CASE REPORT

In Vivo Corneal Confocal Microscopy: Pre- and Post-operative Evaluation in a Case of Corneal Neurotization

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ABSTRACT

In this report, we analyse the pre- and post-operative corneal changes observed using in vivo confocal corneal microscopy in a patient with neurotrophic keratitis submitted to a corneal reinnervation surgical procedure. We describe favourable trophic changes observed at different levels of the patient's cornea, particularly in the sub-basal nerve plexus; complete absence of these neuro-logical structures was observed before surgery, but appeared largely restored six months thereafter.

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Introduction

Corneal anaesthesia is a very harmful condition that encompasses a high risk of deleterious injury to the cornea. In recent years a new corneal reinnervation procedure has been described. This procedure uses a contralateral- and uninjured-trigeminal branch that acts as an axon donor in order to reinnervate the affected cornea. Herein we report a case successfully treated using this technique.

Case report

An 11-year-old girl of white European heritage underwent neurosurgery following acute haemorrhage associated with a pontine cavernoma in 2014. At presentation in our department two years later, she was tetra-paretic, and had (1) left facial palsy; (2) complete left trigeminal anaesthesia including the cornea; (3) consequent severe neurotrophic keratitis (NK) affecting the left eye; (4) cerebellar nystagmus; and (5) ophthalmoplegia consistent with one-and-a-half syndrome. At the initial examination performed within our department, visual acuity was 20/20 in the right eye (RE) and 20/400 in the left eye (LE). Biomicroscopy was normal for the RE, while NK grade I-II³ was evident in the LE, with ulcers of

different size, depth and age, together with leukoma and thinning of the cornea. Ocular tension was 12 and 10 mmHg in the RE and LE, respectively. Funduscopic examination was normal bilaterally.

A facial re-innervation procedure had already been performed at the age of 13. Although successful at restoring active facial movement, complete eye occlusion and secondary corneal protection were not achieved following this procedure. The NK also was treated unsuccessfully with artificial tears, lubricants and ointments. Consequently, considering the risks of corneal perforation, a corneal neurotization (CN) procedure was deemed indicated when the patient was 14-years-old.

In the literature, CN had been described for the surgical treatment of NK^{1,2} and the reported results were encouraging. A termino-terminal anastomosis between the contralateral supraorbital nerve and the left cornea using an interposed sural nerve graft (obtained from the patient's right leg) was performed. We preferred to use the supraorbital nerve as donor nerve rather than the supratrochlear (as reported by others) because the former is a more powerful donor that contains a greater number of axons: furthermore its use does not necessitate a significantly longer nerve

graft. We chose the sural nerve as the graft which is by far the most frequently used nerve graft in the literature. Other satisfactory donor nerves can be used, i.e., the great auricular nerve, but the harvesting of this nerve implies a more exposed scar in the neck, in comparison to the relatively hidden location of the sural nerve at the distal lower limb.

The sural nerve was distributed around four quadrants of the perilimbal subconjunctival space, according to the previously described technique (Figure 1). The surgery was well tolerated and no complications were observed, except for transient forehead anaesthesia on the right side after sectioning of the supraorbital (axon donor) nerve, which persisted for three months. Follow-up then was done with *in vivo* confocal corneal microscopy (IVCCM) of both eyes on postoperative weeks 4, 8, and 24 (HRTII/Rostock Corneal Module, <https://business-lounge.heidelberg-engineering.com/int/products/hrt/#Rostock-Cornea-Module>).

Preoperative IVCCM allowed for visualization of a very severe deficit of the sub-basal neural plexus, the corneal epithelium and stroma, and the corneal endothelium in the LE relative to the normal RE. The affected epithelial changes

included volume-incremented cells, organized in blocks, which were fragmented. Probably the most eloquent finding in the preoperative IVCCM was the predominance of dendritic cells (DC) at the sub-basal level and corneal stroma in the LE, indicating a pathological cell immunity reaction.^{3–5} Starting at eight weeks postoperatively, and definitely evident at 24 weeks, IVCCM images demonstrated a gradual increase in nerve sprouts, along with clinically relevant improvement in the trophic state of the left cornea at different levels. At 24 weeks, clear epithelial and stromal improvement was observed, though the appearance of the endothelium failed to exhibit clear changes. Of note, the preoperative pathological finding of dendritic formations had almost disappeared at 24 weeks. It is hypothesized that recovery of the local immune response mediated by corneal re-innervation was directly related to this change (Figure 2). These objective corneal innervation changes were accompanied by a clear subjective reference of sensation recovery referred by the patient, which started at 12 weeks.

Fung *et al.*⁶ have recently presented two cases of CN: in the first case, IVCCM was used preoperatively, but the only absence of the nerve plexus was mentioned; no preoperative use of IVCCM was described for the second patient. The originality of the present report is that it contains a complete preoperative description of the corneal status, followed by a thorough exposition of the trophic changes at different postoperative periods employing IVCCM.

In conclusion, in this report, we describe a 14-year-old girl with NK, we show the absence of the corneal nerve plexus preoperatively; its re-appearance posteriorly (8 weeks); and disappearance of the DC and favourable trophic changes after surgery. Visualisation of these changes was aided by IVCCM, something not reported previously in the literature. IVCCM has been shown to be a non-invasive, reproducible, and highly accurate tool to evaluate the cornea at a cellular level. We strongly recommend using IVCCM for pre-operative evaluation and post-operative follow-up in patients undergoing CN surgery.

Figure 1. In our patient, the left cornea was denervated, so we decided to perform a re-innervation procedure. We used the (normal) right supraorbital nerve as the donor (a), sectioning the nerve distally to the supraorbital notch, and suturing it to a cable graft harvested from the lower limb (sural nerve, B), which was transposed subcutaneously to reach the affected (left) cornea. This nerve was distributed around four quadrants of the perilimbal subconjunctival space.

Figure 2. (a) Right Eye (RE) and Left Eye (LE) *in vivo* confocal corneal microscopy IVCMM images of the cornea pre-operatively (week zero). Altered epithelium in the LE, accompanied by hyper-reflective metaplastic cells, are seen, relative to the RE; the presence of abundant dendritic cells in the LE contrasts with their scarcity in the normal RE. The absence of a sub-basal neural plexus in the LE is apparent, versus the normal appearance on the right. Activated keratocytes are present, on the left, of abnormal size and intercellular spaces, again relative to the RE. Endothelial polymegathism is present in the LE. (b) Post-operative changes in the LE at week 8 (8 wk) and week 24 (24 wk) include improved epithelium with mild superficial metaplasia, as well as a clinically relevant decrease in dendritic cell numbers and a dramatic improvement at the sub-basal neural plexus level, including a great number of new nerves. Keratocyte appearance also is improved, including the presence of activated cells. Polymegathism is still present in the endothelium. (c) Presence of performant nerves (solid white arrows) in the RE. (d) Performant nerves (empty white arrows) in the LE are almost absent preoperatively. (e) New performant nerves seen in the LE at week 8 postoperatively (solid white arrows).

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Declaration of interest

The authors have no conflict of interest.

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