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Case Report

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Aminoglucoside/Imidazole in the Treatment of Acanthamoeba Keratitis

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Abstract

Acanthamoeba Keratitis (AK) is an infrequent corneal infection caused by free living amoeba, it is frequently misdiagnosed and medically/surgical treated with low or no response in advanced cases. In this paper we present five cases of AK with early diagnoses and good response to aminoglucoside/imidazole treatment and achieving acceptable final visual acuity in each case.

Keywords: Acanthamoeba keratitis, Netilmicin, Tobramicin, Itraconazole

Acanthamoeba Keratitis (AK) is an infrequent corneal infection caused by free living amoeba, it is frequently misdiagnosed and medically/surgical treated with low or no response in advanced cases. In this paper we present five cases of AK with early diagnoses and good response to aminoglucoside/imidazole treatment and achieving acceptable final visual acuity in each case.

Introduction

Aminoglycosides and its derivatives have been recommended for *Acanthamoeba* keratitis (AK) treatment, Neosporin (Neomincin, polimixin and B-Gramicidin) since 2005 or tobramycin [1]. Ishibashi in 1990 published 3 cases successfully resolved using Imidazole alone [2]. Topical aminoglucosides in combination with oral imidazoles, (itraconazole) has been sowed as good medical treatment [3]. We describe five cases of culture proved AK and medically treated with netilmicin, a semi-synthetic derivate drug of recent systemic medical use, available in intravenous presentation, and useful in ophthalmic topical drops 0.3% concentration (SIFI Laboratory Scicilia Italy), alone or in some cases combined with an oral imidazole itraconazole.

Material and Methods

We present five cases of AK culture proved, in NNA medium, its clinical diagnosis, treatment and evolution.

Case 1

Female 19 years old, living in Mexico City, contact lens user, she presented with visual acuity loss in both eyes one week before the consultation. She had received topical gatifloxacin 0.3% and netilmicin 0.3% with no specification of dose and time.

At Cornea Department in the Hospital, slit lamp examination: In OD corneal haze and mild keratitis were found; also epithelial edema and perineural infiltrate in temporal inferior quadrant (Figure 1) VA 20/50 (Snellen scale). In OS conjunctiva hyperemia, central cornea stromal opacity and diffuse perineural infiltrate was observed (Figure 3) AV 20/60(.)20/50. Patient was diagnosed as OS herpes simplex keratitis, oral acyclovir was prescribed (oral 400 mg/5 times a day), without clinical response. Sample of both corneas scraps, and both contact lens for bacterial, fungal and *Acanthamoeba* was taken at the first medical consultation in the laboratory of the hospital.

Laboratory report was; *Acanthamoeba spp* growing in NNA agar covered with live E cloacae after 48hs, in both corneas and both contact lens samples, and culture was negative for bacteria in OS. *Stenotrophomonas maltofilia* in OD cornea, and contact lent samples. *Acanthamoeba* strain isolated form cornea sample in OD was identified as *Acanthamoeba royreba*. After laboratory results and AK diagnosis, topical netilmicin 0.3% eye drops for booths eyes, and oral itraconazole (100 mg bid)/15 days were prescribed.

The patient was attended 30 days after, at silt lamp examination were observed in OD epithelial edema and perineural infiltrate in temporal inferior quadrant, 30 days after she presented a little inflammatory ring and the perineural infiltrate in the same site described before. 12 days after there was observed haze for paracentral corneal, and vascularization, total superficial epithelization of cornea surface in OD, and 6 weeks later she referred no pain, in the next visit the patient showed no ulcer in OD, inflammatory reaction and perineuritis diminished (Figure 2) within 100 days in total. In OS cornea at 30 days after the first visit the patient showed no ulcer in OS cornea, an inflammatory reaction and perineuritis was diminished (Figure 4).

