

“Bowman’s layer transplantation –
a new hope for regaining of correct ocular surface.”

Introduction

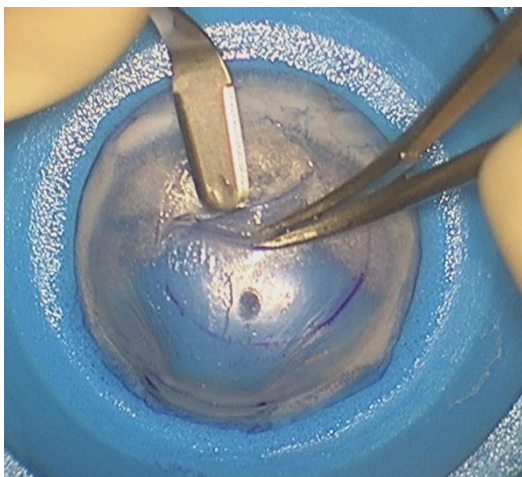
Treatment of corneal ulcers is one of the greatest challenges in ophthalmology. Neurotrophic keratitis (NK) is a corneal degenerative disease, manifested with decreased or even absent corneal sensitivity due to damage of the V cranial nerve, corneal nerve plexus or co-existing chronic metabolic diseases, e.g. diabetes⁽¹⁾. Most untreated NK can lead to decrease in visual acuity or vision lost in some cases. Moreover, NK is also clinically connected with other diseases, such as dry eye disease, decreased frequency of blinking etc. Common treatment of NK comprises mostly conservative methods (lubrication, collagenase inhibitors, therapeutic contact lenses) at the beginning or surgical options, such as tarsorrhaphy, botulinum toxin induced ptosis, amniotic membrane transplantation, autologous conjunctival flap and lamellar or penetrating keratoplasty⁽²⁾. Due to the fact that above mentioned treatment methods do not provide fast recovery in the course of NK, new therapy options are necessary. Selective Bowman's layer transplantation is an innovative surgical treatment applied in advanced neurotrophic keratitis. Acellular structure of Bowman's layer comprises mostly type I, III, V and XII collagen linked up with proteoglycans. Its rigid structure is the most resilient among corneal layers and therefore is physiologically responsible for maintaining the corneal shape. It has been histologically proven that cells of deep corneal epithelial layers are anchored within Bowman's layer⁽³⁾. This provides stability and improves integrity of the corneal surface. Presence of superficial corneal nerve plexus within Bowman's layer provides sensation and trophic factors in anterior corneal layers, which in consequence keeps proper moisturising as well as augments healing processes of the eye surface. Bowman's layer location between corneal epithelium and stroma prevents stromal keratocytes from being exposed to some soluble factors in the tear film, such as epithelial growth factor or factors secreted by autonomic nerve endings in the subepithelial area⁽⁴⁾. Moreover, Bowman's layer acts as a barrier preventing from pathogen penetration or toxin-induced collagen lysis in case of corneal erosions. It is well documented that prolonged exposure to chemical and neurotrophic agents leads to Bowman's layer damage followed by ulcer progression. Taking histological structure and crucial functions of Bowman's layer in stabilisation of the eye surface into account, it can be assumed that its selective transplantation seems to be beneficial in cases of NK.

Case presentation with illustrations and figures

The paper presents the technique and outcomes of selective transplantation of Bowman's layer in patients with neurotrophic keratitis. In brief, Bowman's layer graft preparation starts with placing the donor cornea on an artificial anterior chamber followed by corneal epithelium removal. Surface of the Bowman's layer is then stained with trypan blue solution and planned margins of the graft are incised slightly with a corneal trephine and a crescent knife. The incised Bowman's layer rim is inverted and pulled with a McPherson forceps tangentially to the corneal surface. Underlying stroma is at the same time gently pressed by crescent knife (Fig. A). After successful excision, the Bowman's layer is placed in BSS, where it starts to roll toward the stromal side. The no stitch flap technique of Bowman's layer grafting is achieved by creation of a corneal subepithelial „pocket” around a corneal ulcer in the recipient's cornea (Fig. B). When the proper size of graft is achieved, margins of Bowman's layer are then slipped into the corneal „pocket”. The presented way of tissue transplantation stabilises Bowman's layer in the recipient's cornea with no need of suturing. Once Bowman's layer is introduced in the recipient's cornea, it can be covered with a contact lens.

