

Treatment of spontaneous corneal microperforation linked to autoimmune hepatitis:

The corneal regeneration with Cacicol

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INTRODUCTION

Corneal perforations can be derived from a variety of disorders and may lead to devastating ocular sequelae. After infectious and traumatic, inflammatory eye perforations are the most frequent etiology and they presented in the context of systemic autoimmune diseases as rheumatoid arthritis, systemic lupus erythematosus or with granulomatosis polyangiitis among others. Less commonly they may occur as secondary complications of severe dry eye disease, idiopathic or associated with Sjögren's syndrome, neurotrophic keratopathy or corneal ectasia.

We report a case of spontaneous eye micro-perforation in a patient without previous ocular diseases, with diagnosis of autoimmune hepatitis as only pathological history.

Autoimmune hepatitis is a rare disorder, with an incidence of 0.1-0.9 per 100,000 persons per year, which usually affects middle-aged women. According to immunologic pattern differs in types 1 and 2. The most common form in adults and globally is the type I, characterized by hypergammaglobulinemia and positive antinuclear antibodies (ANA) and/or positive anti smooth muscle (AMS), and the type 2 is most common in children have positive liver-kidney microsomal type 1 antibodies (LKM) (1,2). Autoimmune hepatitis may present with keratoconjunctivitis sicca in the context of associated Sjogren syndrome (3,4), in which if described aggressive cases of sterile corneal melting leading to spontaneous perforation, especially when the diagnosis is delayed (4). However there have been no published cases of ocular perforation with corneal thinning associated with underlying immune disorder in patients with autoimmune hepatitis. Described in the literature there are two anterior uveitis cases associated with autoimmune hepatitis, one before the era of diagnostic tests for hepatitis C (5) and another later , which is associated the presence of uveitis with corneal stromal injury secondary to autoimmune hepatitis without details of corneal involvement (6).

Corneal perforation are emergencies that require immediate attention. It is essential to identify and treat the underlying cause may with orally broad-spectrum antibiotic coverage and referrral to a specialist unit. There are different options for the treatment of corneal perforations less than 2 mm: therapeutic contact lenses, tissue adhesives, the free conjunctival autograft or amniotic membrane.

In our case we present the evolution and results of treatment with topical RGTA-cacicol combined with therapeutic contact lens and autologous serum.

CLINICAL CASE

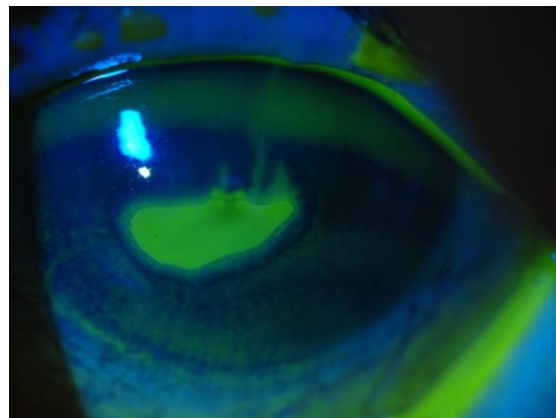
71 year-old woman evaluated at the emergency room of our hospital describing itching and secretion in the left eye (LE) of 2 weeks. The best corrected visual acuity (BCVA) was 0.15. In the slit lamp evaluation we objectify a moderate ciliary hyperemia with a central infiltrated corneal ulcer of 0.5 mm wide by 3 mm high, central descematocele and corneal perforation of 1 mm in diameter with spontaneous positive Seidel. Preservation of the anterior chamber depth without inflammatory reaction was observed. (Figures 1-3).

Fig 1. Central corneal ulcer with thinning, descematocele and central microperforation (arrow). No signs of infection are observed.



Fig. 2. Corneal ulcer with thinning. Corneal microperforation indicated by the arrow.

Fig. 3. Epithelial defect with positive fluorescein staining and positive Seidel's test.



Exploration of the contralateral eye was normal. In the emergency room we put a therapeutic contact lens (TCL), with this anterior chamber remained. The eye was occluded with mydriatics and topical antibiotic coverage plus systemic quinolone

No history of trauma, ophthalmic diseases or previous eye surgeries. Among the pathological systemical history included a diagnosis of autoimmune hepatitis with cirrhosis and secondary portal hypertension. The profile autoimmune antibodies was positive for ANA and SMA and negative for LKM. In biochemistry stands elevated ESR, transaminases, alkaline phosphatase and hypergammaglobulinemia. Liver virus serology was negative. At present, the patient has no systemic treatment of their disease.

