• Letter to the Editor •

Intracameral 5-fluorouracil and viscous dispersive viscoelastic for diffuse epithelial downgrowth management in aphakia

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Dear Editor,

I am Dr. Santiago Montolío-Marzo from FISABIO Oftalmología Médica, Valencia, Spain. I write you to present a case report of epithelial downgrowth in an aphakic patient.

Intracameral epithelial downgrowth is one of the most feared complications in cases of penetrating ocular trauma or recurrent ocular surgeries. Its progress can affect all the ocular structures, giving rise to corneal decompensation, retinal detachment, difficult-to-treat glaucoma or phthisis bulbi and many cases end in enucleation[1]. Fortunately, the incidence of this condition is very low, there being between 0.08% and 0.12% after cataract surgery and 0.25% after penetrating keratoplasty. Its infrequency means that scientific evidence is reduced to case series and the opinions of experts without there being a homogeneous criterion to guide the work of the doctor in charge. For these reasons, epithelial downgrowth is still a diagnostic and therapeutic challenge.

CASE REPORT

Here we present the case of a 73-year-old man with epithelial downgrowth in his only eye. The patient was referred to our center due to retinal detachment and corneal decompensation of the left eye. His visual acuity was hand movements. His medical history presented complicated phacoemulsification surgery (postoperative aphakia and areflexic mydriasis), repeated surgery for Seidel positive in the main incision and secondary glaucoma with superior temporal Ahmed valve implant. His other eye suffered ocular trauma and he used a prosthesis. We performed pars plana vitrectomy with temporal keratoprosthesis in order to visualize the posterior pole and we applied silicon for the retinal detachment, followed by penetrating keratoplasty during the same surgical procedure. Two months after surgery, the Ahmed valve tube was removed from the anterior chamber and passed to the subconjunctival space because of contact with the endothelium and ocular hypotony. Informed consent was obtained previous to every surgery, in agreement with Declaration of Helsinki.

Two weeks after the last operation, a retrocorneal pigment line, associated with a corneal edema, was explored using a slit lamp. Taking into account that it was possibly a Khodadoust line and endothelial rejection, intensive topical and subconjunctival corticoid treatment was initiated. No improvement was observed at the following appointments and, apart from the corneal edema increasing, the pigment line advanced from the superior temporal region to the inferior nasal region thereby covering the endothelial side of the cornea (Figure 1). The optical computerized tomography of the anterior segment (AS-OCT Visante™, Carl Zeiss, Germany) showed a hyperreflective retrocorneal membrane covering the endothelial surface, coinciding with the lesion depicted in the optical biomicroscopy image (Figure 2).

A diagnosis of diffuse epithelial downgrowth was posed in view of the patient's medical history of multiple operations. An attempt was made to obtain confocal and specular microscopy images, in order to visualize epithelial cells, but the images were of insufficient quality to be conclusive. As the pigment line was advancing and as it was an only eye, we decided to treat the downgrowth and attempt to obtain histopathological confirmation[2].

A sample of aqueous humor and a small sample of peripheral Descemet membrane were taken to be sent to the pathological anatomy examination. Then the anterior chamber was irrigated with 5-fluorouracil (5-FU) in a concentration of 1000 mg/0.1 mL in 0.1 mL of a viscous dispersive viscoelastic (DisCoVisc®, Alcon, USA). The choice of a viscous dispersive carrier was

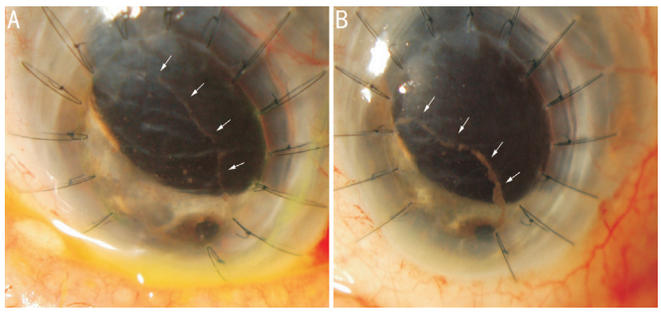

Figure 1 Photo of the anterior segment where one can observe the progression of the demarcation line of epithelial downgrowth A: The beginning of the follow-up; B: After 2mo of progression.

