



Healing of neurotrophic corneal ulcer with autologous serum eye drops

Ahmed ALAMI^{1*}, Amine BENJELLOUN², Mohamed KRIET³, Karim REDA⁴, Abelkader LAKTAOUI⁵, Abdelbaare OUBAAZ⁶

¹Ophthalmology unit, 3rd Military Hospital, Laayoune, Morocco.

²Pulmonology unit, Avicenne Military Hospital, Marrakech, Morocco.

³Ophthalmology unit, Avicenne Military Hospital, Marrakech, Morocco.

⁴Ophthalmology unit, Ophthalmology unit, Mohammed V Military Hospital, Rabat, Morocco

⁵Ophthalmology unit, Moulay Ismail Military Hospital, Meknes, Morocco

⁶Ophthalmology unit, Ophthalmology unit, Mohammed V Military Hospital, Rabat, Morocco

ABSTRACT

Neurotrophic keratitis results from complete or partial denervation of the cornea and can be complicated by chronic ulceration with the risk of perforation. The etiologies are diverse. We report the case of a neurotrophic ulcer secondary to complete corneal denervation by lesion of the fifth cranial pair with total regression under autologous serum eye drops. Such eye drops are easy to prepare, but their use exposes to the risk of infection, which can be reduced by complying with the rules of use.

Keywords: Neurotrophic ulcer; Fifth cranial nerve; Autologous serum eye drops.

INTRODUCTION

Neurotrophic keratitis is a chronic degenerative affection of the corneal epithelium characterized by a delay in epithelial healing, which can be complicated by stromal involvement or corneal perforation. Etiologies are numerous and the management usually difficult.

We report the case of a patient with a chronic neurotrophic ulcer secondary to a damage on the fifth cranial pair, completely healed by autologous serum eye drops.

MATERIALS AND METHODS

Case report:

A 41 year-old woman teacher, consulted for a binocular diplopia and redness of the left eye. On examination, we found a paralytic strabismus of the left lateral rectus muscle associated with a binocular diplopia. The examination of the left eye found a 10 /10 conserved far visual acuity, a

normal pressure and a diffuse superficial punctuate keratitis (SPK) associated with meibomitis at the biomicroscopic examination. The examination of the right eye only found a meibomitis. The proposed diagnosis was: ophthalmic dryness secondary to a blepharitis. A treatment with azithromycin eye drops (2 instillations per day for 3 days), artificial tears (6 instillations per day) and vitamin (A) ointment in the evening were prescribed. Then the patient was oriented for the exploration of her paralytic strabismus (cerebral MRI, Lancaster test, neurological consultation) but she was then lost sight of.

Three months later, she came back for a drop in the visual acuity of her left eye associated with redness and ocular photophobia. She said, she was followed by a neurosurgeon after the discovery at MRI of a meningioma of the left cavernous sinus (Fig. 1), with the involvement of the left nerve VI, treated with radiotherapy. She was then followed by an ophthalmologist for redness and photophobia in her left eye treated as viral keratitis by anti-herpetic treatment (acyclovir ophthalmic ointment for 7 days, prolonged for 3 days) , Tobramycin 0.003 eye drops (4 instillations per day) and eye wash with physiological serum. The keratitis worsened despite this treatment.

On examination, we found visual acuity at 8/10 with persistent paralytic strabismus. The biomicroscopic examination showed a total corneo-conjunctival anesthesia and an ulcer involving the anterior third of the stroma. The ulcer was 3 mm long, oval-shaped, long horizontal, fluo (+) with epithelial margins and edematous epithelial banks that tend to curl; it was surrounded by a stromal edema. (Fig 2.3). The corneo-conjunctival anesthesia was associated with anesthesia of the left hemiface secondary to the involvement of the homolateral nerve V.

The diagnosis of a neurotrophic ulcer secondary to the involvement of the nerve V was made and the patient was treated with hyaluronic acid (6 instillations per day), vitamin (A) ointment (3 applications per day) and ocular occlusion by an eye wash.

After a one month treatment, the ulcer showed no objective improvement. Unfortunately, ReGeneraTing Agent (**RGTA**) eye drops are not available in Morocco, we therefore opted for autologous serum eye drops.

