

CASE REPORT

Three cases of *Acanthamoeba* keratitis diagnosed and treated in the early stage

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Abstract : *Acanthamoeba* keratitis (AK) is a severe infectious corneal ulcer that usually occurs in contact lens wearers. Although the number of AK cases in Japan has been increasing, many of these cases are diagnosed in the early stage and are treated adequately. This is probably because of the increased availability of various diagnostic techniques and the ever-increasing knowledge about AK among ophthalmologists. In this article, we described 3 cases of AK that were diagnosed and treated in the early stages of the disease, and we discuss why 1 of the cases had a less favorable prognosis than the other 2 cases, which had excellent prognoses, from an etiological point of view. *J. Med. Invest.* 56 : 166-169, August, 2009

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INTRODUCTION

Acanthamoeba keratitis (AK) is a rare corneal infectious disease that can cause severe complications in contact lens wearers. Previously, AK was frequently misdiagnosed as herpetic keratitis or keratomycosis and was thought to be an intractable type of corneal ulcer. Therefore, many AK patients would visit one eye clinic after another but would not be cured despite long term administration of several medications (1). In Japan, however, recent developments in diagnostic techniques and the increased knowledge about AK have facilitated early diagnosis and adequate treatment. Herein, we present 3 cases of AK that were diagnosed and treated in the early stages of the disease. Further, we review the differences in the disease course in these cases from an etiological point of view.

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CASES

Case 1

A 23-year-old male who used two-weekly disposable soft contact lenses visited a medical practitioner on September 21, 2007, presenting with conjunctival hyperemia and foreign body sensation in his right eye. He was administered various antimicrobial medications, including an ophthalmic solution of tobramycin 0.3% and moxifloxacin 0.3%, topical and systemic fluconazole, acyclovir 3% ointment and systemic valacyclovir, and fluorometholone 0.1% ophthalmic solution administered. Despite this treatment, his symptoms worsened. He was subsequently referred to Tokushima University Hospital on October 9, 2007. On his first visit to the hospital, the patient presented with a relatively strong pain in his right eye, and his visual acuity was (0.02) in right eye and (1.5) in left. The ocular tension was normal in both eyes. Slit-lamp examination of the right eye revealed radial keratoneuritis, multifocal stromal infiltrates and diffuse corneal edema, and marked ciliary injection (Fig. 1). Fungi flora Y[®] staining and immunostaining with a fluorescence

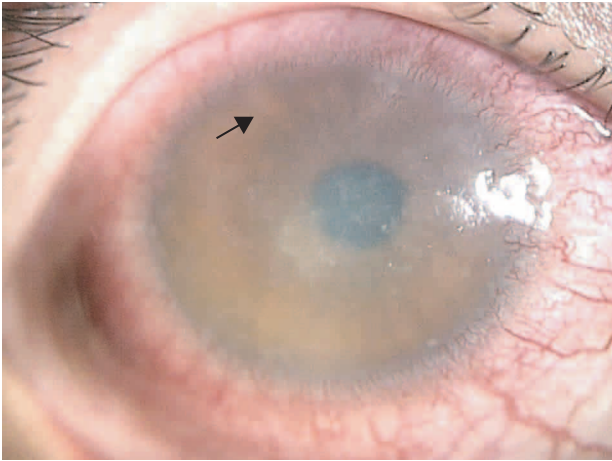


Fig. 1 Marked ciliary injection, multifocal stromal infiltrations, diffuse corneal edema, and radial keratoneuritis (→) in case 1

antibody to detect for herpes simplex virus suggested the presence of an *Acanthamoeba* cyst in the corneal scraping. An isolation culture was performed on the multi purpose solution that the patient used to clean and store his contact lenses. The culture, performed on a Bacto™ Agar plate containing Difco Bacto® yeast extract (Becton, Dickinson and Company Sparks, USA) revealed *Acanthamoeba* cysts and trophozoites (Fig. 2). Treatment for stage 2 AK (2)