The final visual acuity was 20/25 OD and 20/50 OS, perineural infiltrate on left eye continues but was diminished within 3 months: final best corrected visual acuity 20/20 on both eyes, and haze on OD inferior quadrant temporal cornea.

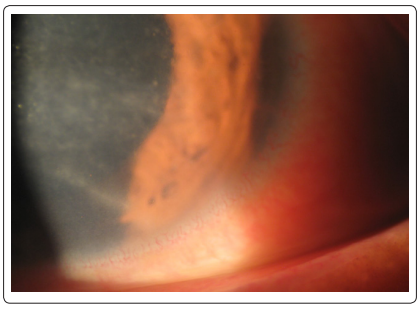


Figure 1: OD corneal haze and mild keratitis, epithelial edema and perineural infiltrate in temporal inferior quadrant

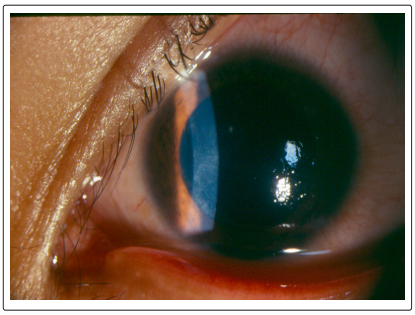


Figure 2: OS conjunctiva hyperemia, central cornea stroma opacity and diffuse perineural infiltrate

Figure 3: OD After treatment, total superficial epithelization of cornea surface in OD, 6 weeks later: and the patient referred no pain

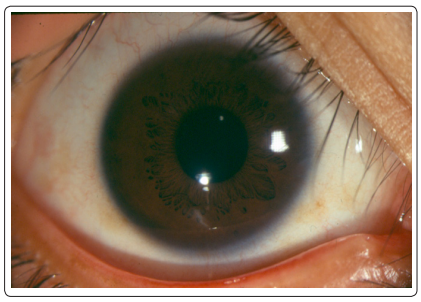


Figure 4: OS Inflammatory reaction and perineuritis was diminished, and clear cornea was observed after 3 weeks of treatment

Case 2

Female 14 year old living in México City, contact lens user, by an acute ocular pain two days before in OS was attended in our hospital. In clinical exploration was observed; OS red eye, with epiphora +++, and acute pain. At slit lamp examination, was observed cornea ulcer in temporal superior quadrant cornea in OS, des-epithelization, and slight infiltrate surrounding the lesion (Figure 5 and 6), she referred the use of CL washed with running water in both LC from both eyes, was administered topical Netilmicin 0.3% and Moxifloxacino 0.3% (Alcon USA) in topical drops each 2hs alternatively, and Ciprofloxacino ointment by night in OS. Cornea samples were taken by scraps for bacteria, fungus and acanthamoeba. Ten days after at consultation it was observed epithelization of corneal ulcer, remaining only a discrete infiltrate. Twenty five days after was observed a superficial inflammatory infiltrate and perineuritis, in direction from infiltrate to central cornea. For the laboratory report, of *Acanthamoeba sp* culture in cornea and contact lens samples, was added to previous medical treatment; Itraconazol 100 mgs bid. Thirty days after the first consultation, patient referred no pain and the corneal ulcer was no visible, there was a superficial leucoma, visual acuity 20/60 Final BCVA 20/25.

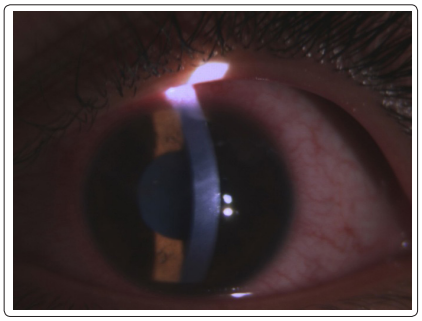


Figure 5: Cornea ulcer in OS in temporal superior quadrant, des-epitelization, and slight infiltrate surrounding the lesion