After the agreement of the patient; autologous serum eye drops were prepared in the hospital laboratory. The reconstitution of the solution is carried out after dilution with physiological saline. This dilution makes it possible to obtain a 20% solution of autologous serum.

The administered dose is six instillations per day during the first two days and then four instillations per day. The patient refused ocular occlusion, we therefore opted for a therapeutic lens as ocular dressing.

The patient was advised that in case of infection signs (redness, secretions, loss of vision, pain), she had to stop instilling the eye drops and go back as soon as possible to the consultation.

In only one week we observed a spectacular resolution of the ulcer, leaving only superficial punctuate keratitis (Fig. 4). The eye drops were maintained at four instillations per day.

At the 15th day control, we observed a total resolution of the ulcer, leaving regular epithelial scarring (Fig. 5, 6).

The autologous serum instillation was stopped and replaced with hyaluronic acid (six instillations per day) with the maintain of the therapeutic lens.

The state of her ocular surface remained stable at one month with no ulcer relapse (Fig. 7)

We then took off the therapeutic lens and the patient was kept under hyaluronic acid treatment(4

instillations per day).

The surgery of strabismus will be postponed after the complete cure of its tumor and after a six month lull period.

RESULT AND DISCUSSION

Neurotrophic keratitis resulting from complete or partial denervation of the cornea can be complicated with chronic ulcer with risk of perforation.

It is of various etiologies, mostly viral. In our patient, the neurotrophic ulcer was discovered when the fifth homolateral cranial pair was involved in a meningioma of the cavernous sinus on the same side. The nerve V denervation of the cornea caused an epithelial involvement (SPK).

Three factors of worsening were noticed in this situation:

- Diagnosis delayed twice (dry eye and then viral etiology);
- Secondary aggravation of keratitis by radiotherapy of the tumor, toxicity of applied eye drops preservatives and dry eye;
- The presence of classical gravity factors in corneal ulcers (reaching the posterior third of the stroma, a dimension greater than 3 mm, a localization in the central 3 mm).

This is why we put the patient under high dose of wetting agents and an ocular occlusion.

Given the inadequacy of this first level and the unavailability of RGTA eye drops in Morocco (recommended in this type of ulcer (3)), we opted for autologous serum eye drops.

This product is currently the only way to bring growth factors to the ocular surface (1). Several growth factors have demonstrated positive effects on epithelial scarring, including EGF (Epithelial Growth Factor) and NGF (Nerve Growth Factor) (2)

The autologous serum treatment provides growth factors and vitamin factors with beneficial effects on the ocular surface. It is sometimes the only solution found to avoid the perforation of certain neurotrophic keratitis (1).

The preparation of autologous serum eye drops is simple: We take a blood sample from the patient. After centrifugation, the reconstitution of the solution is carried out after dilution with physiological saline. This dilution makes it possible to obtain a 20% solution of autologous serum.

Some rules of use are necessary (1):

- Confirmation of sero-negativity for hepatitis B and C viruses and the AIDS virus;
- The elimination of certain systemic diseases because of the risk of perforation under the effect of an essential complement of keratolysis in certain rheumatoid arthritis.
- Putting the solution into sterile, opaque drops (for the proper preservation of vitamin factors), stored in the freezer, except the vial in use which must be stored in a refrigerator;
- Each vial should not be used for more than 10 days;
- The cessation of instillations in case of infection signs (redness, secretions, loss of vision, pain).

The main problems related to the use of autologous serum are the infectious risk and the absence of law regulation (1).

In the case of a chronic neurotrophic ulcer, a blepharography or tarsorrhaphy is usually proposed. Such a solution was completely rejected by the patient. That is why we opted for a therapeutic lens which remains an effective way by acting as a dressing and / or as a reservoir of topical treatment.

CONCLUSION

Autologous serum eye drops remain an effective means of treating neurotrophic ulcers. Its use requires the respect of the prescription rules to minimize the infection risk and a forensic regulation.



Figure 1: Cerebral MRI, axial section showing the presence of a meningeoma of the left cavernous sinus with a sellar extension.



