

# Subconjunctival bevacizumab and argon laser photocoagulation for preexisting neovascularization following deep lamellar anterior keratoplasty

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We report a rare case of deep anterior lamellar keratoplasty (DALK) neovascularization managed with combination of subconjunctival bevacizumab and argon laser photocoagulation. A 24 year old male underwent Deep anterior lamellar keratoplasty for corneal stromal opacity following presumed viral keratitis. Deep corneal neovascularization was observed postoperatively which was successfully managed using a combination of subconjunctival bevacizumab and argon laser photocoagulation within one week of DALK. The neovascularization resolved by 3 months and at 2 years follow up, patient maintained good visual acuity of 6/12 Snellen's without recurrence of vascularization. A combination of bevacizumab and argon laser may be an effective approach to manage neovascularisation in the immediate postoperative phase (Post DALK) and improve graft survival.

**Key words:** Argon laser photocoagulation, corneal neovascularization, corneal scar, deep anterior lamellar keratoplasty, subconjunctival bevacizumab

Deep anterior lamellar keratoplasty (DALK) has become the mainstay for managing superficial diseases of the cornea such as keratoconus, anterior corneal opacities, and dystrophies causing significant visual impairment.<sup>[1]</sup> Although rejection rates have reduced since the advent of DALK compared to full thickness penetrating keratoplasty, one of the most common risk factors that contributes to corneal graft failure is vascularization of the recipient cornea.<sup>[2]</sup> In addition, lymphangiogenesis has also been shown to accompany angiogenesis and increase the risk of graft rejection.<sup>[3]</sup> Measures to inhibit these responses have been shown to improve graft survival in the past.<sup>[4]</sup> We present a case of corneal vascularization post DALK which

was successfully treated with a combination of argon laser photocoagulation and subconjunctival bevacizumab.

## Case Report

A 24-year-old healthy man presented with history of diminution of vision in his left eye for the past 30 days. On examination, the best corrected visual acuity (BCVA) was counting fingers close to face and slit lamp evaluation revealed a 4×4 mm, oval whitish superficial stromal infiltrate with surrounding scarring and superficial vascularization [Fig. 1a]. Corneal sensations were reduced. He gave history of injury with needle and had undergone corneal scraping elsewhere. The scraping report revealed no organisms on KOH/Grams stain. The lens was relatively clear and ultrasound did not reveal any posterior segment pathology. The right eye was essentially normal. The patient was diagnosed to have presumed stromal viral keratitis and was managed medically with oral acyclovir (400 mg) 5 times in a day for 2 weeks followed by 2 times in a day continued for 1 year and topically with fluorometholone acetate 0.1% eye drops in weekly tapering dose over 4 weeks and carbonylmethylcellulose 0.5% eye drops over 6 months. Preoperative anterior segment optical coherence tomography (AS-OCT) after healing showed central corneal thickness of 420 μ with scar depth of 370 μ [Fig. 1b]. At 1 month, the active keratitis healed with a residual vascularized corneal scar [Fig. 1c].

After 1 year of quiescence, left eye underwent predescemet's DALK. Big bubble DALK was attempted but failed to achieve. The surgery was completed by layer-by-layer dissection manual DALK. On first postoperative day, deep vascularization with lipid keratopathy was seen in the DALK interface [Fig. 1d] and documented using AS-OCT [Fig. 1e]. In view of vascularization, subconjunctival bevacizumab (1.25 mg/0.05 mL) was injected on the third postoperative day followed by argon laser photocoagulation of efferent blood vessels on the seventh postoperative day using 150 mw power, 200 ms duration of exposure, and spot size of 100 to 200 μ [Fig. 1f]. Corneal vessels started regressing within a week and disappeared by 3 months [Fig. 2a]. Patient was then followed up at three monthly intervals for 2 years and alternate suture removal was done at 6 and 9 months follow-up. At 2 years, his BCVA was 6/12 with -2.0 sphere and -3.5 cylinder at 150°. Recurrent neovascularization or lipid keratopathy was not seen again, and there were no recurrence of viral keratitis [Fig. 2b]. AS-OCT at 2 years showed normal graft architecture [Fig. 2c], pachymetry showed a graft thickness of 590 μ and specular microscopy showed a cell density of 1802 cells/mm<sup>2</sup>.