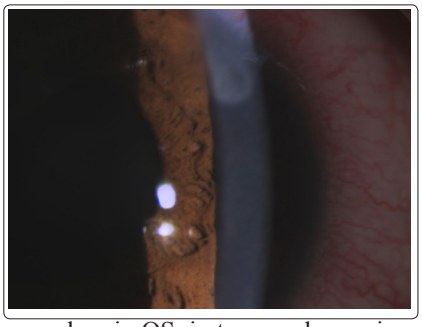
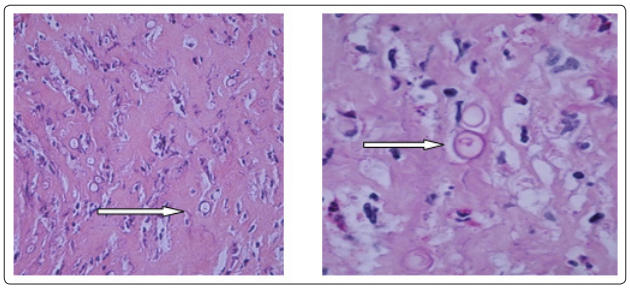


Figure 6: Cornea ulcer in OS, in temporal superior quadrant, des-epitelization, and slight infiltrate surrounding the lesion

Case 3

Female 17 years old, living in Mexico City, contact lens user, she was attended after 21 days of onset by pain++ in OD, palpebral edema, and conjunctiva hyperemia +++. At slit lamp examination in OD was observed, cornea perineural inflammation, corneal ring surrounding a central des-epithelization, after laboratory *Acanthamoeba* sp. culture confirmation in corneal sample, was started topical Brolene, Netilmicin and artificial tears each 2 hours alternatively, an oral Itraconazole 100 mgs each 2 hours. Because perforation risk in OD the patient was submitted to TPK (tectonic), the corneal tissue, was submitted to laboratory studies cultures and microscopic observation (Figure 7A and B) after three weeks, it was adjusted one corneal suture, and presented in central donor cornea a visible des-epithelization. For a peak of intraocular pressure was installed by surgery an intraocular Ahmed valve in OD with the regularization to 10 mmHg pressure, after 6 months the central donor cornea was epithelization again and the patient was maintained only

in observation, remaining a visible central scar in her OD cornea.



A B

Figure 7A and B: *Acanthamoeba* cyst (arrows) in corneal tissue hematoxilin-eosin stain X40, and cyst in x100

Case 4

Female 14 years old, soft contact lens user in right eye, 45 days before she had foreign body sensation, and a central corneal ulcer. She was diagnosed as corneal ulcer related to seasonal conjunctivitis, and received medical therapy with topical prednisolone and sodium cromoglycate, after increasing pain and loss vision, the patient was attended in Corneal service of our hospital. At slit lamp examination OD; infectious 5.6 and 6.3 mm in diameter central ulcer in the right eye, immune ring with light infiltrate surrounding the ulcer, inflammation in anterior chamber, hypopyon (Figure 8), VA; HM, severe conjunctivitis, and pain. In the smears from cornea scrap sample taken was observed *Acanthamoeba* cyst (Figure 9). For medical treatment was administered topical Tobramycin 0.3% (Laboratorios Sophia, Mexico) each 2 hours day and night, and oral itraconazole 100 mgs /15 days bid, and was recommended do not use the contact lens in the right eye. Laboratory reported; culture positive for *Acanthamoeba castellani*. Twenty four days after was observed conjunctiva hyperemia, ciliary reaction 360o, some clear cornea, and no ulcer (Figure 10) was suspended oral itraconazole, and was added topical dibromo propamidine-isetionate (brolene) each 4 hours for 6 months and the final VA taken was; FVA 20/40(.)20/80.

