CLINICAL FEATURES OF *ACANTHAMOEBA* KERATITIS IN CONTACT LENS WEARERS AND NON-WEARERS

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Abstract. Clinical presentations of patients with *Acanthamoeba* keratitis (AK) attending the Faculty of Medicine Siriraj Hospital during 1996-2006 were reviewed. The studied parameters included history of ocular trauma, use of contact lenses, associated eye diseases, systemic diseases, visual acuity, symptoms, signs, treatment, visual outcomes, and sequelae. Data were analyzed by comparing non-contact lens (nCL) and contact lens (CL) wearers with eachother. Twenty-two patients (24 affected eyes) (68.2% female) had AK, 9 (37.5%) were nCL and 15 (62.5%) were CL. Both groups had similar basic characteristics; however the nCL group was significantly older (48.3±14.5 *vs* 30.6±15.3 years old, p=0.006), and tended to have a longer duration of symptoms with more severe clinical findings, but this was not statistically significant. Eleven had severe ciliary injection (nCL 55.5%, CL 40.0%), 3 had satellite lesions (nCL 22.2%, CL 6.7%), 2 had radial keratoneuritis in the CL group (13.3%), 1 ring infillrate in the nCL group (11.1%) and 1 pseudodendrite in the CL group (6.7%). The mean duration of follow-up was 8.2±7.9 (ranging 0.3-29) months. Therapeutic measures included anti-*Acanthamoeba* medications (5/9 for nCL, 8/15 for CL), penetrating keratoplasty due to uncontrolled infections (1/9 for nCL, 2/15 for CL) and corneal perforation (1/9 for nCL), and enucleation due to endophthalmitis (1/9 for CL). At the last follow-up visit, the CL group had slightly better visual acuity (55.5% *vs* 66.7%). In conclusion, AK among patients who do not use contact lenses may have a delayed diagnosis, resulted in more severe ocular manifestations and poorer prognosis. Physicians should be aware of *Acanthamoeba* infection as a cause of keratitis in any patient, not just contact lens wearers. Long periods of follow-up are recommended to observe for recurrent episodes and proper management of AK patients.

Keywords: *Acanthamoeba* keratitis, clinical manifestation, contact lens wearers, non-contact lens wearers

INTRODUCTION

Acanthamoeba keratitis (AK) has been reported to be increasingly worldwide, not only among contact lens (CL) wearers in developed countries, but also in non-contact lens (nCL) wearers in developing countries (Joslin *et al*, 2006; Ibrahim *et al*, 2007; Carvalho *et al*, 2009). The incidence of AK among contact lens wearers has been increased since 2004, among patients with moisture plus contact lens solution, contaminated water, poor hygiene and inappropriate care of contact lenses (Joslin

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et al, 2007; Hasler *et al*, 2009; Por *et al*, 2009; Verani *et al*, 2009). The clinical outcome of AK depends on early diagnosis and proper treatment (Radford *et al*, 1998). AK is somewhat difficult to diagnose. The clinical features of AK can be confused with other infectious keratitis, such as herpes, fungal or bacterial infections. Since AK is often associated with contact lens wearing, ophthalmologists may misdiagnose cases among non-contact lens wearers delaying treatment until complications occur. As a result, patient may have a poor outcomes with long-term sequelae, such as sclerokeratitis or chorioretinitis (Moshari *et al*, 2001; Lee *et al*, 2002; Awwad *et al*, 2007a).

The diagnosis of AK is made by a positive culture or histopathological findings between 30-70% (Radford *et al*, 2002; Butler *et al*, 2005). The diagnosis of AK using culture may require some time, particularly in cases with few protozoa. The diagnosis of AK can be delayed due to bacterial or fungal coinfection. Confocal microscopy is a rapid, noninvasive diagnostic technique with high sensitivity and specificity, but requires a trained technician, experienced ophthalmologist and cooperative patients (Parmar *et al*, 2006; Tu *et al*, 2008a).

Proper treatment of AK requires long-term use of anti-*Acanthamoeba* medications. Relapse of the disease is common, since the amebic cysts resist treatment. The disease can relapse after penetrating keratoplasty (Perez-Santonja *et al*, 2003). Because of the increase in incidence and the difficulty in diagnosis and treatment, AK should be included in the differential diagnosis of all corneal ulcerations.