## Discussion

To the best of our knowledge, this is the first report on the successful use of bevacizumab and argon laser applications for the treatment of corneal neovascularization in the graft-host

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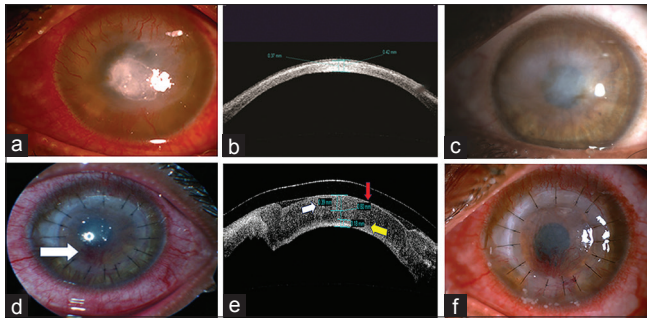
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**Figure 1:** (a) Active viral keratitis; (b) preoperative AS-OCT; (c) healed viral keratitis; (d) post DALK deep vascularization (white arrow); (e) post DALK ASOCT (showing central corneal thickness—red arrow, superficial scar thickness—white arrow, and endothelial bed thickness—yellow arrow); and (f) post argon laser marks

interface post DALK. A single application of this combination therapy lead to complete resolution of neovascularization without recurrence over a 2-year follow-up. Bevacizumab has been used previously in different routes including subconjunctival, topical, and intrastromal for managing corneal neovascularization in humans as well as animal models.<sup>[5-7]</sup> Postulated mechanisms by which bevacizumab inhibits corneal neovascularization include inhibition of smooth muscle cells and pericytes around newly formed vessels and direct inhibition of VEGF (vascular endothelial growth factor) along with VEGFR1 and VEGFR2 receptors.<sup>[7,8]</sup>

Argon laser photocoagulation of corneal vessels has been described previously.<sup>[9]</sup> However, combining it with subconjunctival bevacizumab has been described only once before by Gerten *et al.*<sup>[10]</sup> However, they used this form of treatment in two eyes as a preoperative measure before penetrating keratoplasty. The rationale of combining two anti-angiogenic treatments is to attain additive effect and improve graft survival, with bevacizumab having an immediate effect and the influence of the argon laser coming into effect in a few weeks. In addition, we also believe that the mild but undesirable inflammatory response after argon laser photocoagulation would have been negated by the bevacizumab. Finally, bevacizumab may also play a role in inhibiting corneal lymphangiogenesis and aid in improving graft survival.

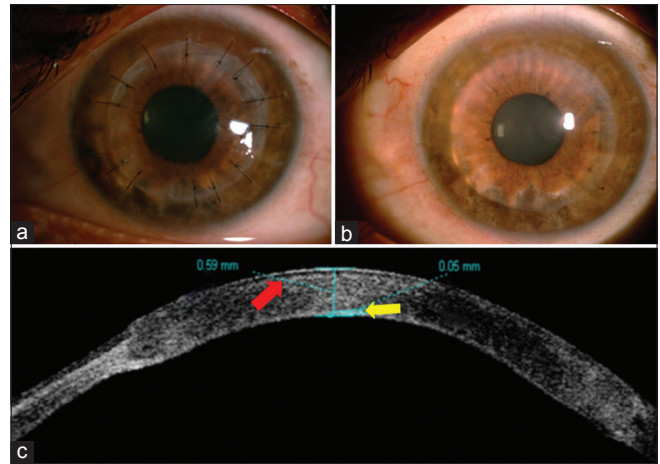
Interestingly, our patient did not require any repeat treatments with either bevacizumab or argon laser over a 2-year period suggesting that there may have been a transient VEGF surge after the DALK procedure as a part of wound healing. Combining therapies may have also lead to excellent resolution with just one injection, a phenomenon often observed in retinal diseases.

## Conclusion

In conclusion, combined bevacizumab and argon laser photocoagulation may be very useful in treating post DALK corneal neovascularization, thereby improving graft survival. However, larger case series are required to confirm these findings.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients



**Figure 2:** (a) 3 months postop with clear interface and no new vessels or lipid keratopathy; (b) 2 years postoperative follow up; (c) AS-OCT showing central corneal thickness—red arrow and faint scar—yellow arrow

understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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