Acanthamoeba Keratitis Presenting as Dendritic Keratitis in a Soft Contact Lens Wearer

Edward Yip Yeung, MD; Samuel Chao-Ming Huang, MD; Ray Jui-Fang Tsai, MD

Acanthamoeba keratitis is a rare cause of corneal infection in Taiwan, which can result in devastating visual outcomes. A 37-year-old woman, who wore soft contact lenses, suffered from severe pain in her left eye. Biomicroscopy revealed dendritic keratitis, radial keratoneuritis, and fine keratic precipitates on her cornea. Culture, using non-nutrient agar plate seeded with Escherichia coli, resulted in heavy growth of Acanthamoeba. The inpatient treatment, including topical neomycin-polymyxin B and metronidazole (0.5%) eyedrops, oral ketoconazole, and then oral prednisolone, successfully controlled the corneal infection. The best-corrected visual acuity was 0.9 without any evidence of recurrence of infection after 21 months of follow up. Acanthamoeba keratitis can present as dendritic keratitis, which mimics herpes simplex infection, thus, delays appropriate treatment. Early diagnosis and judicious treatment are essential for restoring the vision and avoiding the subsequent need of penetrating keratoplasty. *(Chang Gung Med J 2002;25:201-6)*

Key words: Acanthamoeba keratitis, corticosteroid, dendritic keratitis, metronidazole.

Acanthamoeba keratitis is a chronic corneal infection caused by members of the genus Acanthamoeba. It was first reported in 1973.[1] The number of cases has increased gradually from 1981 through 1984 with a dramatic rise beginning in 1985 after the association with contact lens wear was first recognized by Moore et al..[2] Acanthamoeba keratitis has rarely been seen in Taiwan, and all of the cases reported previously ultimately required therapeutic penetrating keratoplasty.[3-5] We present a case that was diagnosed in the very early stage and was successfully treated with medications only. The patient regained her satisfactory best-corrected visual acuity without either therapeutic or optical penetrating keratoplasty.

CASE REPORT

A 37-year-old female had been wearing conventional daily wear soft contact lenses for more than 8 hours per day for more than 10 years. She cleaned the lenses with commercial disinfecting solutions, but sometimes just with tap water. She came to our ophthalmic clinics because of redness and severe pain in her left eye for 1 week. No history of ocular trauma was documented. Biomicroscopic examination revealed central dendritic keratitis (Fig. 1). Herpes simplex keratitis was presumed, and acyclovir ointment was prescribed. The patient was then referred to a cornea specialist.

When she was referred to us 3 days after treat-

From the Department of Ophthalmology, Chang Gung Memorial Hospital, Chang Gung Memorial Hospital, Taipei.
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Address for reprints: Dr. Samuel Chao-Ming Huang, Department of Ophthalmology, Chang Gung Memorial Hospital. 5, Fu-Shin Street, Kweishan, Taoyuan, 333, Taiwan, R.O.C. Tel.: 886-3-3281200 ext. 8666; Fax: 886-3-3287798

ment, there was no improvement in eye pain. Biomicroscopic examination showed limbitis, central dendritic keratitis with anterior stromal infiltrate, paracentral radial keratoneuritis, and fine keratic precipitates on the endothelium (Fig. 2). Decreased corneal sensation could also be demonstrated. No ring ulcer or hypopyon was noted. Topical neomycin-polymyxin B ointment and oral mefenamic acid were added. Bacterial and fungal cultures were performed as well as a non-nutrient agar culture seeded with Escherichia coli.

Heavy growth of Acanthamoeba on non-nutrient agar seeded with E. coli was noted 9 days after gathering, but there was no growth on the other culture media (Fig. 3). The patient was then admitted to our ophthalmic ward for further management and closer observation. Initial treatment included topical neomycin-polymyxin B and metronidazole (0.5%) eyedrops (every hour), oral ketoconazole (twice per day) and acetaminophen. Severe pain was relieved partially 1 week after starting treatment. Corneal dendritic keratitis gradually healed with some residual superficial punctate keratitis. Anterior stromal infiltration faded out to form scattered and mild

