VOLUME-6 | ISSUE-2 | FEBRUARY-2017 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 78.46

CLINICAL CHARACTERISTICS AND THERAPEUTIC OUTCOME IN ACANTHAMOEBA KERATITIS

Ophthalmology

KEYWORDS: Acanthamoeba keratitis, culture, epidemiology, microscopy, risk factors.

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ABSTRACT

Purpose : To report the clinical characteristics, predisposing factors and therapeutic outcome in a series of patients diagnosed with acanthamoeba keratitis(AK).

Materials and Methods: The data was collected from the clinical records of patients admitted with infective keratitis at Regional Institute of Ophthalmology, Trivandrum from December 2012 to May 2013. In this retrospective case series analysis, medical and microbiology records of forty consecutive patients with acanthamoeba keratitis(AK) were reviewed and analyzed. All cases with a micro biologically proven acanthamoeba corneal infection either by direct microscopy or by culture following standard protocols were included for analysis.

Results: Among the 40 patients,thirty four patients had coexistent fungal keratitis and four were isolated AK. Sixty percentage of patients had a predisposing factor with history of trauma or contact with foreign bodies. No patients in our series were contact lens users. Twenty two patients (55%) had central corneal ulcers with size greater than 3mm.Twenty three patients (57.5%) had a best corrected visual acuity(BCVA) less than 6/60 at presentation. Majority (80%) of these patients responded well with adequate healing of ulcer and visual improvement(60%) to a combination therapy of Chlorhexidine 0.02% and Neomycin (98%).

Conclusion: Till recently acanthamoeba infections were considered as a rare cause for infective keratitis compared to fungal and bacterial keratitis in this part of the world. This recent report highlights a significant rise in occurrence of Acanthamoeba keratitis among our corneal ulcer patients. Most of the patients in our series lacked the typical clinical characteristics of acanthamoeba keratitis. High index of clinical suspicion helped us in the accurate diagnosis of this co existing mixed parasitic infection. Addition of specific amoebicidal drugs like Chlorhexidine and Neomycin or Poly hexa methylene biguanide to the conventional anti fungal therapy gave very good response with favorable therapeutic outcome in majority of these patients, as demonstrated in our series.

Acanthamoeba is an ubiquitous free-living protozoa of the subphyla Sarcodina. [1,15] Because of the wide spread distribution of this parasite in the environment, human contact with the organism is very common[2,3,10]. Ocular infection by Acanthamoeba is reported more from developed countries including USA and UK.[10,13] Acanthamoeba keratitis is a potentially devastating corneal infection leading to severe visual loss. This vision threatening disease shows wide geographic variations and several outbreaks had been reported worldwide mostly through contaminated contact lens solutions or through domestic water sources. However, in developing countries important risk factors are either trauma or exposure to contaminated water [4,7,11]. An understanding of the region-wise epidemiological features and risk factors of Acanthamoeba keratitis will be of great help in the diagnosis, prevention and appropriate management of this disease entity.

The purpose of this study was to determine the clinical features, risk factors, epidemiological characteristics and therapeutic outcome of Acanthamoeba keratitis in a series of patients presenting at a tertiary eye care referral center in the southernmost part of India (Thiruvananthapuram, Kerala).

Materials and Methods

A retrospective case series study of 40 consecutive cases of micro biologically confirmed Acanthamoeba infections among the total 264 infective keratitis cases, treated at Regional Institute of Ophthalmology, Thiruvananthapuram, Kerala, South India over a period of 6 months from December 2012 to May 2013 were included for analysis. Clinical and microbiological data of the study population was collected after obtaining the approval of Institutional Review Board.

A standard protocol of data collection was followed for each patient. Socio-demographic features, duration of symptoms, predisposing factors, clinical features, associated ocular conditions, systemic diseases and previous treatment data were collected. All patients were examined under the slit-lamp biomicroscope. The size of the epithelial defect and depth of the stromal infiltrate were measured with the variable slit beam and recorded in millimeters and documented diagrammatically. The presence or absence of a hypopyon was recorded and the height measured in millimeters. Specific predisposing factors for corneal ulceration including trauma, use of contact lenses, topical steroid use and the nature of domestic water sources were enquired and documented.

