Role of oral doxycycline and large diameter bandage contact lens in the management of early post-trabeculectomy bleb leak

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SUMMARY
A 27-year-old man with juvenile open angle glaucoma and medically uncontrolled intraocular pressure (IOP) underwent a trabeculectomy with mitomycin C in his right eye. One week postoperatively, he developed ischaemic necrosis of the conjunctiva with a bleb leak. This was managed conservatively with oral doxycycline 100 mg twice daily along with a topical low-dose steroid, antibiotic and cycloplegic and a large diameter bandage contact lens (BCL). There was dramatic improvement in the bleb appearance, the necrosis healed and the leak resolved. The patient had well-controlled IOP with a diffuse healthy bleb at 4 weeks, which was maintained at 2 years. This case illustrates the utility and importance of oral doxycycline in the management of early post-trabeculectomy conjunctival necrosis and the use of BCL in the management of a bleb leak. This safe and non-invasive method not only hastened the recovery but also helped in maintaining good bleb function.

BACKGROUND
A bleb leak is a well-known complication after any glaucoma filtering surgery. Leaking blebs have become increasingly common with the widespread use of antimetabolites in glaucoma filtering surgery.1 Bleb leaks may occur early in the postoperative period or years after the surgery. An early postoperative bleb leak is associated with increased risk of hypotony and bleb failure.1 These complications can be prevented by appropriate and timely intervention. Conjunctival ischaemia or necrosis is an uncommon complication that can occur in the early or late postoperative period. The predisposing factors for early postoperative conjunctival necrosis are poor conjunctival health prior to the surgery, intraoperative inadvertent cautery or mitomycin C (MMC) exposure to the conjunctival edges. Conjunctival necrosis predisposes the eye to infection (blebitis) and endophthalmitis in the presence of poor lid hygiene.

The management of early bleb leaks varies from simple observation to the use of a large diameter bandage contact lens (BCL) or surgical intervention. The choice of treatment depends on the severity of the leakage, type of conjunctival flap (limbus or fornix based), position of leakage and the health of the surrounding conjunctiva. The management of an ischaemic or necrotic bleb is essentially surgical, requiring bleb excision with conjunctival advancement or autograft.1 The use of oral doxycycline in the management of conjunctival erosion following glaucoma drainage device use has been described.2 However, its role in the management of post-trabeculectomy conjunctival necrosis or bleb leak has not been reported so far. We report a case of juvenile open angle glaucoma (JOAG) with conjunctival necrosis and bleb leak 1 week following trabeculectomy with MMC. The use of oral doxycycline and large diameter BCL helped in conservative management with complete resolution of the bleb leak, obviating the need for surgical intervention. It also helped in maintaining good bleb morphology and function.

CASE PRESENTATION
A 27-year-old man with JOAG presented with intraocular pressure (IOP) of 30 and 15 mm Hg in the right and left eyes, respectively, on maximal topical antiglaucoma medications (combination of dorzolamide 2% and timolol maleate 0.5% twice daily, latanoprost 0.005% once at bed time and brimonidine tartarate 0.1% twice daily) and oral acetazolamide. Visual acuity was finger counting at 1 m in the right eye and 20/20 in the left eye. Gonioscopy showed near total glaucomatous optic atrophy in the right eye and 0.8:1 cup to disc ratio with thin superior and inferior rims in the left eye with corresponding visual field defects. A trabeculectomy with MMC (0.04% for 3 min) was performed using a fornix based conjunctival approach. Wide area application of MMC was performed, precautions were taken to avoid contact of MMC to the conjunctival edges and copious wash was given with ringer lactate after removal of the sponges. A 4 x 4 mm, triangular scleral flap was dissected up to the clear cornea, a 2 x 2 mm deep scleral block was excised and peripheral iridectomy was performed. The scleral flap closure was performed with single 10-0 nylon suture and water tight conjunctival suturing was performed with 8-0 vicryl wing sutures. On postoperative day 1, the visual acuity was 20/200, IOP was 12 mm Hg and there was a diffuse well-formed bleb. One week postoperatively, the bleb was flat, with conjunctiva showing an ischaemic area measuring 3 x 1 mm with surrounding congested conjunctiva (figure 1). The IOP was 6 mm Hg, anterior chamber was shallow, there was minimal flare but no cells and a brisk bleb leak was noted by Seidel’s test.

INVESTIGATIONS
Humphrey visual field in the right eye showed advanced field loss and left showed incomplete biarcuate scotoma sparing fixation.

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DIFFERENTIAL DIAGNOSIS
It would be prudent to rule out ‘Blebitis’ in such a presentation. Blebitis presents with necrotic or ischaemic conjunctiva with surrounding conjunctival and ciliary congestion, which is most intense around the bleb edge. It is usually associated with purulent discharge and chemosis. In severe cases could be associated with anterior chamber reaction including keratic precipitates and hypopyon. When these features are associated with vitreous involvement it is termed as bleb-related endophthalmitis. A positive Seidel’s test is common. In our case, blebitis was unlikely as there were no other signs of periorcular or intraocular inflammation apart from the localised necrotic conjunctiva and bleb leak.