Figure 2.

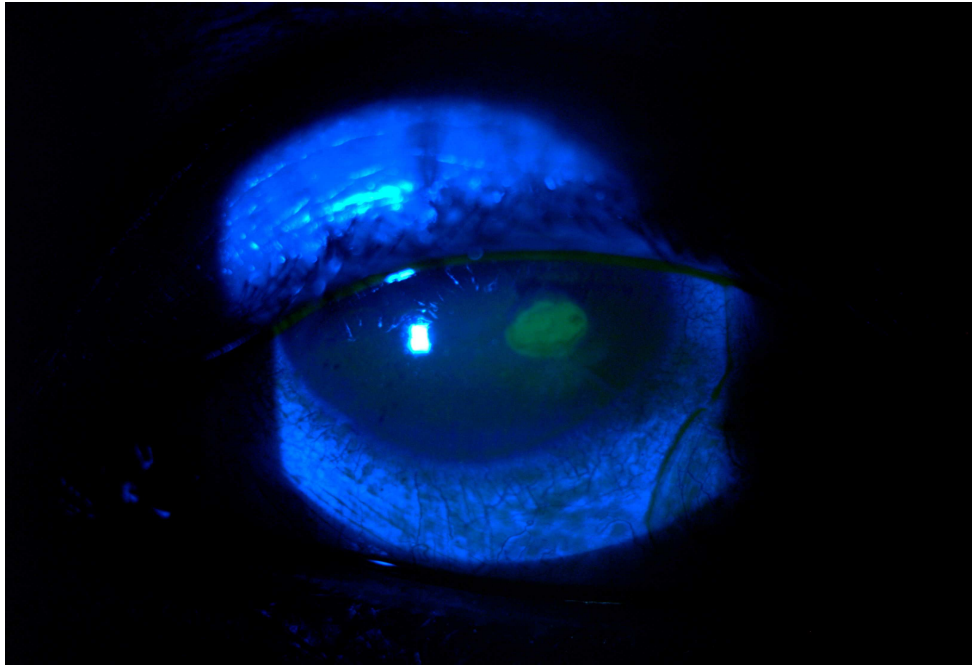


Figure 3:

Figure 2.3: Neurotrophic ulcer in the central region of oval shape, long horizontal axis, fluo (+) with epithelial margins and edematous epithelial banks that tend to curl; it was surrounded by a stromal edema