Specimens for smear and culture were obtained by scraping the corneal ulcer under aseptic conditions using sterile number 15 BP blade following instillation of 0.5% proparacaine hydrochloride in the conjunctival sac. The material was scraped under slit lamp from the edge and the base of each ulcer, spread onto labeled slides in a thin, even manner to prepare a 10% potassium hydroxide (KOH) or normal saline wet mount, Gram-staining and Giemsa-staining and direct microscopy was performed without any delay in our laboratory. The remaining specimen was inoculated onto the surface of solid media such as 7% sheep blood agar, chocolate agar, Sabouraud dextrose agar and nonnutrient agar with E. coli overlay in a row of "C"-shaped streaks. Acanthamoebae infections confirmed either by direct microscopy and or culture were included for this analysis. Microbiological diagnosis of acanthamoeba was based on presence of specific microscopic features of trophozoites including it's motility and presence of double walled cysts for immobile acanthamoeba cysts under the low-power (10 X) objective using a light microscope. Amoebal migration tracks, bacterial clearing show where the amoeba have been grazing were the other signs considered to be positive for Acanthamoeba growth in culture media. The fungal and bacterial cultures were considered positive if growth of the same organism was demonstrated on more than one solid phase medium and/or if there was confluent growth at the site of inoculation on one solid medium and/or if growth of one medium consistent with direct microscopy findings. All laboratory procedures followed standard recommended protocols.

All microbiologically confirmed acanthamoeba keratitis were treated with combinations of reconstituted chlorhexidine 0.02% and neomycin eye ointment. Propamidine(Golden eye drops) were also added in a few non healing AK cases. Mixed infective keratitis were treated with additional topical antifungal therapy using topical Natamycin 5% and Voricanazole eye drops. Broad spectrum antibiotic eye drops, cycloplegics, antiglaucoma measures, systemic antifungal therapy and other supportive treatment with analgesics were given based on individual case requirements.

For the purpose of analysis, the corneal ulcers were grouped to mild, moderate and severe according to size of ulcer in millimeters, location and severity of associated anterior segment inflammation. Corneal ulcers with a size less than 3mm, peripheral corneal location and less than 2+ cells in anterior chamber were graded as mild, those with a size more than 3 upto 5mm, central or paracentral in location and 3+ or above cells in anterior chamber were graded as moderate in severity. All corneal ulcers above 5 mm in size, located anywhere on cornea with or without hypopyon were graded as severe ulcers.

Therapeutic outcome measures were defined as good or poor according to healing response, course of illness and visual outcome. Ulcers healed with opacification with medical treatment were considered as good healing response and those which progressed to complications or required surgical intervention while on treatment were considered as poor outcome. Course of illness was graded according to duration of hospital stay as <2 weeks,2-4 weeks and >4 weeks. Best corrected visual acuity(BCVA) at time of admission and after treatment were documented and included for outcome analysis. Cases with prolonged hospital stay for more than 4 weeks and occurrence of complications while on treatment with reduction in final BCVA were reported as poor outcome. Favorable outcome was reported on cases with less hospital stay showing adequate healing with opacification and stable or improved BCVA after treatment.

Results

During the study period, a total of 264 patients were micro biologically evaluated for infective keratitis in our Institute. Among them, presence of acanthamoebae infections were confirmed in 40 patients by direct microscopy (n=24) or by culture (n=16).

Microbiological data analysis showed that among the 40 patients positive for acanthamoeba, majority had co existing polymicrobial infections (n=36). In our series, acanthamoeba infections were coexisting with fungal keratitis in majority of patients. (34/40). Four patients had isolated acanthamoeba keratitis and 2 patients had mixed infections. Among fungal keratitis, fusarium species (19/40) showed predominance over aspergillus infections (11/40). The two cases of mixed keratitis had co existing bacterial infections also.

