



# Management of severe epithelial versus fibrous downgrowth following trabeculectomy: Case report and literature review

Christos N. Theophanous, Ema Avdagic, Asim V. Farooq, Dimitra Skondra, Mary Qiu\*

Department of Ophthalmology and Visual Science, University of Chicago Medical Center, Chicago, IL, USA

## ARTICLE INFO

### Keywords:

Trabeculectomy  
Epithelial downgrowth  
Fibrous downgrowth

## ABSTRACT

**Purpose:** To describe the presentation and management of a patient with epithelial versus fibrous downgrowth following trabeculectomy surgery and review relevant literature regarding this complication after intraocular surgery.

**Observations:** A 52-year-old monocular African-American woman was referred for management of presumed epithelial versus fibrous downgrowth following trabeculectomy surgery. The patient was initially treated with intracameral injections of 5-fluorouracil (x2) and bevacizumab (x1). Cataract extraction, membranectomy, and a third intracameral 5-fluorouracil injection were performed. Intraocular pressure (IOP) elevation was subsequently managed with a superotemporal Ahmed FP7 glaucoma drainage device in the sulcus, followed by an inferonasal Baerveldt 350 glaucoma drainage device in the sulcus. The downgrowth has not progressed and the intraocular pressure remains controlled at the most recent follow-up.

**Conclusions:** This case underscores the risk of this complication following trabeculectomy, the role of a combined medical and surgical approach to management, and the possible need for multiple surgical interventions to control IOP. A review of the literature regarding epithelial and fibrous downgrowth after intraocular surgery was conducted, which highlighted the aggressive nature of these conditions and the range of therapeutic approaches that have been described.

## 1. Introduction

Epithelial downgrowth is a rare complication of intraocular surgery or trauma characterized by invasion of surface epithelial cells into the anterior chamber (AC) of the eye.<sup>1</sup> The membranous spread of these conjunctival or corneal epithelial cells can be difficult to control and lead to devastating consequences including end-stage glaucoma and permanent vision loss.<sup>2</sup> Fibrous downgrowth is a similar but somewhat less aggressive condition characterized by fibrovascular connective tissue invading into the eye. Patients with these conditions can present with decreasing visual acuity, pain, tearing, photophobia, foreign body sensation or flashes of light.<sup>2</sup> Previous reports have described epithelial downgrowth following glaucoma surgery.<sup>3-7</sup> Herein, we report the medical and surgical management of a case of severe epithelial versus fibrous downgrowth following prior trabeculectomy surgery.

## 2. Case report

A monocular 52-year-old African American woman with primary

open angle glaucoma (POAG) was referred to the anterior segment service for evaluation of a membrane growing into the AC from a superior trabeculectomy site in her only-seeing left eye (OS) performed 10 months prior. Visual acuity (VA) was 20/125 and intraocular pressure (IOP) was 24 mmHg on four topical antihypertensive agents. She was also using prednisolone acetate 1 % and cyclopentolate 0.5 % once daily for low-grade AC inflammation. She had previously undergone selective laser trabeculoplasty (SLT) OS with initial improvement in IOP; however, after being lost to follow-up for 18 months, the IOP had increased to 29 mmHg so she underwent a superior fornix-based *ab externo* trabeculectomy with subconjunctival injection of mitomycin-C (MMC) (0.1 mL of 0.4mg/mL). Her post-operative course was notable for hypotony with IOP of 7 mmHg, a shallow AC, self-limited choroidal effusions, and persistent low-grade AC inflammation. Five months after surgery, the angle was documented to be synechially closed for 360-degrees.

On slit lamp examination, a membrane covering the anterior lens capsule was noted, originating from the superior trabeculectomy site with neovascularization on the membrane. This was concerning for an inflammatory membrane, fibrous downgrowth, or epithelial

\* Corresponding author. Department of Ophthalmology and Visual Science University of Chicago Medical Center, 5841 S. Maryland Ave, Chicago, IL, 60637, USA.  
E-mail address: [maryqiu@bsd.uchicago.edu](mailto:maryqiu@bsd.uchicago.edu) (M. Qiu).

downgrowth (Fig. 2). An inflammatory workup for Lyme disease, syphilis, tuberculosis, and sarcoidosis was negative. Diagnostic argon laser applied to the iris surface was consistent with the diagnosis of epithelial downgrowth. Confocal microscopy did not reveal a retrocorneal membrane.