The presented data illustrate the results obtained in 3 consecutive patients suffering from NK and treated with selective Bowman's layer transplantation in the Department of Ophthalmology.

A.



B.

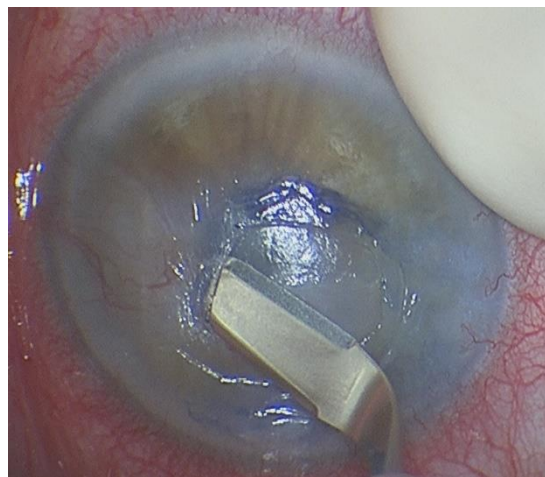


Figure A: Peeling of Bowman's layer. The inverted flap is pulled backwards tangentially, stroma is pressed with a crescent knife simultaneously.

Figure B: Creation of subepithelial corneal “pocket” in the recipients cornea for placement of tailored Bowman's layer graft.

Case 1

A diabetic, female suffering from neurotrophic corneal ulcer in the course of viral keratitis in her left eye presented significantly decreased visual acuity (to counting fingers) and hypoesthesia around the area of ulceration in the affected eye. A slit-lamp examination (Fig. C) and OCT scans (Fig. E) revealed a paracentral corneal ulcer with corneal pachymetry diminished to 309 μm within its central part and 640 μm in its margins. Ulceration was covered partially by fibrovascular changed tissue. Postoperatively corneal transparency improved significantly in the short period of time (Fig. D). Corneal oedema around the ulcer decreased to 420 μm in 3 months after surgery. Stromal restoration and re-epithelialisation were observed in the area covered with transplanted Bowman's layer (Fig. F). Visual acuity increased gradually to 0.4 within 6 months postoperatively. Esthesiometrically proved corneal sensation was detected close to the corneal ulcer margins.

C.



D.

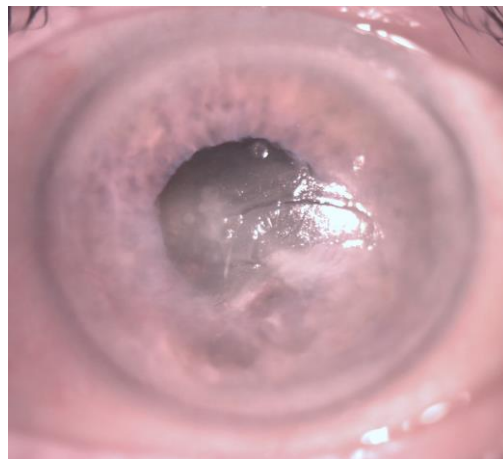
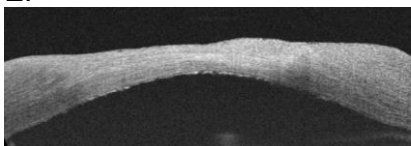


Figure C: Preoperative photography shows corneal ulceration in the inferior-temporal cornea.

Figure D: Photography obtained 6 months postoperatively - Bowman's layer fitting in the recipient bed with visible epithelialisation.

E.



F.