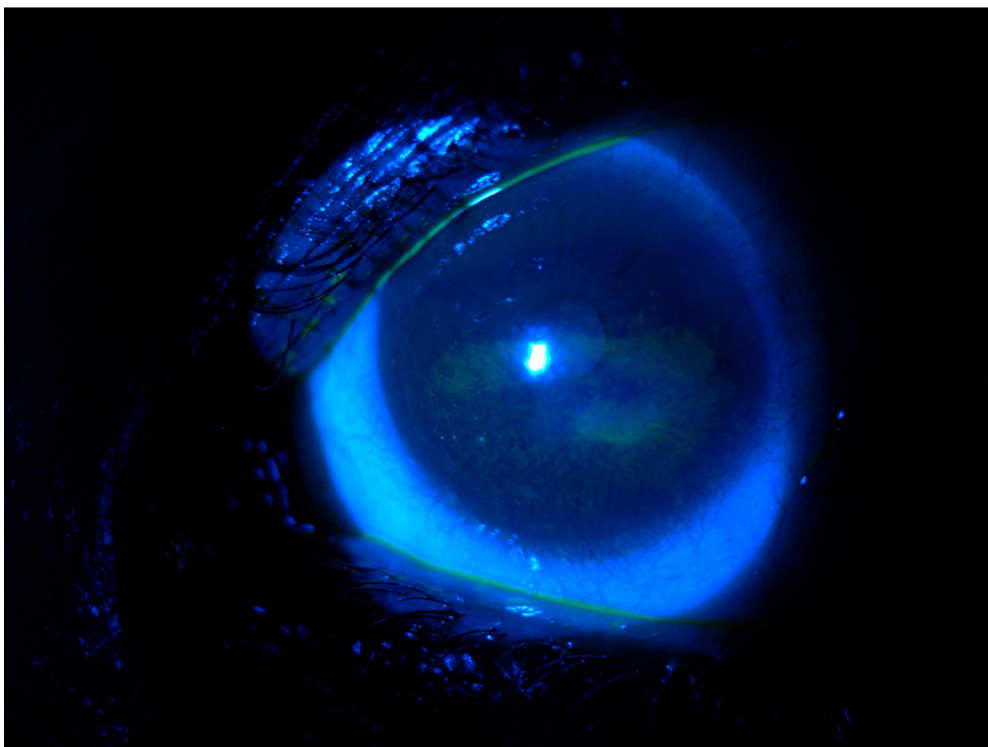


FIG. 4: On the seventh day of instillation of eye drops with the autologous serum: complete regression of the neurotrophic ulcer leaving only a band of superficial punctate keratitis



Figure 5

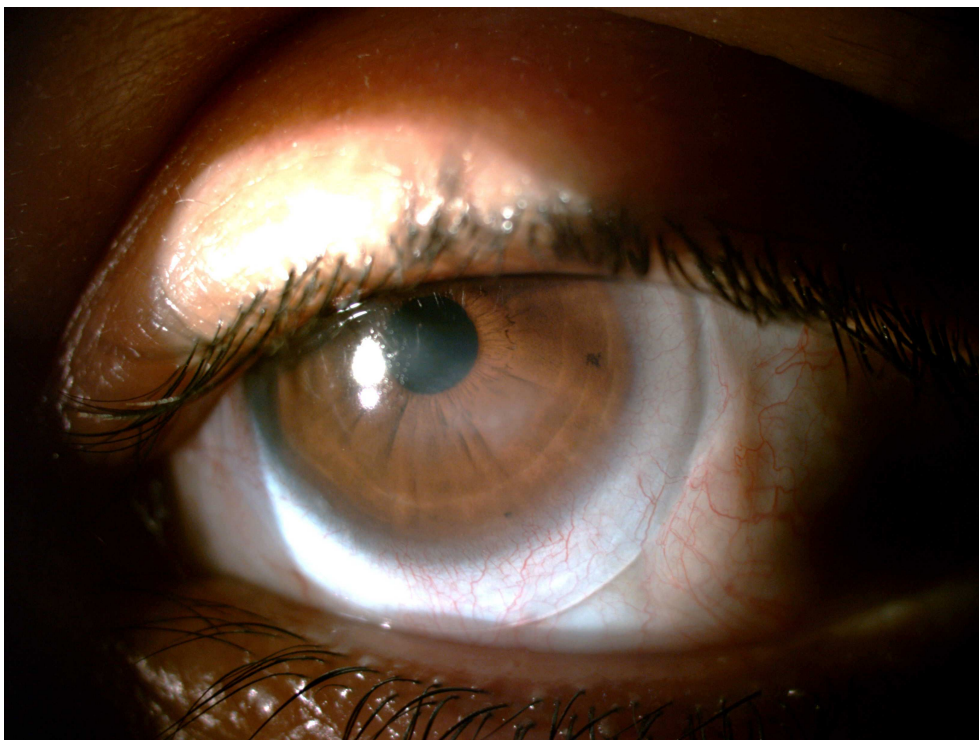


Figure 6

Figure 5.6: The 15th day of autologous serum eye drop instillation: we observe a total resolution of the ulcer leaving regular epithelial scarring.



Figure 7: Control of one month: total cure of the neurotrophic ulcer.

REFERENCES

- [1] Catherine Creuzot-Garcher. collyre au serum autologue N°133 - Tome 15 - mars **2010** - RéfleXions Ophtalmologiques.
- [2] Bonini S, Lambiase A, Rama P, et al. Topical treatment with nerve growth factor for neurotrophic keratitis. *Ophthalmology* **2000**;107(7):pp 1347-51; discussion 51-2.
- [3] Pison A, Feumi C, Bourges JL. Healing of a resistant neurotrophic corneal ulcer using a new matrix therapy agent. *J Fr Ophtalmol.* **2014**;37(7):pp 101-4.