TREATMENT
The patient was continued on topical moxifloxacin 0.5% four times daily, cyclopentolate hydrochloride 1% twice daily and he was also started on a low dose topical steroid, loteprednol etabonate, 1% four times daily (tapered over 4 weeks) along with oral doxycycline 100 mg (Capsule Doxt SL, Dr Reddy’s Laboratories Ltd) twice daily for 2 weeks.

OUTCOME AND FOLLOW-UP
There was improvement in the area of conjunctival necrosis by day 3 after starting doxycycline (figure 2). However, the Seidel’s test was still positive. Hence a large diameter soft BCL (15.5 mm, Plano, Hydrogel BCL from Silk lens manufacturer) was placed and the rest of the treatment was continued. Two weeks later the BCL was removed, the conjunctiva was healthy with no signs of necrosis and the leak had subsided. The slit-lamp photograph at this visit was 12 mm Hg and the visual acuity was 20/100.

DISCUSSION
This case illustrates that an early postoperative bleb leak with conjunctival necrosis following trabeculectomy can be successfully managed with oral doxycycline and BCL. This approach obviates the need for surgical intervention, which would be challenging and likely to compromise long-term bleb function. There is one case report on the utility of oral doxycycline in the management of conjunctival melt 1 month following Ahmed valve implantation with exposed scleral patch graft in an eye with neovascular glaucoma.2

Doxycycline (6 deoxy-5-hydroxytetracycline) is a semi-synthetic tetracycline, a protein synthesis inhibitor and a broad spectrum antibiotic. In a submicrobial dosage (20 mg twice daily), doxycycline is known to exhibit anti-inflammatory and anticollegenolytic properties. It is also used in the management of ocular surface diseases such as recurrent epithelial erosions, rosacea, keratitis sicca, meibomian gland disease and sterile corneal melts.3

Matrix metalloproteinases (MMPs) are a family of zinc dependent extracellular endoproteinases that play a vital role in the wound healing process. MMPs and their specific inhibitors, known as tissue inhibitors of metalloproteinases (TIMPs), are synthesised and secreted locally by tissue cells or by inflammatory cells.4 TIMPs interact with the MMP enzyme and inhibit proenzyme activation and thus regulate MMPs. Doxycycline can differentially inhibit the members of the MMP family, in particular MMP9 activity. MMPs are expressed by fibroblasts and play a role in the degradation of ECM and basement membrane components, tissue remodelling, wound healing and inflammatory and immunological reactions.4 Overexpression of MMPs results in excessive extracellular matrix degradation, leading to tissue destruction. Collagenases and other metalloproteinases require cations (calcium, zinc and magnesium) to maintain their activity, so chelation of these ions could result in the reduced action of these enzymes.4

Doxycycline is best taken on an empty stomach at least 1 h before or 2 h after a meal. Tetracyclines have a high affinity to form chelates with polyvalent metallic cations. Antacids, calcium supplements (including dairy), iron products and laxatives containing these cations interfere with doxycycline absorption. Doxycycline is contraindicated in pregnant women, infants and in children under 8 years of age due to its potential to
interfere with bone and tooth development. It is also contraindi-
cated in people with history of photosensitivity.

The reported adverse effects of doxycycline are gastrointes-
tinal symptoms, nephrotoxicity due to its catabolic effect,
photosensitivity, discoloration of the enamel of teeth and
depression of bone growth. However, our patient did not report
any of these side effects.

We presume that the rapid resolution of the conjunctival
necrosis in our case with oral doxycycline is possibly due to its
ability to inhibit collagenolysis, thereby stopping tissue break-
down and promoting healing. Although long-term usage of
submicrobial dosage of 20 mg twice daily has shown benefit in
conditions like acne rosacea, the dosage and duration of doxy-
cycline use in the treatment of conjunctival necrosis is not clear.

In the report on conjunctival erosion following a glaucoma
drainage implant, the dose used was 100 mg twice daily for
2 weeks followed by once daily for 4 weeks. However, the
rationale for the dose and duration was not mentioned.

Complete resolution of conjunctival necrosis in our case within
2 weeks prompted us to stop doxycycline after 2 weeks. The
BCL helped in the mechanical tamponade and aided in faster
resolution of the bleb leak. In the presence of a bleb leak, the
BCL acts by its mechanical ability to tamponade the area of
aqueous leakage and allows epithelial restoration. Shoham et al
have successfully treated post-trabeculectomy bleb leak with a
large diameter soft contact lens in 22 of 24 patients.

This case illustrates that oral doxycycline is a new addition to
the armamentarium in the medical management of early bleb
leak with conjunctival necrosis following trabeculectomy.

**Learning points**

- An early postoperative bleb leak is a serious
  post-trabeculectomy complication and a high risk of
  suspicion is important for the early diagnosis of this
  complication. Early intervention is warranted in order to
  avoid serious vision threatening sequelae requiring surgical
treatment.
- Conjunctival necrosis following trabeculectomy is rare and
  should be differentiated from blebitis, since the management
  is different.
- Oral doxycycline is a viable alternative in the conservative
  management of conjunctival necrosis.
- A large diameter bandage contact lens is very useful in the
  management of an early postoperative bleb leak.

**Competing interests** None.

**Patient consent** Obtained.

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**REFERENCES**

   erosions with inhibitors of matrix metalloproteinase-9, doxycycline and