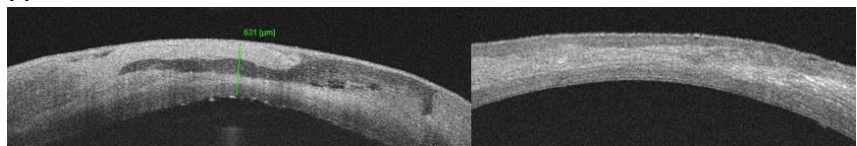


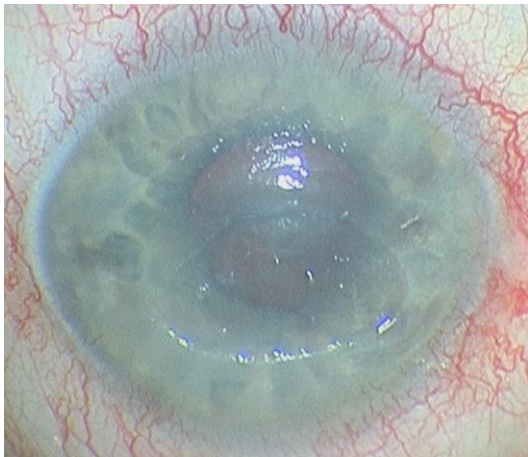
Figure E: Preoperative OCT scan presenting corneal thinning.

Figure F: 2 OCT scans obtained on 14th day and 6th month postoperatively show increase in corneal thickness with restoration of corneal stroma and complete re-epithelialisation.

Case 2

A 50-year-old patient presented with neurotrophic corneal ulcer (Fig. G) due to recurrent, viral keratitis. Lack of corneal sensitivity was confirmed esthesiometrically on the whole corneal surface. OCT scans revealed elevated, oedematous corneal epithelium covering corneal ulcer and significant thinning of the remaining corneal stroma (Fig. I). The performed selective Bowman's layer grafting was completed with removal of degenerative epithelium. Postoperatively, a correct adhesion of the graft was observed (Fig. H). Two weeks postoperatively the central corneal thickness decreased from its preoperative level of 700 μm to 305 μm . OCT scans confirmed intensive epithelialisation and stromal restoration (Fig. J). The results remain stable with visual acuity improvement from hand movement preoperatively to 0.2 up to 3-month follow-up.

G.



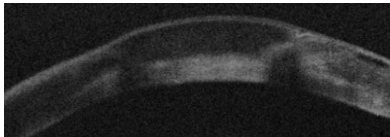
H.



Figure G: Appearance of corneal ulceration due to neurotrophic keratitis.

Figure H: Corneal picture obtained 3 months after selective Bowman's layer transplantation – complete epithelialisation and partially improved thickness of corneal stroma.

I.



J.

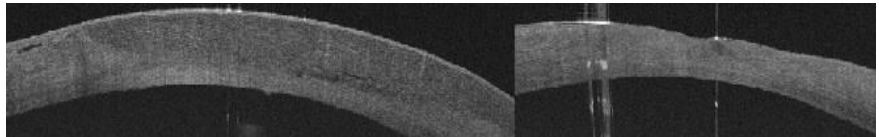


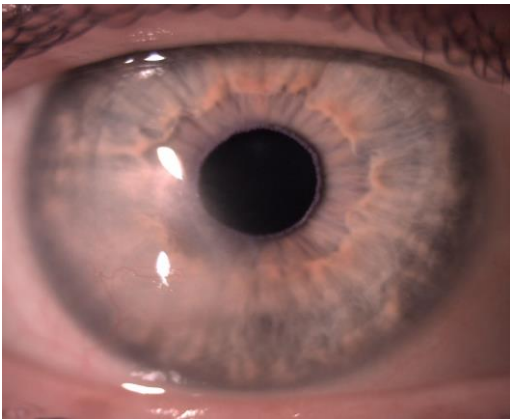
Figure I: Preoperative OCT scan - subepithelial cyst, oedema of the anterior stroma and increased corneal thickness.

Figure J: 2 postoperative OCT scans obtained on 14th day and 3rd month - gradual stromal restoration and signs of epithelialisation.

Case 3

A 35-year-old woman was admitted to the hospital due to painless decrease in visual acuity and a corneal ulcer. Medical history revealed long time intake of tetryzoline containing eye drops for cosmetic reasons. A slit-lamp examination (Fig. K) and OCT scans (Fig. M) revealed a wide diameter of the corneal ulceration with stromal thinning to 265 μm . The ulceration was partially covered by thickened, opaque epithelium. Corneal sensitivity was absent in both eyes despite the eyedrops withdrawal. Significant changes in the tear film secretion and decreased TBUT were also noted. The patient was diagnosed with toxic neurotrophic keratitis and planned for selective Bowman's layer transplantation. In the postoperative period a proper adhesion of the transplanted Bowman's layer to the corneal stroma was observed. Partial restoration of corneal stroma and proper epithelialisation were observed in the follow-up (Fig. L, N). Corneal thickness increased to 580 μm within the next 3 months with gradual improvement in visual acuity from 0,4 to 0.9. The corneal sensation was still absent.

