Cyclosporine 0.1% (Ikervis®) as a corticoid-sparing agent in Lyell syndrome with KeraClear® keratoprosthesis

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Abstract:
Cyclosporine 0.1% was used in a patient with Lyell syndrome, which had undergone a KeraClear® keratoprosthesis implant due to the severe ocular involvement to avoid overuse of corticoid agents. To the best of our knowledge, this is the first reported case of cyclosporine 0.1% eye drops to use in Lyell syndrome previously treated with keratoprosthesis implant.

Keywords: Cyclosporine 0.1%, KeraClear, keratoprosthesis, Lyell syndrome

Introduction
Lyell syndrome or toxic epidermal necrolysis is a rare idiosyncratic hypersensitivity reaction being bullous cutaneous lesions, mucositis, and conjunctivitis its main clinical manifestations. In most cases, it is associated with drug intake.[1,2]

Ophthalmological symptoms may lead to corneal blindness for which numerous therapeutic options have been described, although not satisfactory in many cases. KeraClear® keratoprosthesis, an episcleatal prosthesis that is implanted into a stromal pocket, is part of the available therapeutic spectrum.[3] being our patient the first one suffering from Lyell syndrome with ocular involvement in whom a KeraClear® keratoprosthesis was implanted. However, how can we avoid fibrinous reactions from taking place once the prosthesis is implanted?

Case Report
A 39-year-old Caucasian male was referred to our ophthalmology department after Lyell syndrome diagnosis secondary to ibuprofen intake 24 months ago, for which he was hospitalized for over 3 months. Severe ocular and esophageal sequelae remained after the acute episode.

Slit-lamp examination showed symblepharon, trichiasis, and conjunctivalization and neovascularization of the cornea affecting both eyes, which impeded the anterior chamber and fundus examination [Figure 1a]. Visual acuity was light perception. Ocular motility was significantly reduced due to fibrinous adherence.

As topical steroids and previous surgical interventions (oral mucosa grafting) had failed to stop conjunctivalization and neovascularization and graft rejection risk is

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very high in this type of disease, we decided to implant a KeraKlear® keratoprosthesis in his right eye to restore vision. A stromal pocket was created after intensive debridement to place the epidescement prosthesis, and symblepharon half rings were used to aid fornix reconstruction.

Follow-up reviews after keratoprosthesis implantation showed no signs of extrusion [Figure 1b]. However, although mechanical debridement was daily carried out associated with topical steroids and anti-glaucomatous eye drops, extensive pseudomembranous conjunctivitis affecting the patient’s ocular surface appeared. Symblepharon half rings were removed, and a conformer covering the prosthesis was placed instead to avoid new conjunctivalization and further symblepharon formation.

The conformer was again not enough to avoid fibrosis and conjunctivalization of the patient’s ocular surface [Figure 1c], being the risk of surgical failure very high as if the fibrinous reaction consolidated it would cover the prosthesis’s optic area.

We then decided to use out-of-label 0.02% mitomycin C, which we applied twice using impregnated sponge spears. Mitomycin C use slowed down pseudomembrane’s formation and improved ocular motility as new adherences were not being formed [Figure 1d]. However, after having undergone so many procedures to stop fibrinous reactions from taking place, we did not consider abandoning anti-inflammatory medication, and we decided to use cyclosporine 0.1% (Ikervis®) eye drops as corticoid-sparing agents once a day. Topical steroids were tapered down over a period of 4 weeks after introducing cyclosporine 0.1%. Eight weeks after their use, ocular inflammation and fibrin formation are stabilized for the first time since the process began [Figure 2].

**Discussion**

Cyclosporine is an immunosuppressant agent that prevents T-cell immunity activation[4] and its use in ophthalmology has been described in inflammatory diseases such as dry eye disease.[5]

Its use in toxic epidermal necrolysis has been mostly described when administered orally, has shown to increase survival rates.[6] However, its role in controlling ophthalmological symptoms has been reported to a lesser extent in medical literature, focusing on its role in acute inflammation[4,7] (showing promising results) and not as a long-term treatment.

We decided to use cyclosporine 0.1% in our patient as after so many therapeutic options had failed due to excessive fibrinous reactions taking place, we considered that long-term management of ocular surface inflammation was fundamental. Steroid eye drops would be the best option to minimize the high relapse risk, but continuing their use would mean high intraocular pressure (IOP) and optic nerve damage.

It is important to take into account that IOP is very difficult to measure in patients with keratoprosthesis being fundus examination as well as digital palpation of IOP of extreme importance in these cases. However, digital palpation is inaccurate, and waiting for optic nerve damage to take place means irreversible vision loss taking place. Therefore, the use of corticoid-sparing agents such as cyclosporine could aid surface inflammation control without rising IOP, which is difficult to monitor in these patients. The fact that corticoid-induced elevations of IOP cannot be easily examined in keratoprosthesis users makes it of extreme importance to avoid or reduce long-term corticoid use in these patients and associate

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**Figure 1:** Right eye with severe ocular involvement. (a) Decreased eye-opening and extensive corneal neovascularization, conjunctivalization, and symblepharon have shown with fluorescein stain. (b) Eye-opening and ocular surface improvement after KeraKlear® keratoprosthesis implant. (c) Conformer over keratoprosthesis with fibrinous reaction reappearing and decreased eye-opening due to the formation of new adherences. (d) Ocular surface improvement after mitomycin use

**Figure 2:** Stabilization of fibrin formation 8 weeks after starting topical cyclosporine
their use to anti-glaucomatous eye drops whenever possible.

In addition, it is also very important to take into account the inflammation that we are triggering due to the manipulation of the patient’s eye. This is why we decided to use KeraKlear® keratoprosthesis in this patient, as it is an epidescement prosthesis that does not need to associate a corneal graft as other prostheses do, meaning less manipulation, and hence less induced inflammation.

To the best of our knowledge, the use of topical cyclosporine 0.1% as a long-term corticoid-sparing agent in patients with Lyell syndrome and KeraKlear® keratoprosthesis implant has not been previously reported.

The importance of reporting this case relies on the fact that new therapeutic options have to be explored to manage different forms of corneal blindness, for example, in patients with severe ocular involvement secondary to Lyell syndrome due to the high rates of therapeutic failure.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal the identity, but anonymity cannot be guaranteed.

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Conflicts of interest
The authors declare that there are no conflicts of interests of this paper.

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