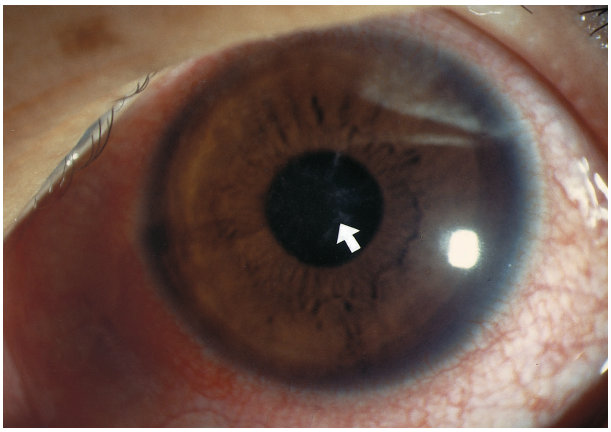

Fig. 1 The patient presented with central corneal dendritic keratitis, limbitis, and conjunctival infection (Arrow).

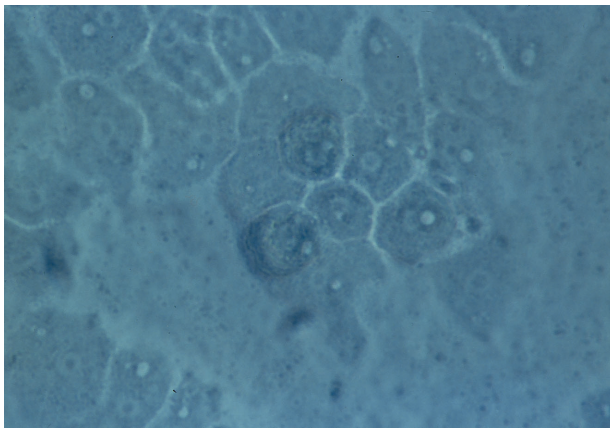

Fig. 3 The Acanthamoeba trophozoites grew on the non-nutrient agar seeded with *E. coli,* and some of them condensed to form cysts. (No staining, Light Microscope ¡ 400)

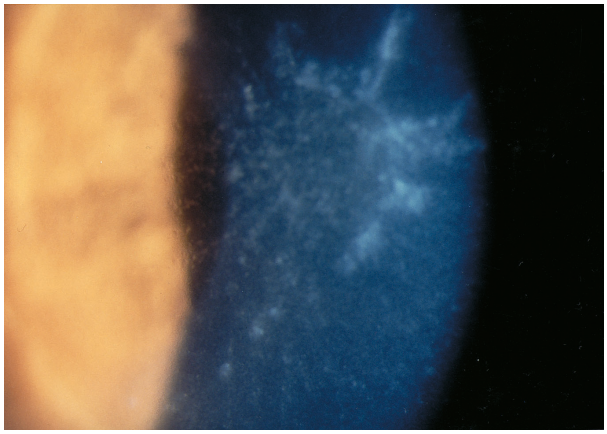

Fig. 2 Biomicroscopic examination shows central dendritic keratitis with anterior stromal infiltrate, paracentral radial keratoneuritis and fine keratic precipitates on endothelium.

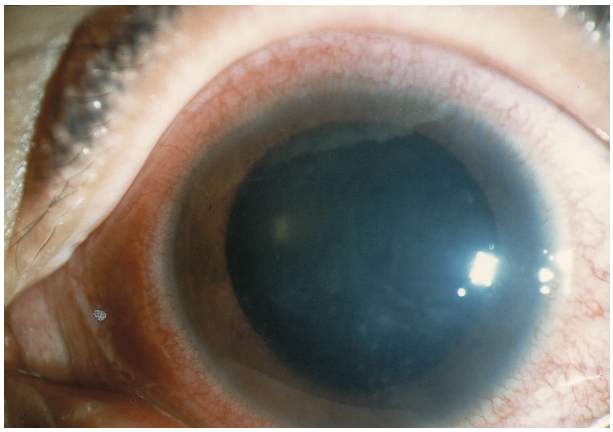

Fig. 4 After treatment, anterior stromal infiltration faded out to form scattered and mild subepithelial opacities.

subepithelial opacity. Fine keratic precipitates on the endothelium resolved later. The topical and oral regimens were then tapered gradually. Oral prednisolone was added 2 weeks after the beginning of the treatment, and all pain subsided completely. The patient was then discharged and followed up at our clinics.

The topical agents were maintained at lower frequency for another one and a half months. Only scattered and faint subepithelial opacities were noted during the follow-up period (Fig. 4). She did not want to wear contact lens any more, and later she received refractive surgery at another hospital. After 21 months of follow up, her best-corrected visual acuity was 0.9 in her left eye.