In Thailand, data regarding the clinical features and outcomes of AK are limited (Kosrirukvongs *et al*, 1999; Jongwutiwes *et al*, 2000). The present study was conducted to evaluate the clinical features, treatment, and complications of AK among Thai patients, comparing CL wearers with nCL wearers.

MATERIALS AND METHODS

This retrospective study was approved by the Institution Review Board of the Faculty of Medicine Siriraj Hospital, Mahidol University (No. Si 331/2007). Medical records from 22 patients diagnosed with AK by culture on non-nutrient agar overlaid with *Escherichia coli* between 1996 and 2006 were reviewed, including the cases of five patients previously reported in 1999 (Kosrirukvongs *et al*, 1999).

The study included all patients who had positive findings for *Acanthamoeba*, including corneal scraping specimens, contact lens pieces, contact lens solution in contact with lens cases, specimens examined under light microscope to identify living or stained amebae and specimens cultivated on non-nutrient agar overlaid with *Escherichia coli* (de Jonekheere and van de Voorde, 1977).

The studied parameters included demographic data, predisposing factors, associated eye diseases, systemic diseases, clinical manifestations, uncorrected and best corrected visual acuities (BCVA) using a Snellen chart, intraocular pressure, treatment, visual outcomes, and sequelae.

Data are presented as means ± standard deviation (SD), numbers (n) or percents, when appropriate. Data were analyzed using SPSS for windows version 13.0 (SPSS, Chicago, IL). Chi-square and Mann-Whitney U test were used for analyzing data comparing the nCL and CL groups. A p-value < 0.05 was considered statistically significant.

RESULTS

We reviewed 22 cases of AK, 20 monocular cases and 2 binocular cases; 11 right eyes (45.8%) and 13 left eyes (54.2%). Co-infection with bacteria was found in 8 eyes (33.3%); four of which had mixed bacterial infection (2 eyes had 2 species, and 2 eyes had 3 species). The co-infecting bacteria included *Pseudomonas aeruginosa* (n = 5), nonfermentative gram-negative rods (n = 4), *Stenotrophomonas maltophilia* (n = 3), *Serratia marcescens* (n = 2), *Klebsiella oxytoca* (n = 1), *Escherichia coli* (n = 1), and alpha hemolytic *Streptococcus* (n = 1).

The characteristics of the 22 patients are shown in Table 1. There were 8 patients (36.4%) in the nCL group, and 14 (63.6%) in the CL group. The mean age of the patients was 37.0±17.1 (range 17-76) years; the nCL group had a significantly older mean age (48.3±14.5 *vs* 30.6±15.3 years, p=0.006) than the CL group. Fifteen patients (68.2%) were female; the nCL group had a slightly lower proportion of female patients (50.0% *vs* 78.6%, p=0.343). No associated eye diseases were found more often in the CL group (50% *vs* 78.6%, p=0.076). Two patients had a history of ocular trauma: one (nCL) was injured by a piece of stick and the other (CL) was exposed to mud. Regarding the contact lens wearers, seven patients used monthly contact lenses, five patients used overnight contact lenses, and six patients had a history of improper care of contact lenses. The CL group consulted the ophthalmologist much earlier (within one week) than the nCL group did (nearly one month). Fifteen patients were admitted to the hospital for an average of 1.6±1.4 months; the nCL group tended to have a longer length of stay (2.4±1.7 *vs* 1.1±1.0 months, p=0.073). The mean duration of follow-up was 8.2±7.9 months, ranging from 0.3 to 29 months.

Data regarding the 24 affected eyes are shown in Table 2. There were 9 eyes (37.5%) in the nCL group, and 15 eyes (62.5%) in the CL group. Severe ciliary injection, satellite lesions, stromal melting, ring infiltrates and hypopyon were present at slightly higher frequencies in the nCL group than in the CL group, whereas radial keratoneuritis, pseudodendrite epithelial lesions, multiple subepithelial infiltrates and hazy or ground glass appearance were slightly more often encountered in the CL group, but without statistical significance. Corneal epithelial ulcers tended to be larger in size in the nCL group. A high intraocular pressure (secondary glaucoma) was found equally in both groups (33.3%).

Anti-*Acanthamoeba* eye drops (chlorhexidine, polyhexamethylene biguanide or propamidine) were not administered in 11 eyes due to delay in diagnosis and the patients were lost to follow-up before the results of *Acanthamoeba* cultivation were obtained (Table 3).