K.



L.

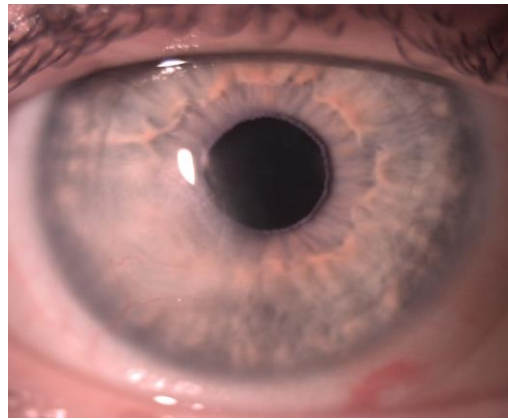
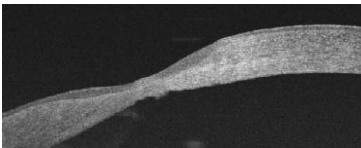


Figure K: Huge area of corneal ulceration due to toxic neurotrophic keratitis.

Figure L: Picture of the eye surface obtained 3 months after selective Bowman's layer transplantation - restoration of stroma and correct corneal surface were observed.

M.



N.

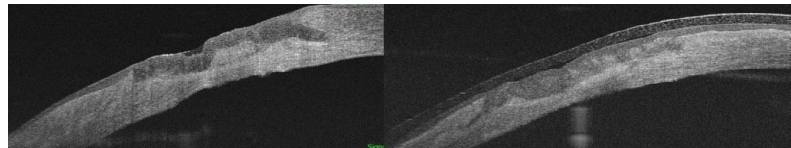


Figure M: Preoperative OCT scan shows corneal thinning to 265 μm .

Figure N: 2 OCT scans taken on 14th day and 3rd month postoperatively – good adaptation of

transplanted Bowman's layer to recipient bed with gradually increased corneal thickness.

Discussion

Selective Bowman's layer transplantation presented by the author is a novel surgical method among corneal transplantation procedures in the treatment of neurotrophic corneal ulcers. Based on presented herein cases, the technique demonstrates a high success rate. Common postoperative observations reveal significant and fast corneal epithelialisation as well as restoration of stroma. Despite being a sutureless procedure, the transplanted Bowman's layer is properly stabilized within subepithelially created pocket, preventing additional suture-related complications, such as infections, neovascularisation or graft rejection. Postoperative pharmacotherapy comprises topical steroid and antibiotic treatment, however it is less intensive and tapered quicker compared to a standard corneal grafting. My observations allow to point out that the procedure promotes regeneration of corneal stroma and epithelium by providing a healthy, fully developed selective Bowman's layer, which has been damaged in the course of neurotrophic/degenerative processes. Physiological location of the superficial corneal nerve plexus at the level of Bowman's layer may suggest its important role as a framework for corneal nerve bundle regeneration⁽⁵⁾ followed by restoration of corneal sensitivity postoperatively (unpublished data of the author). From the immunological point of view, acellular structure of Bowman's layer potentially does not activate immune reactions, which results in a low risk of graft rejection and has an advantage over traditional allogenic keratoplasties in such cases. The presented procedure of selective Bowman's layer transplantation does not require sutures to stabilise the graft. Moreover, restored continuity of Bowman's layer after its transplantation creates a tight barrier preventing from corneal damage caused by infectious pathogens or toxins.

Conclusion

Thanks to unique features of Bowman's layer, the novel technique of selective corneal grafting presented here seems to be an interesting and innovative treatment option in neurotrophic keratitis. Further studies are needed to expand our clinical observation and to ensure whether corneal regeneration and neuroregeneration mechanisms progress.

References

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