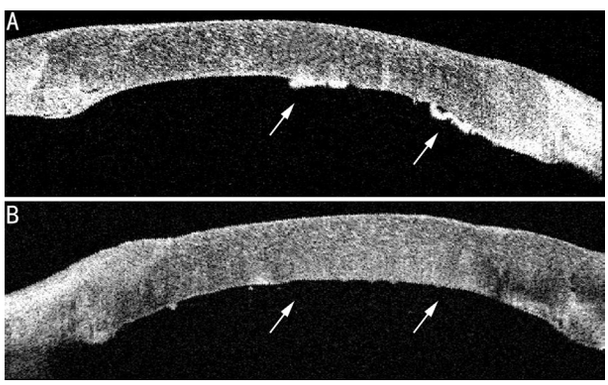

Figure 2 OCT of the anterior segment prior to 5-FU treatment (A) and 2wk after such treatment (B) in which resolution of the retrocorneal membrane of epithelial downgrowth can be objectivized.

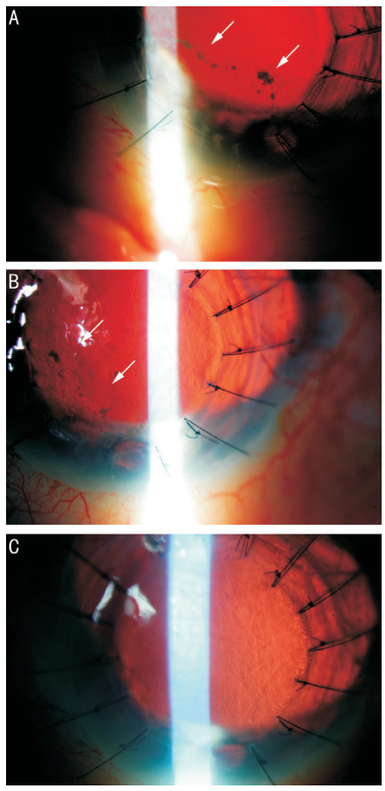

Figure 3 Photo of the anterior segment in retroillumination where the retrocorneal membrane can be observed prior to treatment (A), after the first 5-FU injection (B) and after the second intervention, showing complete resolution (C).

taken in order to concentrate the 5-FU in the retrocorneal space and prevent it from moving to the posterior pole due to the aphakia. Fifteen days later a new dose of 5-FU was administered following the same technique, even though the pathological anatomy laboratory results were inconclusive. The dispersive characteristics of the carrier allowed a proper coating of the posterior cornea, whereas the cohesive properties would have enabled an easier removal of the medication if needed. At two weeks of follow-up, a progressive regression of the hyperreflective line in the AS-OCT imaging (as well as the disappearance of the pigment line visible using a slit lamp) was observed until it totally disappeared one month after surgery (Figures 2 and 3). However, the possible endothelial toxicity of the medication caused the corneal edema to increase, bringing about a decrease in visual acuity; consequently the patient is awaiting new keratoplasty.

DISCUSSION

Cases of intracameral epithelial downgrowth in a sheet-like fashion like the case we present are usually more aggressive and more difficult to diagnose and treat. Given that these cases have a greater tendency to recur, they require a high degree of clinical suspicion for early diagnosis and treatment. Presentation symptoms of epithelial downgrowth are non-specific and insufficient for diagnosis. In our case, the presence of a progressive retrocorneal membrane and a corneal edema were indicative signs. But above all, the history of multiple intraocular operations, repetition of Seidel in one of the incisions and hypotony made us feel highly suspicious[3].