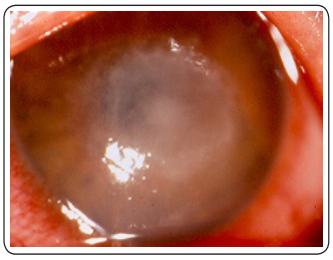


Figure 8: In the first consultation: Central cornea ulcer in OD, immune ring with light infiltrate surrounding the ulcer, inflammation in anterior chamber, hypopyon, and severe pain

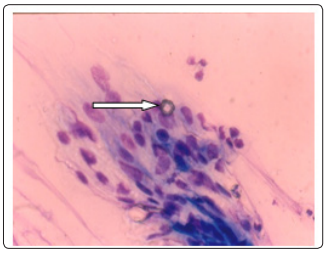


Figure 9: In Giemsa stain at smears from scrap sample taken we observed *Acanthamoeba* cyst (Arrow)

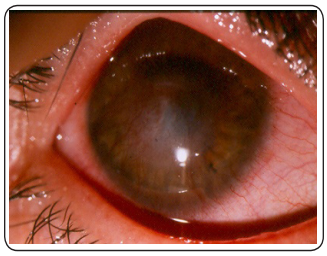


Figure 10: Twenty four days after was observed conjunctiva hyperemia, ciliary reaction 360°, some clear cornea, a central leucoma surrounded by vascularization and no ulcer was visible

Case 5

Female 30 years old, refractive contact lens user in OS, referred intense pain 24 hours before, VA 20/200. At slit lamp observation; Ciliary 360° inflammatory reaction, central and superior paracentral cornea infiltrates in OS, VA 20/300(.)20/200, Tyndall +, Cells in anterior chamber +, slight immune ring, and perineuritis (Figure 11). Samples for CL cultures was taken and yielded abundant colonies of P *aeruginosa* and cyst and trophozoites of *Acanthamoeba* sp, the diagnosis was bacterial and acanthamoeba keratitis, medically treated with topical netilmicin 0.3%, neomycin 0.3% eye drops each 2 hours, the evolution taken 74 days, and was good. The patient showed central slight leucoma, FBCVA 20/20 (Figure 12).

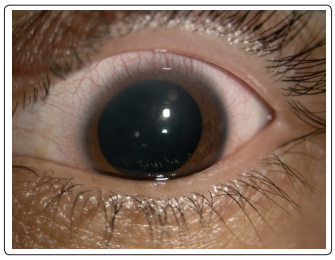


Figure 11: Ciliary 360° inflammatory reaction, central and superior paracentral cornea infiltrates in OS, VA 20/300(.)20/200, Tyndall +, Cells in anterior chamber +

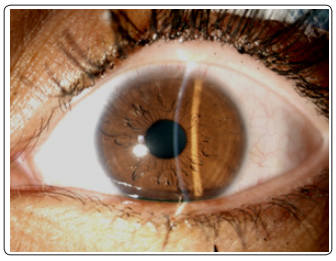


Figure 12: After medical treatment, cornea in OS, superior and central slight leucoma

Discussion

Nowadays, there are no a single drug that eliminate from the cornea lesion *Acanthamoeba* cyst and triphozoites at the same time, for all the drugs tested the susceptibility is higher for trphozoites than for the cyst. Aminoglucosides interfere with the normal process of ribosomal function, and imidazols change the pathway at the synthesis of ergosterol in *Acanthamoeba* cells membrane [4]. The combination is synergistic, and finally the action over the new *Acanthamoeba* trophozoites and cyst replicating in the cornea tissue, is expressed healing the cornea lesion in cases of early *Acanthamoeba* diagnosis.

Conclusion

In early diagnosis of AK the topical 0.3% netilmicin/oral itraconazole 100 mgs/12 hs bid, are good choice for medical treatment in cases of early *Acanthamoeba* diagnosis. Both medical drugs; ophthalmic netilmicin 0.3% or Itraconazole 100 mgs tablets, have pharmaceutical presentation available in Mexico and are not so expensive.

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