DISCUSSION

The three major risk factors for Acanthamoeba keratitis are contact lens use, exposure to contaminated water, and corneal trauma.[2] Ninety-five percent of the patients with Acanthamoeba keratitis had at least one of these risk factors. Eighty-five percent of the cases wore contact lenses. It occurred in patients who wore all types of soft or hard contact lenses.

The initial symptoms of Acanthamoeba keratitis include photophobia, tearing, and pain.[6] The pain is typically very severe, seeming to be disproportionate to the signs.[1] The early signs include pseudo-dendritic epithelial lesion,[7,8] radial keratoneuritis,[9] limbitis, and sometimes a low-grade anterior uveitis[6] along with the finding of decreased corneal sensation.[10] Therefore, herpes simplex keratitis is the most common misdiagnosis because of the similarity of its early signs to Acanthamoeba keratitis.[7-9] Misdiagnosis may delay the appropriate treatment. The ring corneal infiltrate, which is the hallmark of the disease, may then appear, but it is a relatively late sign.[11] Patients in the late stage may also demonstrated frank ulceration, anterior uveitis, and often with hypopyon.[12]

In addition to extreme awareness, the diagnosis of Acanthamoeba keratitis is mainly based on the clinical pictures and laboratory investigations. The most common method is to culture the tissue obtained from corneal lesion scraping on to a non-nutrient agar plate seeded with *E. coli*. Using this method, 75 % of patients had cultures positive for Acanthamoeba, either directly from corneal tissue or from their contact lens, case, or solution.[12] It can also be diagnosed directly by staining the tissue obtained from corneal biopsy with a number of dyes, such as calcafluor white, lactophenol blue, or even with gram or Giemsa stains.[1] Other methods of diagnosis include immunostaining, polymerase chain reaction, and confocal biomicroscopy, all of which require more complicated techniques and expensive equipment.[1]

Before 1985, medical treatment of Acanthamoeba keratitis was difficult due to the lack of specific anti-amoebal agents. A large proportion of the patients ultimately required penetrating keratoplasty.[11] However, recurrent postoperative infections had become a serious problem that required repeat transplantation in 30% of the patients. Wright et al reported the first successful medical control of Acanthamoeba keratitis with the diamidine compound propamidine isethionate (Brolene) in 1985.[13] Since then, a trial of specific anti-amoebic medical therapy that was the first choice for management of Acanthamoeba keratitis before corneal transplantation.[11] Other aromatic diamidines that have proven to be effective against Acanthamoeba include petamidine, dibromopropamidine, and hexamidine. Effective treatment regimens for Acanthamoeba keratitis also included propamidine in combination with other agents, such as the aminoglycosides neomycin and paromomycin, or the imidazole derivatives miconazole (topical), clotrimazole (topical), ketoconazole (systemic), and itraconazole (systemic).[13]

At present, the recommended triple medication therapy of Acanthamoeba keratitis should include cationic antiseptic agents, chlorhexidine (0.02%) or polyhexamethyl biguanide (PHMB) (0.02%), in combination with propamidine isethionate (0.1%) and neomycin.[13] Unfortunately, with the exception of neomycin, the recommended topical agents are neither officially licensed, nor commercially available for topical use in the eye in Taiwan and most other countries.[1] Moreover, toxicity and resistance to these agents may sometimes compromise the effectiveness of the treatment.[11] Metronidazole (Flagyl) 0.5% eyedrops together with other anti-amoebal agents has been reported to have successful outcomes in the treatment of Acanthamoeba kerati-

tis.[14-16] It is readily available in our hospital and is easily prepared for topical use. We found that it was equally effective as other anti-amoebal agents used in the treatment of Acanthamoeba keratitis.