Evolution control is performed by anterior segment photographs and OCT (Triton Swept Source OCT). At 24 hours anterior chamber depth is maintained without Seidel.

The possibility of treating microperforating with cyanoacrylate or amniotic membrane arises, but given the anterior chamber depth maintenance without progression of corneal thinning, we decided conservative treatment including artificial tears and Cacicol 1 drop every 48 hours, associated with TCL and topical antibiotic coverage (ofloxacin every 6 hours).

Progressively decreases both epithelial defect and the size of the perforation. On the third day of treatment, in the absence of TCL, not Seidel was observed. In the anterior segment OCT, we observed an epithelial closure, anterior and posterior, by a fibrous bridge leaving an anterior intrastromal defect in the area of maximum thinning. (Figure 4).

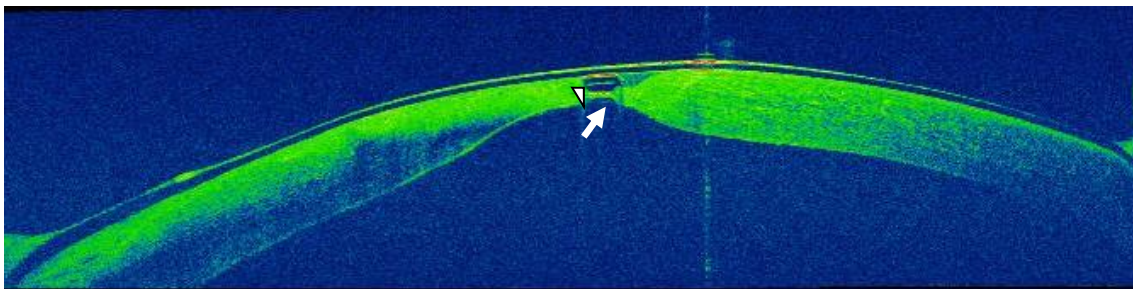


Fig 4. Anterior segment OCT (Triton DRI OCT) on the third day of treatment. Under the TCL, we observe anterior epithelial closure and posterior closure by a fibrous bridge (arrow) leaving an intrastromal defect of (arrowhead).

During the first week begins progressive epithelialization of the ulcer (Figure 5) with a pattern of diffuse superficial keratitis associated, and progressive corneal stroma regeneration with decrease of thinning (Figure 6)

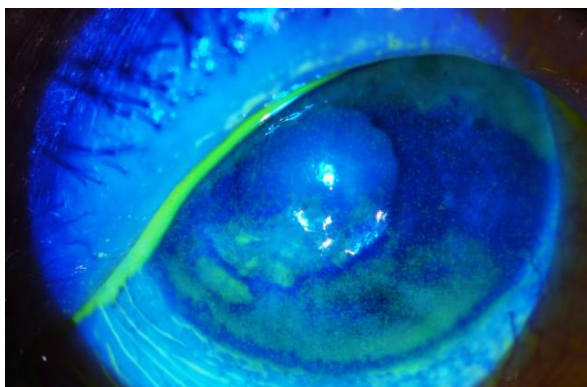


Fig 5. Epithelialization of the corneal ulcer with negative Seidel test. Irregular distribution of fluorescein is appreciated and diffuse keratitis associated.

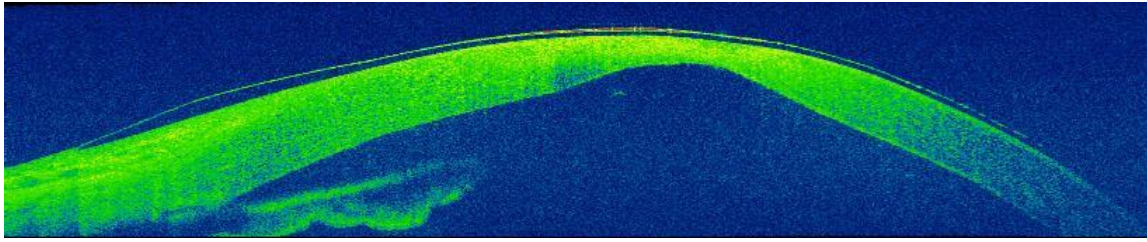


Fig 6. Anterior segment OCT at day 10 of treatment. Regeneration of the anterior corneal stroma is observed with complete resolution of intracorneal visible defect in Figure 3.

By possible association with Sjogren's syndrome we ask an autoimmune hepatitis analysis and internal medicine evaluation. The results showed a positive antiRo antibodies and the diagnosis of secondary Sjögren's syndrome is confirmed.