The patient underwent intracameral injection of 0.05mL of 5-Fluorouracil (5-FU) followed by intracameral injection of 0.05mL of bevacizumab two weeks later, and a second intracameral injection of 0.05mL of 5-FU one month later. Her IOP OS increased to 29 mmHg, so topical prednisolone acetate was discontinued due to a concern for steroid response. Over the next eight months, the appearance of the fibrous membrane remained stable, the patient's VA OS fluctuated between 20/300 and count fingers, and IOP ranged from 15 to 23 mmHg.

The patient subsequently underwent membranectomy, cataract extraction with implantation of a one-piece intraocular lens in the capsular bag, and another intracameral injection of 0.05mL of 5-FU. The membranectomy involved visco-dissection and excision of the membrane using a cystotome and MST scissors. Histopathologic analysis identified the sample as a hypocellular collagenous tissue with small vessels and focal pigment deposition (Fig. 3).

One month after surgery, the patient's IOP OS was 38 mmHg on four topical antihypertensive medications, and she was referred to a new glaucoma provider (MQ). Steroid response was considered given prolonged use of prednisolone acetate. Gonioscopy revealed 360-degrees of synechial closure with fibrous tissue extending from the trabeculectomy sclerostomy site to the superior aspect of the anterior capsule. Oral acetazolamide 500mg twice a day was started, but IOP remained elevated at 33 mmHg. The patient underwent implantation of a superotemporal Ahmed FP7 glaucoma drainage device (New World Medical, Rancho Cucamonga, CA) with the tube tip in the sulcus, scleral patch graft, and Kenalog 20mg injected intra-tenons over the plate to reduce encapsulation. The following day, IOP was 17 mmHg OS.

By post-operative week five, IOP increased to 25 mmHg on 4 topical antihypertensive medications and oral acetazolamide 250mg four times per day, so the patient underwent implantation of an inferonasal Baerveldt 350 implant (Johnson & Johnson Vision Care Inc., Jacksonville, FL) with the tube tip in the inferonasal sulcus, split thickness half-moon corneal patch graft, and 3-0 Prolene ripcord suture in the tube lumen to prevent hypotony when the ligating suture dissolves, which is this surgeon's standard protocol for Baerveldt tubes. Concurrent revision of the Ahmed FP7 was also performed by excising the capsule over the plate and injecting Kenalog 20mg to reduce aqueous outflow resistance and

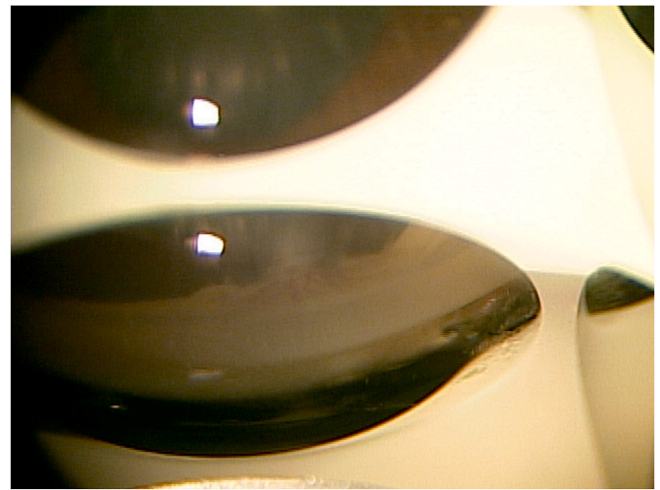


Fig. 2. Gonioscopic photograph of left eye demonstrating membranous growth from trabeculectomy site.

future encapsulation. The goal was to achieve early IOP lowering in the first 6 weeks before the Baerveldt opened.

At post-operative week one, the IOP was 12 mmHg; however, one week later, the IOP decreased to 3 mmHg, the ripcord suture was absent although the patient did not recall removing it herself, and there was a robust AC inflammatory reaction with fibrinous material at the tip of the inferonasal tube, not occluding the tube (Fig. 2). The patient was treated medically with frequent topical steroid and atropine. By post-operative week three, the IOP increased to 16 mmHg, and the AC inflammation subsided. Throughout this period, the AC remained deep, and no choroidal effusions or suprachoroidal hemorrhage were seen. By post-operative week six, the ligating suture dissolved, as expected, and the inferonasal Baerveldt tube was fully functioning. By postoperative month seven, the patient's best-corrected VA was 20/50, and the IOP was 11 mmHg on five topical antihypertensives (brinzolamide/brimonidine 3x per day, Timolol 2x per day, netarsudil/latanoprost at bedtime) and no oral agents. No recurrence of the downgrowth was noted, the fibrinous AC reaction had resolved, and both tube tips were patent in the sulcus (Fig. 4). A new 24-2 Humphrey Visual Field, this time with a size V stimulus, demonstrated that she still retained a central island of vision in this eye (Fig. 1).