Early diagnosis and treatment of Acanthamoeba keratitis are essential for successful medical treatment[8,11] because 50% of patients with late diagnosis compared with less than 10% with early diagnosis required penetrating keratoplasty.[6] We started the appropriate treatment (topical neomycin-polymyxin B ointment) within 10 days following the manifestation of symptoms. The initiation of specific therapy 1 to 4 weeks from the start of the infection was effective in the eradication of Acanthamoeba.[12] The rationale in initial treatment of this keratitis is to saturate the cornea with the drug in an effort to kill the trophozoites, to encourage encystment, and to maintain a drug level high enough to kill any emerging trophozoites should the cysts persist and later cause recurrence of the keratitis.[17] Most anti-amoebal agents are effective against trophozoites in vivo, but only PHMB and chlorhexidine are effectively cysticidal in relatively low doses.[13] Therefore, it was suggested that anti-amoebal regimens should be maintained at a low dose for at least 3 to 6 months after all signs of inflammation have disappeared.[12] We tapered medications gradually and then maintained them for one and a half months to prevent recurrence. Then the treatment was suspended to minimize the ocular toxicity of these agents. Furthermore, the patient was closely followed up at our ophthalmic clinics, and we could properly responded when any evidence of recurrence occurred.

The use of corticosteroids in Acanthamoeba keratitis is still controversial. Some authorities believed that the corticosteroids were relatively contraindicated in the treatment of Acanthamoeba keratitis.[18] They did not use topical corticosteroids because they considered the host defenses important in eradicating the organisms, and corticosteroids may inhibit neutrophil and macrophage responses.[17] However, other authorities suggested that topical corticosteroids could be carefully introduced into the therapy although the exact role was unclear.[19] Topical corticosteroids, when used concurrently with anti-amoebal agents, were very effective in treating the severe pain of Acanthamoeba keratitis.[19] Corticosteroids were also used with benefits for some other specific indications including limbitis and scleritis, perineural infiltrates, uveitis, stromal lysis, and after penetrating keratoplasty.[1,6,13] Cases of steroid sensitive Acanthamoeba keratitis were reported.[19] Recurrent flare-ups of inflammation were noted when corticosteroid therapy was tapered or discontinued. This suggests that a component of the corneal reaction in Acanthamoeba keratitis might be immunologically mediated. Although the mean anti-amoebal therapy duration that was significantly longer has been reported, topical corticosteroids were not associated with a higher rate of medical treatment failure.[19] Moreover, no significant differences were noted with respect to visual outcome, incidence of perforation, or incidence of penetrating keratoplasty. Rather, poor outcome was significantly related to diagnostic delay. Oral corticosteroids were prescribed in our patient in order to reduce the subjective severe pain and decrease the ocular immune response-related inflammation. We chose oral forms of medication because they minimally interfere other topical treatment.

Wide epithelial debridement performed for Acanthamoeba keratitis before topical medications not only provided adequate tissue for diagnosis, but also debulked the load of infectious organisms, facilitated the delivery of topical medications, and enhanced the resolution of diseases.[1,8,13] We selectively debrided only suitable amounts of tissue over the lesion of keratitis to avoid prolonging wound healing time.

A medical cure can sometimes be achieved in Acanthamoeba keratitis using specific anti-amoebal agents, but the cornea often remains scarred and requires optical penetrating keratoplasty for visual restoration.[20] Much evidence pointed out that successful recovery of excellent vision depended mainly on early diagnosis and appropriate treatment.[6,8,11] Our patient was diagnosed and treated during very early stage. Thus, although even no therapeutic or optical penetrating keratoplasty was performed, the patient recovered her visions satisfactorily.

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隱形眼鏡配戴者感染以樹枝狀角膜炎爲表現之棘狀阿米巴角膜炎

楊 曄 黃朝銘 蔡瑞芳

棘狀阿米巴角膜炎是一種罕見但可以造成嚴重視力影響之角膜感染。一位37歲女性軟式隱形眼鏡配戴者主訴左眼劇烈疼痛，與表徵不成正比。裂隙燈檢查可見樹枝狀角膜炎、放射狀角膜神經炎及細微之角膜內皮沉積物。經由鋪滿大腸桿菌之非營養性培養皿培養出許多棘狀阿米巴原蟲。病患住院治療包括使用局部的 neomycin-polymyxin B及metronidazole (0.5%) 眼藥水、口服 ketoconazole及後期口服類固醇後，角膜感染獲得了良好的控制。在經過21個月之追蹤後，未見有復發之跡象，而病患之最佳矯正視力可以達到 0.9。棘狀阿米巴角膜炎可以有類似泡疹感染之樹枝狀角膜炎表現，並可能因此延誤治療。早期診斷及適當治療是恢復視力及避免最終需要角膜全層移植術的最關鍵方法。(長庚醫誌 2002;25:201-6)

關鍵字：棘狀阿米巴角膜炎，類固醇，樹枝狀角膜炎，metronidazole。

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