Corneal Epithelial Hyperplasia after 5-Fluorouracil Injection

Dania A. Bukhari, Sarah K. Alessa, Safaa I. Beheiri

Keywords
Ophthalmology · Cornea · 5-Fluorouracil

Abstract

**Background:** 5-Fluorouracil (5-FU) is a pyrimidine analogue which selectively inhibits DNA synthesis, RNA synthesis, and VEGF antibodies. 5-FU is widely used in ophthalmology for inhibition of postoperative corneal scarring and scleral bleb fibrosis. **Case Presentation:** In this case report, we describe an unusual case of a 65-year-old male who presented to the clinic with progressive decrease of vision after he underwent a revision of scleral bleb with the administration of 0.05 mL 5-FU (2.5 mg) injection and was diagnosed with corneal epithelial hyperplasia. The patient had a history of glaucoma managed by deep sclerotomy and phacoemulsification with intraocular lens implantation. **Conclusion:** Our case demonstrates an unusual consequence of corneal epithelial hyperplasia developed after 5-FU injection.

Introduction

5-Fluorouracil (5-FU) is a pyrimidine analogue which selectively inhibits DNA synthesis in phase S and G2 of the cell cycle, RNA synthesis, and VEGF antibodies [1]. 5-FU is widely used in ophthalmology for inhibition of postoperative corneal scarring and scleral bleb fibrosis. It is used postoperatively in refractive procedures to decrease the risk of corneal haze.
Here, we report an unusual case of a male presenting with corneal epithelial hyperplasia following needling procedure with the application of 5-FU.

**Case Presentation**

A 65-year-old Somalian patient with diabetes, hypertension, and glaucoma on antiglaucoma medication (Alphagan 3/day and Lumigan 4/day) presented to our clinic with progressive decrease of vision in his left eye 1 week after he underwent a revision of scleral bleb with the administration of 0.05 mL 5-FU (2.5 mg) injection. He lost his vision in the right eye secondary to refractory glaucoma. The patient had deep sclerotomy and phacoemulsification with intraocular lens implantation in the left eye on January 2017. He presented to the clinic 4 months later for left bleb suture removal.

On physical examination, the patient had no light perception in his right eye and 20/50 visual acuity in his left eye. Tonometric left eye pressure was 28 mm Hg. The eyelids, lashes, and lacrimal glands were normal on slit-lamp examination. Left-eye bleb vascularization was noticed while the left-eye anterior chamber was deep and quiet. The patient continued on antiglaucoma medication, and needling for the left eye bleb was planned for the following week.

During the next visit, vision improvement in the left eye was noticed as it became 20/30, and needling of the left eye bleb with 0.05 mL 5-FU (2.5 mg) injection was done. The patient came to the clinic after 1 week complaining of decreased vision in the left eye. Physical examination showed no light perception in the right eye, with 20/50 visual acuity in the left eye. Tonometric right and left eye pressures were 11 and 22 mm Hg, respectively. The eyelids, lashes, and lacrimal glands were normal on slit-lamp examination. The conjunctiva in the left eye showed bleb form, and a left corneal central epithelial defect of 2–3 mm was noticed. The patient was managed with liberal lubrication.

Four days later, the patient returned and was still complaining of decrease of vision with haze in the left eye. Visual acuity of the left eye was 20/200. A central corneal opacity with Dellen effect in the left eye was detected by slit-lamp examination. The patient was advised to continue on his antiglaucoma medication and Pred Forte was also prescribed.

The next day, his left eye vision improved to 20/100. Slit-lamp examination of the left eye cornea showed healing of the central corneal epithelial defect and the formation of central white opacity and mesh-like subepithelial fibrosis which, without fluorescence staining, was diagnosed as corneal epithelial hyperplasia. The patient was started on cyclosporine 1% 4/day as well as lubrication. Visual acuity of the left eye improved to 20/50 during the following 2 weeks and thinning of the central corneal opacity was noticed on slit-lamp examination. The patient missed his follow-ups and showed up after 3 months with complete resolve of the corneal opacity.

**Discussion**

5-FU is an antimetabolite agent which inhibits cell replication by interfering with DNA synthesis and cellular mitosis [4]. 5-FU is used for various applications in ophthalmic practice. It interferes with fibroblast proliferation, which plays an important role in the scarring process in cases of failed glaucoma filtering procedures due to scarring at the surgical site [1]. 5-FU has been used as an anticancer drug to inhibit actively replicating cells [4].
epithelium cells replicate constantly [4], which make them susceptible to 5-FU toxic effects as it prevents their proliferation and growth. Corneal epithelial defects were reported as complications following 5-FU therapy in several studies [5–7]. In our case, hyperplasia of the corneal epithelium was evident following the administration of 5-FU. In 1987, 4 cases of corneal complications after 5-FU administration following glaucoma filtering surgery were reported in cases with pre-existing corneal abnormalities. Microbial keratitis, sterile perforation and ulceration, and anterior stromal scarring in the bed of a persistent epithelial defect were the reported complications [5]. However, in this case the patient did not have pre-existing corneal diseases. Anand and Khan [8] reported late ocular complications in a retrospective study among 70 procedures after 5-FU needle revision of trabeculectomy blebs that included bleb leaks, blebitis, persistent choroidal effusions, unexplained loss of vision, and corneal decompensation. Corneal hyperplasia, as presented in our case, was not reported. Moreover, Bell et al. [9] evaluated 45 patients who underwent trabeculectomy augmented with a single intraoperative application of 5-FU (25 mg/mL) and described postoperative complications in the form of hypotony maculopathy, leaking bleb, and giant bleb.

Hence, this case demonstrates an unusual corneal response to 5-FU in the form of hyperplasia that was treated successfully with cyclosporine 1%.

**Statement of Ethics**

The authors have no ethical conflicts to disclose.

**Disclosure Statement**

The authors report no conflicts of interests.

**References**

1. Gressel MG, Parrish RK, Folberg R: 5-fluorouracil and glaucoma filtering surgery. I. An animal model. Ophthalmology 1984;91:378–383.
2. Lee SY, Pak JH, Tchah H, Kook MS: Mitomycin C, ceramide, and 5-fluorouracil inhibit corneal haze and apoptosis after PRK. Cornea 2006;25:55–60.
3. https://www.aao.org/eyenet/article/reduce-scarring-with-5-fu.
4. Hickey-Dwyer M, Wishart PK: Serious corneal complication of 5-fluorouracil. Br J Ophthalmol 1993;77:250.
5. Knapp A, Heuer DK, Stern GA, Driebe WT: Serious corneal complications of glaucoma filtering surgery with postoperative 5-fluorouracil. Am J Ophthalmol 1987;103:183–187.
6. Shapiro MS, Thoft RA, Friend J, Parrish RK, Gressel MG: 5-Fluorouracil toxicity to the ocular surface epithelium. Invest Ophthalmol Vis Sci 1985;26:580–583.
7. Lee DA, Hersh P, Kersten D, Melamed S: Complications of subconjunctival 5-fluorouracil following glaucoma filtering surgery. Ophthalmic Surg 1987;18:187–190.
8. Anand N, Khan A: Long-term outcomes of needle revision of trabeculectomy blebs with mitomycin C and 5-fluorouracil: a comparative safety and efficacy report. J Glaucoma 2009;18:513–520.
9. Bell RW, Habib NE, O’Brien C: Long-term results and complications after trabeculectomy with a single per-operative application of 5-fluorouracil. Eye 1997;11:663–671.
10. https://www.drugs.com/sfx/bimatoprost-ophthalmic-side-effects.html.