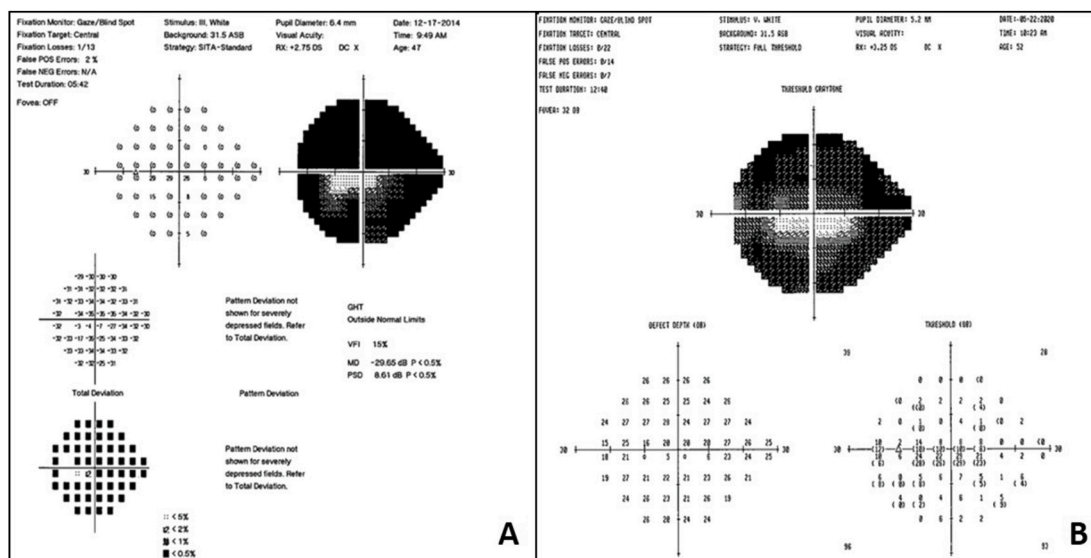
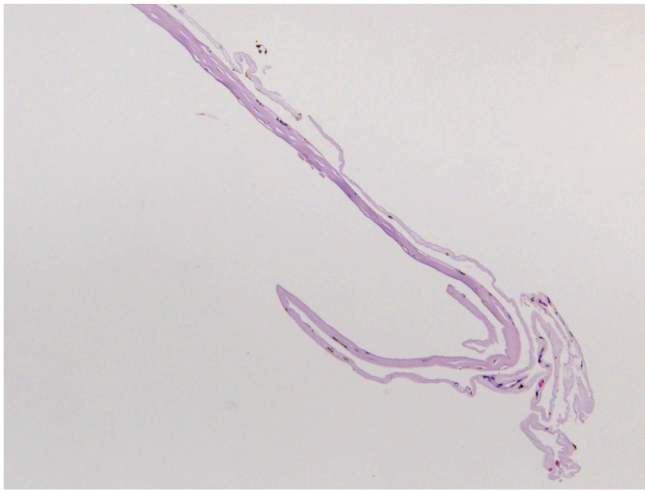


Fig. 1. A) Pre-trabeculectomy Humphrey Visual Field 24-2 of left eye. B) Post-treatment Humphrey Visual Field 24-2 of left eye.





**Fig. 3.** Histopathology image of membrane resected during combined membranectomy and cataract extraction with intraocular lens implant from left eye stained with hematoxylin and eosin at 10x magnification.