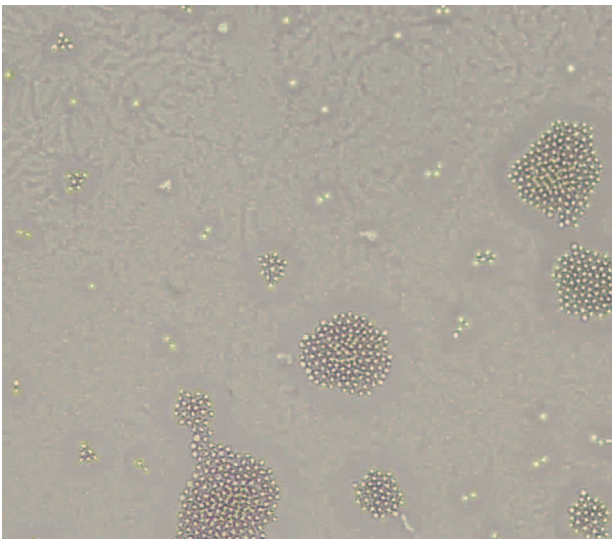


Fig. 2 Colonies of *Acanthamoeba* and moving tracks of trophozoites (original magnification 100×)

was initiated ; the treatment involved corneal scraping and frequent use of eye drops of chlorhexidine 0.02%, moxifloxacin 0.3% (5 times daily) and topical application of ofloxacin ointment 0.3% at bedtime. During a follow-up visit on October 22, the corneal

findings gradually improved, however marked ciliary injection persisted. The next examination on November 14 indicated recovery, after which the patient was lost to follow-up. Five months later, on April 14, 2008, the patient visited our hospital once again, presenting with marked ciliary injection and superficial punctate keratitis in the central area of his right cornea. Repeat treatment with the abovementioned medications reduced ciliary injection decreasing and increased visual acuity in the right eye to (0.1). A topical steroid, fluorometholone 0.1% ophthalmic solution, which is not commonly used to treat AK, was administered to treat persistent inflammation of the anterior chamber of the eye on October 22, 2008. Thereafter, the patient did not visit our hospital regularly.

Case 2

A 29-year-old female who used two-weekly disposable soft contact lenses developed pain and blurred vision in her right eye on March 25, 2007. She visited a medical practitioner on the next day and was administered levofloxacin 0.5% and bromfenac sodium 0.1% ophthalmic solutions to treat corneal edema and opacity. On March 26, she was referred to Tokushima University Hospital because of faint ring infiltration suggestive AK. On the first visit, she presented with a relatively strong pain in her right eye and visual acuity was (0.4) in the right eye and (1.0) in the left eye. Ocular tension was normal in both eyes. Slit-lamp examination of the right eye revealed faint ring infiltrates and marked ciliary injection (Fig. 3). Staining of the corneal epithelial specimen with Diff Quick® revealed the presence of an *Acanthamoeba* cyst. Treatment for stage 1 or early stage 2 AK was initiated ; this involved corneal

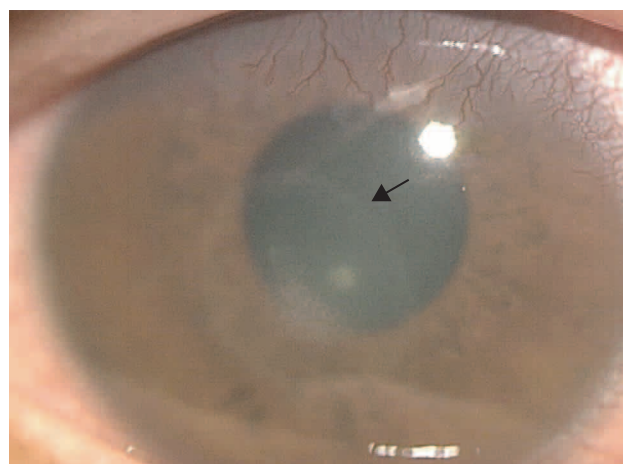


Fig. 3 Ciliary injection and faint ring infiltration (←) in case 2

scraping and the frequent use of eye drops of chlorhexidine 0.02% and levofloxacin 0.5% ophthalmic solution (5 times a day), and ofloxacin 0.3% ointment (twice a day). The corneal infiltration decreased gradually, and it disappeared completely on May 21, 2007.