A penetrating keratoplasty was performed in four patients due to uncontrolled eye infection (nCL = 1 case, CL = 2 cases) and corneal perforation (nCL = 1 case). Enucleation was unavoidable in one CL patient due to endophthalmitis. This patient developed corneal infection after falling into a muddy pond and developed a coma for several days without removing the CL.

Table 4 shows the visual outcomes of the 24 affected eyes. Prior to treatment, none of the nCL group had a normal best corrected visual acuity (BCVA of 6/6) but 20% of the CL group did. After treatment, both groups had improvement in visual acuity (VA) but the proportion with normal BCVA was still lower in the nCL

Table 1
Demographic data of patients with *Acanthamoeba* keratitis.

Characteristics	*n* (%)		*p*-value
	nCL (8 cases)	CL (14 cases)	
Mean age ± SD (years)	48.3 ± 14.5	30.6 ± 15.3	0.006
Gender			
Male	4 (50.0)	3 (21.4)	0.343
Female	4 (50.0)	11 (78.6)	
Right eye	4 (44.4)	7 (46.7)	1.000
No associated eye disease	4 (50.0)	11 (78.6)	0.076
No systemic disease	5 (62.5)	10 (71.4)	0.203
Duration of admission ± SD (months)	2.4 ± 1.7	1.1 ± 1.0	0.073
Duration of symptoms before consultation ± SD (days)			
Red eye	24.9 ± 22.9	6.9 ± 8.6	0.149
Painful eye	26.7 ± 30.3	6.7 ± 9.2	0.684
Decreased vision	30.3 ± 24.6	6.6 ± 6.9	0.234

nCL, non-contact lens wearers; CL, contact lens wearers

Table 2
Clinical features of patients with *Acanthamoeba* keratitis.

Clinical features	*n* (%)		*p*-value
	nCL (9 eyes)	CL (15 eyes)	
Ocular symptoms			
Decreased vision	9 (100)	9 (60.0)	0.052
Red eye	7 (77.8)	14 (93.3)	0.533
Painful eye	5 (55.5)	13 (86.7)	0.150
Ocular signs			
Severe ciliary injection	5 (55.5)	6 (40.0)	0.675
Epithelial defect	7 (77.8)	10 (66.7)	0.669
Microcystic epithelial edema	3 (33.3)	2 (13.3)	0.326
Ground glass appearance	2 (22.2)	8 (53.3)	0.210
Satellite lesion	2 (22.2)	1 (6.7)	0.533
Stromal edema	1 (11.1)	1 (6.7)	1.000
Multiple subepithelial infiltrate	0 (0)	2 (13.3)	0.511
Radial keratoneuritis	0 (0)	2 (13.3)	0.511
Pseudodendrite	0 (0)	1 (6.7)	1.000
Ring infiltrate	1 (11.1)	0 (0)	0.375
Stromal melting (perforation)	1 (11.1)	0 (0)	0.375
Hypopyon	3 (33.3)	3 (20.0)	0.635
Secondary glaucoma	3 (33.3)	5 (33.3)	1.000
Corneal epithelial ulcer area ± SD (mm^2)	20.6 ± 18.6	12.0 ± 12.9	0.240
Mean intraocular pressure at the first visit ± SD (mmHg)	20.0 ± 2.8	13.4 ± 5.7	0.145

nCL, non-contact lens wearers; CL, contact lens wearers

Table 3
Treatments of patients with *Acanthamoeba* keratitis.

Treatments	*n* (%)		*p*-value
	nCL (9 eyes)	CL (15 eyes)	
No anti-*Acanthamoeba* medication	4 (44.4)	7 (46.7)	1.000
Only antibiotic	1 (11.1)	6 (40.0)	0.191
Only antifungal	2 (22.2)	0 (0.0)	0.130
Antibiotic + antifungal	1 (11.1)	1 (6.7)	1.000
With anti-*Acanthamoeba* medication	5 (55.6)	8 (53.3)	1.000
Only anti-*Acanthamoeba*	2 (22.2)	0 (0.0)	0.130
Antibiotic + anti-*Acanthamoeba*	2 (22.2)	6 (40.0)	0.657
Antibiotic + antifungal + anti-*Acanthamoeba*	1 (11.1)	2 (13.3)	1.000

nCL, non-contact lens wearers; CL, contact lens wearers

Table 4
Visual acuities before and after treatment in *Acanthamoeba* keratitis patients.