**3. Discussion**

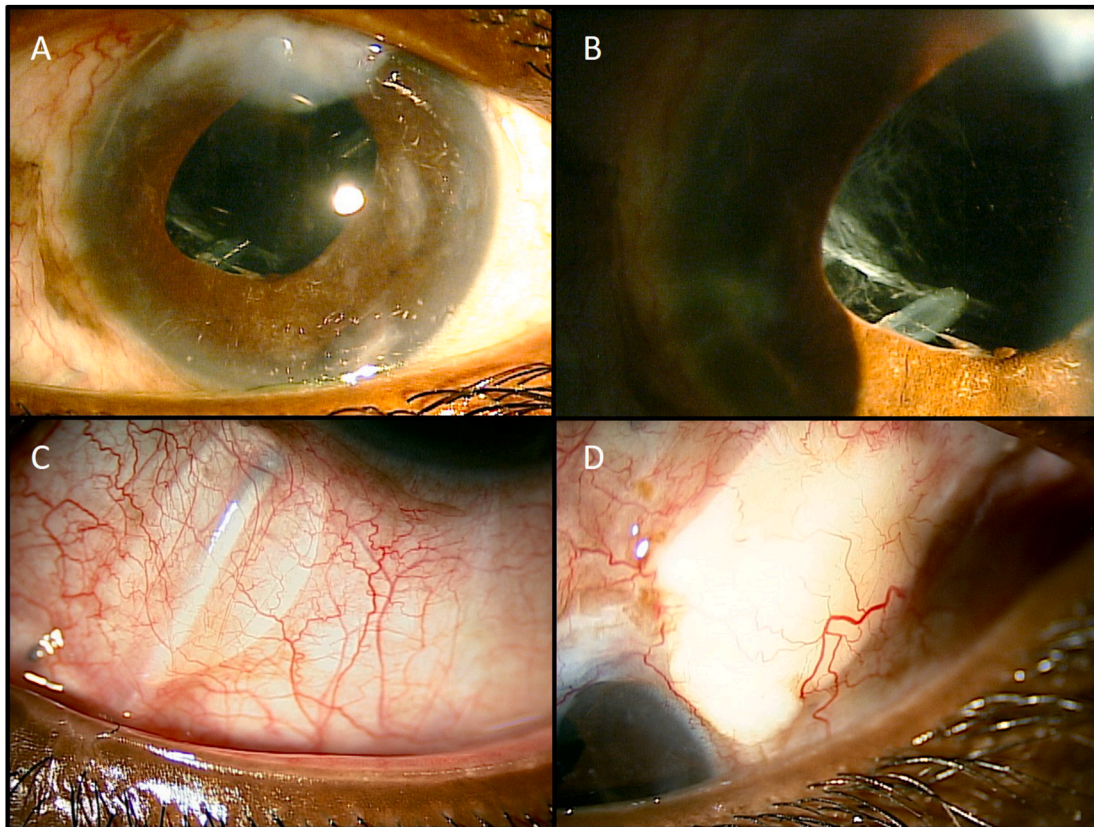
Epithelial or fibrous downgrowth after glaucoma surgery is rare. Most cases of epithelial downgrowth occur after trauma or intraocular surgery such as phacoemulsification, penetrating keratoplasty, and Descemet stripping automated endothelial keratoplasty.<sup>8-10</sup> Rare cases have been reported after aqueous aspiration and pterygium removal.<sup>2</sup> A 30-year pathologic review of epithelial downgrowth by Weiner et al. found that 82 % of cases present within a year of intraocular surgery. In

the study, a retro-corneal membrane was the most common presenting sign, followed by glaucoma, corneal edema, and a positive Seidel sign.<sup>2</sup> Fibrous downgrowth present similarly but differs by the histopathologic presence of fibroblastic instead of epithelial cells.<sup>11</sup>

This case describes epithelial versus fibrous downgrowth identified ten months after trabeculectomy that was successfully treated with a staged medical and surgical approach. One case of epithelial downgrowth after trabeculectomy with MMC was previously reported by Ruderman et al. in a retrospective case series of 43 trabeculectomies.<sup>7</sup> In that case, a leak at the flap was seen and treated with a pressure patch, but after a subsequent conjunctival leak was found and the patient refused treatment, the eye eventually became phthisical.<sup>7</sup>

Epithelial downgrowth after implantation of a glaucoma drainage device has been reported. Jewelewitz et al. described a case of tissue confirmed epithelial downgrowth in an 84-year-old patient seen four months after Ahmed FP7 implantation.<sup>4</sup> Hu et al. described a case of epithelial downgrowth presenting as a peritubular vascular membrane after Ahmed FP7 implantation.<sup>3</sup> Giaconi et al. reported epithelial downgrowth presenting as a cyst after goniotomy and Ahmed valve revisions in a child with congenital glaucoma that was treated by *ab externo* drainage and repeated cryotherapy after recurrence.<sup>12</sup>