Case 3

A 43-year-old female who used two-weekly disposable soft contact lenses visited a medical practitioner on October 2, 2007, presenting with a foreign body sensation and visual disturbance in her right eye. On the same day, a gatifloxacin 0.3% ophthalmic solution was administered to treat superficial punctate keratitis. An acyclovir 3% ointment was administered the following day. Three days later, linear and ring opacities were observed, and the patient was then referred to Tokushima University Hospital. On the first visit, she presented with an intense pain in the right eye, and her visual acuity was (0.4) in right and (1.0) in the left eye. Ocular tension was normal in both eyes. Slit-lamp examination of the right eye revealed ring infiltration, and marked ciliary injection (Fig. 4). We suspected AK because of

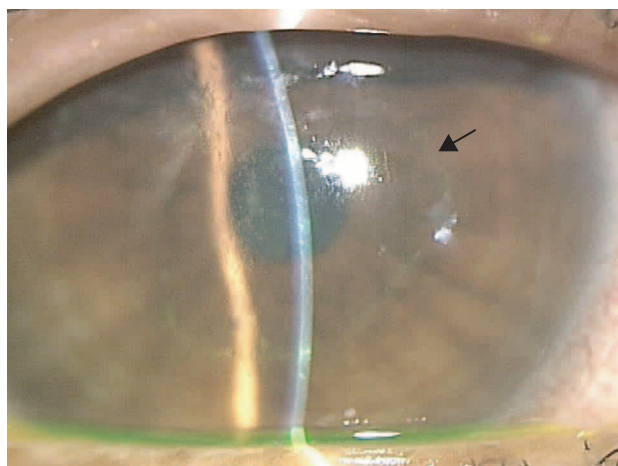


Fig. 4 Ring infiltration (←), superficial punctate keratopathy and ciliary injection in case 3

the ring infiltration and the intense pain in her eye. Specimen of a corneal epithelial scraping stained with fungi flora Y[®] revealed an *Acanthamoeba* cyst (Fig. 5). Treatment for stage 2 AK was initiated; this involved a corneal scraping and the use of hourly eye drops of chlorhexidine 0.02% during daytime and gatifloxacin 0.3% ophthalmic solution (5 times a day). Ten days later, ring infiltrates disappeared and the patient's visual acuity increased; but

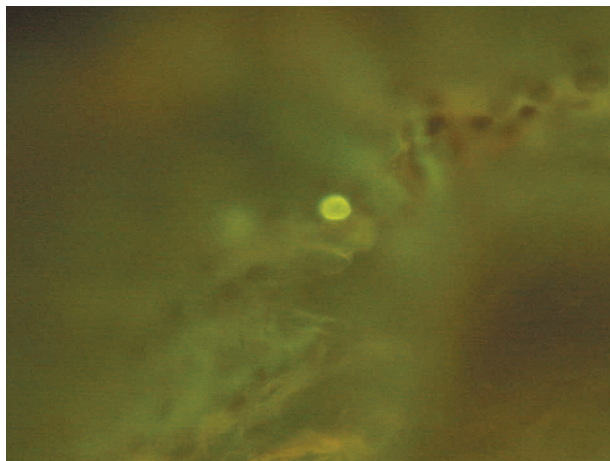


Fig. 5 Fungi flora Y[®] staining of *Acanthamoeba* cyst in corneal scraping in case 3 (original magnification 200×)

a radial keratoneuritis persisted. The visual acuity in her right eye increased to (1.5) seven days after the second visit, and all treatment was ceased on December 12, 2007.

DISCUSSION

Advanced stage AK is relatively easy to diagnose because of the presence of ring infiltrates or ring ulcers, which are most specific to AK (3) and the presence of *Acanthamoeba* cysts, which can often be detected in corneal specimens by light microscopy. On the other hand, the clinical features of early-stage AK are nonspecific and the condition may present with various morphological manifestations such as epithelial microerosions, irregularities, opacities, microcystic edema and stromal infiltrate. Although a radial keratoneuritis is thought to be pathognomonic for early-stage AK, a similar manifestation has also been reported in *Pseudomonas* keratitis previously (4). Therefore, it is possible to confuse the symptoms of AK with those of other corneal diseases, especially with herpetic keratitis as described in case 1. In recent years, however, the availability of various diagnostic techniques and the increased knowledge about AK presumably has facilitated early diagnosis and adequate treatments of the condition. This is reflected in cases 2 and 3, wherein the patients were referred to our hospital within 5 days after treatments were initiated by local medical practitioners. Furthermore, it is necessary to create awareness about the importance of the early diagnosis of AK because of potential increase in the number of cases of AK among young contact lens

wearers in Japan.