Visual acuities	*n* (%)		*p*-value
	nCL (9 eyes)	CL (15 eyes)	
Before treatment			0.358
BCVA 6/6	0 (0)	3 (20.0)	
6/9-6/36	3 (33.3)	4 (26.7)	
≤ 6/60	6 (66.7)	8 (53.3)	
After treatment			0.313
BCVA 6/6	1 (11.1)	6 (40.0)	
6/9-6/36	6 (66.7)	5 (33.3)	
≤ 6/60	2 (22.2)	4 (26.7)	
Improved VA	5 (55.5)	10 (66.7)	0.678

nCL, non-contact lens wearers; CL, contact lens wearers; BCVA, best corrected visual acuity; VA, visual acuity

group than the CL group (11.1% *vs* 40.0%).

DISCUSSION

In this study of Thai patients, AK was found more frequently among CL wearers than nCL wearers. However, patients in the nCL group had more ocular signs and symptoms, and poorer outcomes. This may be due to a delay in diagnosis and treatment. The nCL patients were older and tended to have more associated systemic diseases and eye diseases.

The clinical features of AK may lead to misdiagnoses of other microbial keratitis, including herpes, fungal, bacterial, and mixed infections (Srinivasan *et al*, 1997; Hargrave *et al*, 1999; Rumelt *et al*, 2000; Sharma *et al*, 2000; Rumelt *et al*, 2001;

Radford *et al*, 2002; Perez-Santonja *et al*, 2003). Findings highly suspicious for AK include radial keratoneuritis, herpes like infiltrations, and corneal ring infiltrations, particularly in patients with negative results for fungal or bacterial infection. Diagnosis of AK requires a laboratory investigation to identify the organism. It is noteworthy, we found 33% of AK had co-infection with at least one bacterium. Therefore, the final diagnosis of infectious keratitis should not rely solely on initial positive results of microbial culture. Clinicians should review laboratory findings promptly. Although bacterial growth may be initially reported, investigation for *Acanthamoeba* is still suggested because of the possibility of co-infection. AK should be considered in patients with infectious keratitis that have partial or no response to antimicrobial therapy. Ophthalmologists should consider AK in patients with chronic corneal ulcers where laboratory results show no growth. AK patients need specific, appropriate treatment and long-term follow-up. Although some AK patients in our study respond well with only antibiotic and/or antifungal medication, long term follow-up is still necessary to observe for recurrent episodes. Long duration combined medical therapy should be given to eradicate infection. (Sun *et al*, 2006; Awwad *et al*, 2007b; Thebpatiphat *et al*, 2007; Tu *et al*, 2008b).

We found AK patients in the CL group had shorter duration of eye symptoms prior to consultation, less severe clinical features, and better improvement in visual outcomes. These may result from awareness of ophthalmologists for early detection of AK among contact lens wearers. Our findings are different from a previous study where the delay in diagnosis of AK was nearly a month in the CL group, resulting in more severe ocular manifestations with ring infiltrates in up to 50% (Butler *et al*, 2005). Similar to other studies, patients with delayed diagnosis had ring infiltrates, worse visual outcomes and required surgical treatment (Sharma *et al*, 2000; Radford *et al*, 2002). Patients with deep stromal infiltration and ring infiltrates had worse visual results than those with epithelial infiltration (Tu *et al*, 2008b). Contrary to another report, severe cases of ring ulcers or stromal infiltrations accounted for 40% of CL wearers and had worse visual results (Thebpatiphat *et al*, 2007). These might be due to an initial misdiagnose of herpes keratitis (70%).

Compared to previous reports, the present study had fewer cases of complications, including secondary glaucomas, corneal perforations, and endophthalmitis. This might be due to the fact the patients were lost to follow-up during the initial phase of treatment.

A limitation of the present study was the small sample size. There was not enough power to detect statistical significance in many parameters that seemed to have clinical significance. A number of patients were also lost to follow-up and did not receive appropriate medication.

AK is a devastating ocular infection. AK in nCL patients tends to be more severe and have a poorer prognosis than that in CL users. This may be due to delayed diagnosis. Therefore, physicians should be aware of AK as a cause of keratitis, even in those not wearing contact lenses.

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