On histopathology, epithelial downgrowth typically appears as a multilayered membrane of nonkeratinized, stratified, squamous epithelial sheets.<sup>1</sup> It may also be seen as cysts or scattered islands of cells. Clinically, these sheets appear as a translucent or gray membrane with a smooth border and rolled edges. These membranes can occlude the trabecular meshwork or cause peripheral anterior synechiae formation leading to secondary angle closure glaucoma. Fibrous downgrowth, the spread of fibrocytes through a fistula, can present similarly but the membranes are typically thicker with irregular borders. They tend to grow more slowly and carry a more favorable prognosis.<sup>1</sup> In this case, although no epithelial cells were seen on histopathology, it is



**Fig. 4.** Post-operative slit lamp photographs showing (A) superotemporal and inferonasal tube insertions in sulcus and superior trabeculectomy site; (B) fibrinous deposit at inferonasal tube tip; (C) inferonasal Baerveldt 350 tube with corneal patch graft; (D) superotemporal Ahmed FP7 tube with tutoplast scleral patch graft.

unclear whether this is due to treatment with 5-FU or if epithelial cells were never present. Epithelial downgrowth was more suspected due to the characteristic whitening of the membrane with argon laser and smooth iris appearance with loss of normal architecture.

Various treatments have been attempted for epithelial and fibrous downgrowth including surgical excision, cryotherapy, irradiation, and laser photocoagulation.<sup>13,14</sup> Hu et al. employed tube shunt explanation with surgical excision of the fibrovascular membrane with no noted recurrence 6 weeks post-operatively.<sup>3</sup> Several reports have noted successful use of 5-FU.<sup>15–19</sup> Sivaraman et al. reported three patients with localized epithelial downgrowth treated with partial lamellar sclero-kerato-uvectomy.<sup>20</sup> Yu et al. reported successful use of MMC for cystic epithelial downgrowth after cataract surgery.<sup>21</sup>

The initial treatment of the downgrowth with intracameral injections of 5-FU, followed by bevacizumab, followed by a second dose of 5-FU, did not resolve the membrane, which was not unexpected given the extent of AC invasion. However, the sheet did not progress after these treatments, and given the aggressiveness of epithelial downgrowth, we deem halting the spread as a demonstration of treatment success. Of note, intracameral or intravitreal methotrexate was considered, but since the membrane was not progressing after the 5-FU injections, methotrexate was not deemed necessary.

The patient was originally noted to have PAOG, however after the trabeculectomy, the angle had become synechially closed, potentially due to AC shallowing after the trabeculectomy or the persistent AC inflammation and downgrowth. The elevated IOP prior to Ahmed implantation may also have been due in part to steroid response from use of prednisolone acetate after the cataract extraction and membranectomy. A valved Ahmed FP7 implant was preferred to a non-valved Baerveldt 350 implant since the advanced stage of her glaucoma demanded rapid pressure reduction. A second trabeculectomy was considered but deemed likely to fail in the setting of active neovascularization and persistent inflammation. Considering the synechial angle closure, sulcus placement of the Ahmed tube tip was preferred.

Although initially successful, the IOP increased again after the Ahmed FP7, likely due to encapsulation of the plate and possible steroid response. A Baerveldt 350 implant was deemed more likely to achieve better long-term IOP control than a second Ahmed FP7,<sup>22,23</sup> and concurrent revision of the Ahmed capsule could achieve early IOP lowering before the Baerveldt opened, with less risk of hypotony than aggressive fenestrating slits in the Baerveldt. This patient experienced early transient hypotony due to suspected inadvertent removal of her own ripcord suture. Fortunately, the AC never shallowed, there were never any chorioretinal folds, choroidal effusions, or suprachoroidal hemorrhage, and the transient fibrinous AC reaction resolved with topical steroids and never occluded the tube lumen. Ultimately, this case emphasizes the aggressiveness of membranous downgrowth following trabeculectomy surgery, the possible need for a combined medical and surgical approach to management, and the potential necessity for multiple surgical interventions to control IOP after this complication.

#### Patient consent

Consent to publish the case report was not obtained. This report does

not contain any personal information that could lead to the identification of the patient.

#### Acknowledgements and Disclosures

No funding or grant support was received. The following authors have no financial disclosures: (CT, EA, DS, MQ). One author is a consultant to GlaxoSmithKline in a capacity unrelated to this manuscript (AF). All authors attest that they meet the current ICMJE criteria for Authorship.

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