Figure 1: MICROBIOLOGICAL ANALYSIS OF AK

Acanthamoeba infections were predominant (65%) among males (n=26) compared to females (n=14). Majority of affected patients in our series were adults in the working age group. Twenty six patients in our series (65%) belonged to 30-60 years age group and 13 patients (32.5%) were above 60 years of age. Fifty seven percentage of study population were engaged in outdoor occupations (n=23).

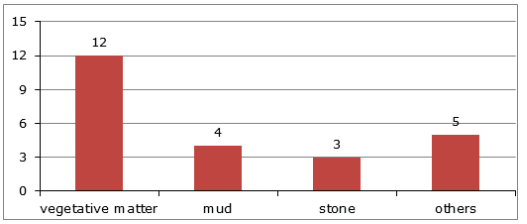
Table 1: DEMOGRAPHIC DATA

DEMOGRAPHIC FACTORS	*Number of cases*
GENDER	
MALE	26
FEMALE	14
TOTAL	40
AGE	
<30 yrs	1
30-60yrs	26
>60yrs	13
TOTAL	40

A positive history of trauma or contact with foreign bodies was the major predisposing factor in 60% of patients (n=24). Among this group of patients, twelve patients(50%) gave history of contact with vegetative matter, 4 patients with mud and 3 patients with stone particles. (Figure 2). None of the patients in our series were using contact lenses.

Seventy five (n= 30) percentage of patients in our series were from rural areas and the rest were from semi urban areas. All patients in our series were using well water for their domestic purposes and a few patients also gave exposure to water from ponds and lakes while at work.

Figure:2 PREDISPOSING FACTORS



Majority (55%) had severe vision threatening keratitis with involvement of visual axis and stromal ulceration (n=22). Among them, eleven patients had large corneal abscess with hypopyon (27.5%). Among the rest, nine patients had moderate severity (22.5%) with mid peripheral location of ulcer and significant associated anterior chamber inflammation. Nine patients had small peripheral ulcers with minimal anterior chamber inflammation(22.5%).

Seventy five percentage (n=30) of patients had pre treatment from local hospitals with antibiotic and antifungal eye drops before seeking care from our centre. Also about 60% of patients (n=18) among them were treated at our institute as fungal keratitis initially as scrapings were positive only for fungi. Repeat scrapings from the above 18 poorly responding cases demonstrated acanthamoeba parasites subsequently. In two cases where surgical intervention was needed, diagnosis of acanthamoeba infection was possible only by culture of the corneal button or anterior chamber aspirate.

Once presence of acanthamoeba infections were confirmed by microscopy or culture, all patients were treated with topical amoebicidal drugs.Thirty eight patients (95%) were treated with combinations of reconstituted Chlorhexidine 0.02% eye drops and Neomycin eye ointment. Two patients showing very poor response were given PolyHexaMethyleneBiguanide 0.02% eye drops in addition to above combination. Coexistant fungal and bacterial keratitis were treated with topical Natamycin 5% and or Voriconazole eye drops and fortified or broad spectrum antibiotic drops respectively as per requirement along with other supportive measures.

BCVA was poor in majority of patients at presentation and 23 patients (57.5%) had a best corrected visual acuity less than 6/60 to hand movements, nine patients (22.5%) had vision in range 6/24-6/60 and eight patients had BCVA better than 6/18. (Table:3).

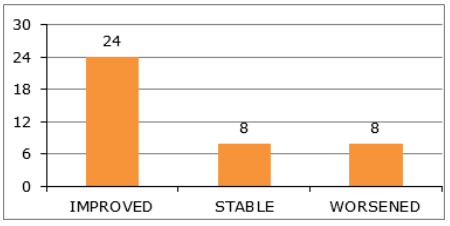
Following treatment, 60% patients (n=24) showed improvement in vision ,20% patients had stable vision(n=8) and 20% patients showed worsening in vision(n=8) (Figure 4)

Chronic course of illness was noted in 40% patients(n=16) as inpatient hospital care and disease course was prolonged for more than 4 weeks, 50% patients (n=20) had adequate healing response within 2-4 weeks and 10% patients(n=4) got cured of the disease in less than 2 weeks.