The most reliable diagnostic tool is the anatomopathological analysis which would show one to multiple layers of non-keratined scaly epithelial tissue on the posterior corneal surface, providing a firm diagnosis. However, neither the sample of aqueous humor nor the peripheral Descemet membrane (descemetorrexis) was conclusive in our case. It must be taken into account that this lesion usually appears in eyes with previous anatomical and functional distortion, thereby making it difficult to take adequate samples in places that are difficult to access[4].

Other non-invasive techniques, such as specular microscopy, confocal microscopy and AS-OCT, can be used[5]. In our case, obtaining imaging by specular microscopy was impossible due to overlying edema. In the case of confocal microscopy, the increase in corneal pachymetry caused by the corneal edema made the distance from the optical system to the lesion greater than its focus depth, and therefore it was impossible to make a diagnosis using this technique. As described previously, AS-OCT is an excellent tool for helping to diagnose and follow up symptoms. In our case, the SA-OCT image showed a

retrocorneal hyperreflective line and its subsequent resolution after applying the treatment (Figure 2). As there was no histopathological confirmation, other diagnoses, such as retrocorneal fibrous downgrowth or endotheliitis could have been considered, but the clinical history and progress of the symptoms suggested epithelial downgrowth.

Treatment of epithelial downgrowth continues to be a diagnostic and therapeutic challenge. It usually tends to recur and consequently requires several interventions; in some cases, it leads to enucleation. Moreover, treatment of the sheet-like, diffuse types of epithelial downgrowth, such as in the case we present, are a greater challenge because they are poorly defined and have to be completely destroyed to avoid recurrence. In our case, surgical resection, cryotheraphy or laser intervention would have meant a higher risk of phthisis, thus antimetabolite treatment was a good alternative.

As 5-FU can inhibit proliferating cells, its use in epithelial downgrowth has been postulated. Other antimetabolites has been used in few case reports, as methotrexate which has recently shown success in one patient[6]. Only 5-FU has been tested to assure a range of doses between 500 μg and 1.0 mg which are known to be safe. It is probable that there will be a recurrence after the first therapeutic attempt, because only the proliferating cells are attacked; others in a latent phase that generate a recurrence may still be present[7]. Therefore, the usual treatment guideline is to repeat such injections at least twice, as we did in this case.

Another crucial factor in the therapeutic approach of this specific patient was the absence of an anatomical delimitation between the anterior and posterior poles. This patient has aphakia, areflectic mydriasis and has undergone vitrectomy. As a result, the medication, which is conveyed in a serum, could easily spread around the eyeball thereby increasing the posterior toxicity without acting on the lesion. Facing aphakic patients few options has been reported: gas-fluid exchange prior to irrigation in order to push the medication into the retrocorneal space, with the patient lying in the prone position for thirty minutes, or using dispersive viscoelastic as a carrier (Viscoat®, Alcon)[8]. We propose using a viscous dispersive viscoelastic (DisCoVisc®, Alcon) as a carrier meaning we can take advantages of both its cohesive and dispersive properties. The dispersive behavior enables proper coating of the posterior cornea limiting the treatment to the anterior chamber and without the patient having to lie in a specific position. Its cohesive characteristics would let us aspirate easily the medication if needed due to the likely misplacement of the mixture after injection in an eye with no anatomical landmarks between anterior and posterior chamber.

At present, no recurrence of the epithelial downgrowth has been objectivized using the slit lamp nor with the AS-OCT after nine months of follow-up. The patient, however, does present a larger corneal edema due to the possible endothelial toxicity of 5-FU[9]. In cases in which the treatment causes decompensation, one could resort to endothelial subsequent keratoplasty. In our case the patient awaits a new penetrating keratoplasty[10].

CONCLUSION

Repeated instillation of 5-FU 1.000 mg/0.1 mL in the anterior chamber is a good therapeutic option for treating diffuse types of epithelial downgrowth. A viscous dispersive viscoelastic as a carrier shows a combination of dispersive and cohesive characteristics that could help delimiting the effect of antimetabolites to the retrocorneal space, ease intraoperative management and reduce the potential toxicity in other parts of the eyeball. A suspicion diagnosis and early treatment are important when attempting to control its progression and stop its impairing other ocular structures.

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