Since very specific and potent anti-*Acanthamoeba* drugs have not been available for years, various drugs such as neomycin, miconazole, ketoconazole, itraconazole, fluconazole, dibromopropamide, propamide isethionate, polyhexamethylene biguanide or chlorhexidine were used for the treatment of AK. Among them polyhexamethylene biguanide and chlorhexidine are thought to be best, because these two drugs are effective against not only trophozoites, but also cysts. However, medical treatment with these drugs are not always satisfactory. Therefore, recent recommended treatment for AK is a combination of corneal scraping, antifungal drugs and antibiotics. Meanwhile, the use of steroid for AK is pros and contras. Topical steroids are occasionally contraindicated because they can suppress the host immune response. If steroids can inhibit endocytosis as has been reported previously (5), they may prove beneficial for the treatment of AK in the very early stage. However, McClellan, *et al* (6). reported that exposure of *Acanthamoeba* trophozoite and cysts to dexamethasone increases the pathogenicity of these organisms. No standardized guideline describing the optimal protocol for AK treatment with topical steroid, i.e., the type of steroid to be used, appropriate time of treatment, and concentration has been established so far. Therefore, topical steroids ought to be used with caution only when the symptoms of infection are undoubtedly exclusive of the presence of *Acanthamoeba* trophozoite and cysts. In case 1, we used a fluorometholone 0.1% ophthalmic solution as an anti-inflammatory agent because no symptoms of infection remained after long-term treatment with non-steroidal drugs. However, in case 1, the use of topical steroids at the onset of anti-amoebic therapy probably contributed to the unsatisfactory prognosis.

Another possible reason for the poor therapeutic outcomes noted in case 1 is the poor patient compliance. The patient did not revisit the hospital for scheduled follow-up session but only revisited when the clinical symptoms recurred. Moreover, we assume that the patient may have discontinued the treatment and resumed wearing contact lenses as

per his own judgment. It is possible that we did not adequately emphasize to the patient the need for hospitalization, but we think that the patient's nature may have contributed to the poor clinical outcome. Currently, we lose a return appointment for his next examination.

In conclusion, excellent results can be obtained when the AK is appropriately treated in the early stage, as observed in cases 2 and 3. The best therapeutic outcome can be achieved with early diagnosis of AK, adequate treatment, and high level of patient compliance. If necessary, topical steroids can be used with caution when the patient has received sufficient anti-amoebic therapy, after the symptoms of the infections have disappeared. Hospitalization should be considered in cases of poor patient compliance.

REFERENCES

1. Ishibashi Y, Miyanaga Y : *Acanthamoeba* keratitis. *Nihon No Gannka* 79 : 721-726, 2008 (in Japanese)
2. Shiota H, Yano M, Kamada Y, Katayama T, Mimura Y : Classification of clinical stages of *Acanthamoeba* keratitis. *Japanese Journal of Clinical Ophthalmology* 48 : 1149-1154, 1994 (in Japanese)
3. Theodore FH, Jakobiec FA et al : The diagnostic value of a ring infiltrate in *Acanthamoeba* keratitis. *Ophthalmology* 92 : 1471-1479, 1985
4. Feist RM, Sugar J, Tessler H : Radial kerato-neuritis in *Pseudomonas* keratitis. *Archives of Ophthalmology* 109 : 774-775, 1991
5. Osato M, Robinson N, Wilhelmus K, Jones D : Morphogenesis of *Acanthamoeba castellanii* : titration of the steroid effect (abstract). *Investigation of Ophthalmology & Visual Science* 27 (Suppl) : 37, 1986
6. McClellan K, Howard K, Niederkorn JY, Alizadeh H : Effect of steroids on *Acanthamoeba* cysts and trophozoites. *Investigation of Ophthalmology & Visual Science* 42 : 2885-2893, 2001