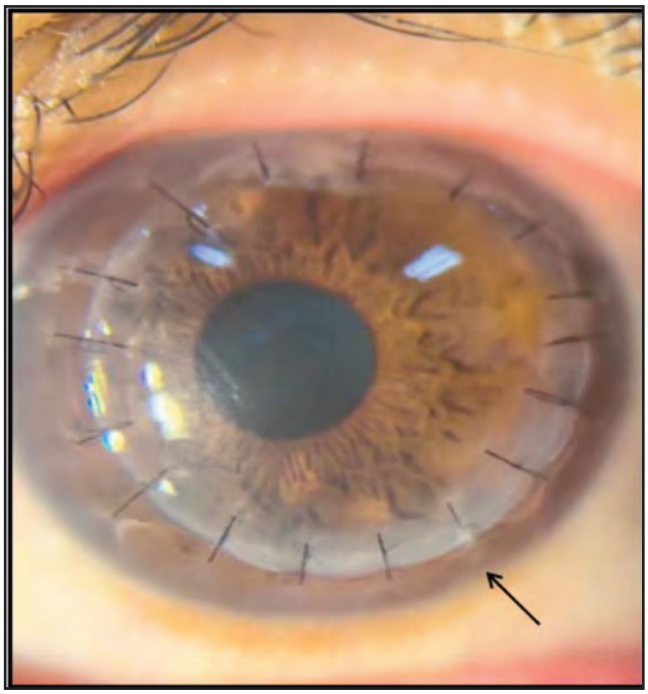

Fig. 2: The left eye showed remarkable resolution of the infiltrate after pulse methylprednisolone (indicated by the arrow)

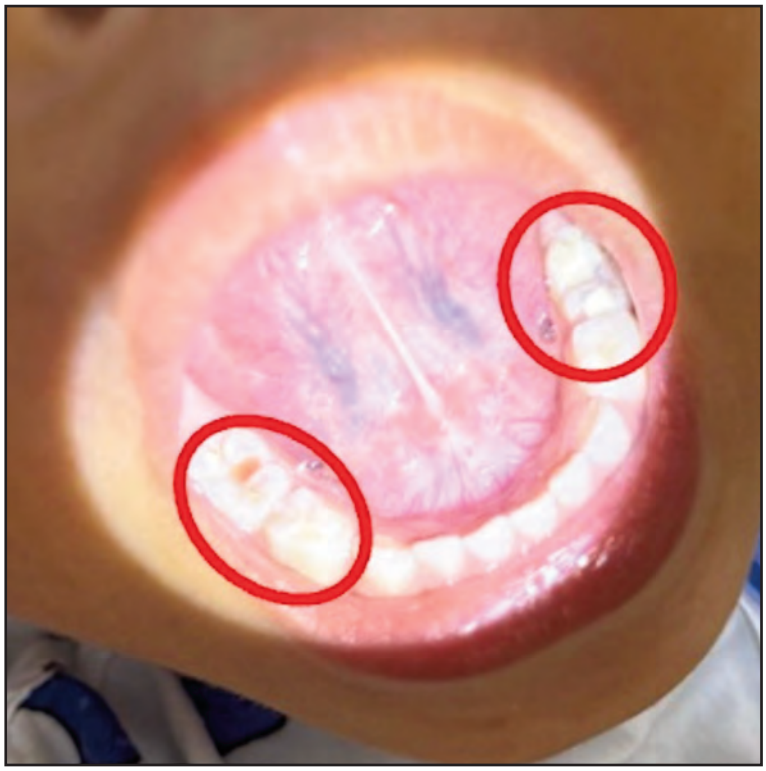

Fig. 3: The left eye demonstrates complete resolution of the corneal infiltrate four months postoperatively, with restored graft clarity and no signs of active rejection

At four months post-PK, the patient's LE vision had improved to 6/12 (pinhole 6/9), with no signs of graft failure. Examination revealed intact sutures, mild subepithelial haze and no significant vascularisation involving the graft-host junction. The RE, affected by severe keratoconus, is planned for corneal cross-linking to prevent further progression. Her treatment regimen included oral prednisolone, topical antibiotics, topical corticosteroid and antiglaucoma medications, with close monitoring of IOP and graft integrity. Regular follow-up was planned to ensure continued recovery and graft stability.

Severe corneal graft rejection has been reported in up to two-thirds of cases, with graft clarity maintained in two-thirds of these.[1] Graft rejections most commonly occur within the first six months after surgery.[4] Acute graft rejection may present with conjunctival injection, anterior chamber activity, keratic precipitates, endothelial rejection line (Khodadoust line) and stromal or epithelial oedema.[4] Early recognition of the signs of rejection is vital, as initiation of early treatment will ensure a better visual prognosis. Systemic corticosteroid is useful in cases of early and severe graft rejection.[4] The rejection reversal rate ranges from 50-80% in patients treated with pulse and oral corticosteroids, suggesting a favourable outcome when using systemic corticosteroid to manage graft rejection.[5] In our case, the patient received high-dose pulse corticosteroid followed by oral prednisolone, leading to successful reversal of graft rejection.

Pulse corticosteroid therapy refers to the administration of a supraphysiological dose of corticosteroid, conventionally 500 to 1000 mg of intravenous methylprednisolone daily for one to three days, given over a short period.[5-9] This achieves faster control of an acute immunological insult while reducing the cumulative steroid burden and the adverse effects associated with prolonged high-dose oral therapy. Pulse therapy is well established in ophthalmology. In acute optic neuritis, intravenous methylprednisolone hastens visual recovery[8], and in sight-threatening thyroid eye disease, single doses of 500 to 1000mg over three days constitute first-line treatment for dysthyroid optic neuropathy.[9] In corneal transplant, Hill et al. demonstrated in a randomised comparison that a single intravenous methylprednisolone pulse was superior to oral steroid alone in reversing rejection and that it reduced the incidence of subsequent rejection episodes.[5] Our management followed this principle.

The quality of the donor corneal tissue merits consideration in this case. Although the preoperative eye bank assessment was satisfactory, the donor cornea was found intraoperatively to have a total epithelial defect and stromal oedema. These changes were most likely due to epithelial loss during storage and handling rather than to endothelial compromise, since the endothelial cell density met our threshold for corneal transplant. Even so, a suboptimal donor cornea at the time of surgery may lead to delayed epithelialisation, persistent epithelial defect and prolonged ocular surface inflammation. Ocular surface inflammation is a known risk factor for rejection. It promotes neovascularisation and neolymphangiogenesis, drawing immune cells into the graft and increasing risk of rejection.[10] Our patient followed a similar course, developing epithelial defect and corneal infiltrates before the rejection episode.

This case highlights the importance of careful donor corneal tissue assessment before grafting, including endothelial cell density, epithelial integrity and stromal clarity. In elective cases such as keratoconus, where the prognosis is otherwise good, it may be preferable to request another donor corneal button rather than accept borderline tissue and risk a good outcome.

CONCLUSION

Early recognition of graft rejection is crucial, as prompt treatment reduces the risk of irreversible graft damage. Pulse corticosteroid therapy offers rapid control of the acute rejection episode while reducing the cumulative side effects of prolonged oral corticosteroids and may lower the risk of further rejection, supporting long-term graft survival.

DECLARATION OF PATIENT CONSENT

The authors confirm that they have obtained all necessary patient consent forms. These forms indicate that the patient has provided consent for their images and clinical information to be published in the journal. The patients acknowledge that their names and initials will not be disclosed and that every effort will be made to protect their identity, though complete anonymity cannot be assured.

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