At present the MAC is 0.05, with nuclear cataract N4, complete epithelization of the lesion with secondary corneal scarring (Figure 7). In the OCT control after 3 months corneal thickness increase is observed in the thinning area, without risk of perforation (Figure 8). Continued monitoring for basic autoimmune hepatitis and treatment is maintained with artificial tears and autologous serum awaiting penetrating keratoplasty and cataract surgery.

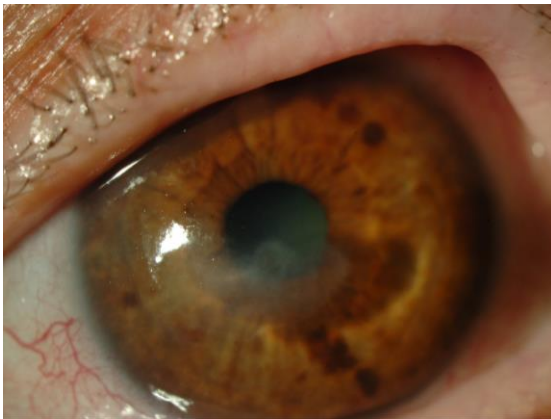


Fig 7. Complete epithelization of the ulcer. Corneal leukoma that compromises the visual axis is observed.

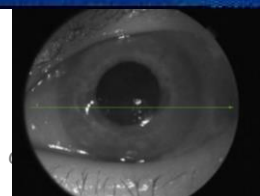
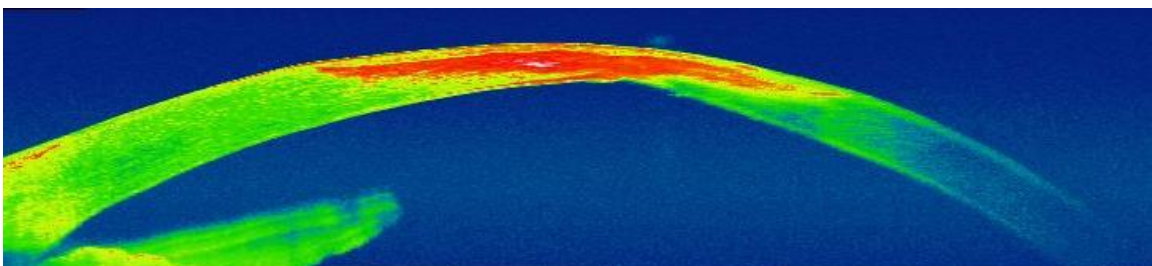


Fig 8. 3-month follow-up anterior segment OCT. We observe restoration of corneal thickness with high reflectivity in the area of corneal leukoma by stromal fibrosis.

DISCUSSION

The unique history of our patient is the autoimmune liver cirrhosis without surgical antecedent, trauma, or previous eye diseases, nor contralateral eye disorders to suspect a clear etiology. It is not rare the corneal involvement for systemic autoimmune diseases, generally as peripheral ulcerative keratitis and occasionally in the center, however to date not been reported corneal ulceration and ocular perforation in the case of autoimmune hepatitis. The known association of this disease with Sjögren's syndrome should make us think of this possibility and should perform appropriate tests.

Therapeutic options for corneal perforation less than 2 mm are TCL, tissue adhesives such as cyanoacrylate, free conjunctival autograft or amniotic membrane. If infected tissue adhesives, this may induce increased neovascularization and generate stromal scarring. The amniotic membrane requires debride the edges of the lesion and as conjunctival autograft requires stitches to the cornea.

Moreover, the GTA therapy restores the balance between the protein matrix and cytokines linked to heparan sulfate and ensures balance in the corneal microenvironment. This in turn prevents degradation of extracellular matrix proteins and promote epithelial and stromal healing. It is administered topically and is usually used in cases of persistent epithelial defects (7,8) and chronic corneal ulcers (9). It has also been used after penetrating keratoplasty (10) and has recently been used successfully in the treatment of corneal ulcers postquirúgicas (11). It is a non-invasive treatment that not induces stroma scarring apparently due to the healing itself.

CONCLUSION

We present a case of micro corneal perforation associated with autoimmune hepatitis basis as only pathological history, a rare disease in which there have been no reported previous cases of corneal perforations. We opted for the non-invasive topical treatment, Cacicol, combined with contact lens and topical lubricants, getting good treatment outcome, with resolution of the corneal perforation and progressive reduction of thinning without resorting to surgery. We could not assess the effect of Cacicol in isolation but it could be an alternative therapy for selected cases of corneal micro-perforations combined with the use of temporary TCL.

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