TABLE 3:VISION AT PRESENTATION

<6/60	23
6/24-6/60	9
Up to6/18	8

Figure:4 VISION OUTCOME



Therapeutic outcome analysis showed good response with adequate

healing and opacification in 80% patients (n=32) with either improvement (n=24)or stabilization (n=8) of BCVA. Eight patients (20%) with poor healing response and worsening needed surgical interventions (n=4) or progressed to complications (n=4) including perforation.

Subgroup analysis of the ulcers which showed poor therapeutic response (n=8) revealed that all of them were of severe grade with stromal ulceration and presented to us very late and had predominant cyst infections on direct microscopy. Among them four patients had to undergo therapeutic keratoplasty for control of infection. One patient also had recurrence of disease in graft and had to have a repeat tectonic corneal grafting later. Two patients refused any surgical intervention and one patient ended up in perforation and lost the eye.

DISCUSSION

Acanthamoeba keratitis is a growing clinical problem both in developed and developing countries[1,15,17].Indian studies reported a prevalence rate of 1 to 4% for acanthamoeba keratitis among culture positive corneal ulcers [4,7,11,12].

Unlike previous reports from south India, majority of patients with AK in our series had poly microbial infections with super added fungal keratitis in majority (n=36). Mixed parasitic and bacterial keratitis have been reported in literature before[16,14] but co existing fungal and acanthamoeba infections are rarely reported. Published reports from developed countries are mostly acanthamoeba infections associated with contact lens use or on pre existing viral keratitis.[7,13]

Acanthamoeba organisms exist in two forms, the active trophozoite form and the resting cystic form. The cystic form is dormant and is resistant to desiccation, extreme temperature and chemicals. The cysts do not exhibit any movements and may remain viable for many years until they are exposed to a food source, where they again assume the trophozoite form.[7,10,13]

Acanthamoeba is encountered in large numbers where other microorganisms are abundant and it has been reported as a waterborne pathogen. Outbreaks of acanthamoeba keratitis from contaminated water sources has been reported in literature from many parts of the world. [2,3,10]

Higher incidence of fungal keratitis due to the humid conditions in this part of the world may be an important reason for increased number of mixed infections with parasite and fungi, observed in our study group.

Corneal injury was the most important predisposing factor in our series which is in accordance with earlier reports from other parts of South India [7,11]. Interestingly none of our patients in this series had a history of contact lens use [11].

With an aim to identify the specific predisposing factor for AK, we collected data regarding the source of water for domestic purposes from these patients. Ninety five percentage of our patients were from rural areas and were using ground water(well water) for their domestic purposes. Many patients also gave history of contact with muddy water and water from ponds and lakes. Polluted domestic water sources may be an important source for acanthamoeba infections in our patients. It has been suggested in many earlier studies that co contamination of Acanthamoeba with a bacterial species is capable of supporting amebic growth in any medium [2,3,10].

Another observation we noted in our study group is lack of classic features of acanthamoeba keratitis as described in literature such as peri neural or ring infiltrates [7,15]. Pain was characteristically present in most ulcers in our series. Presence of co existent fungal infections might have masked the characteristic clinical features of acanthamoeba keratitis.

Among many of our patients microbiological diagnosis of acanthamoeba was obtained after repeated scrapings. This highlight the importance of clinical suspicion for this parasitic infection and to look for them in all non healing ulcers where specific anti microbial therapy is not giving expected therapeutic response. The high index of clinical suspicion of mixed infections and if possible discussions with your microbiologist to look for acanthamoeba is recommended even though an organism is isolated earlier.

The treatment with combination amoebicidal drugs showed good clinical response with adequate healing with opacification[5,6]. Ten percentage of patients underwent surgical intervention as compared to a western report where 35% required surgical intervention. Progression of ulcer to complications occurred in 20% patients and half among them had surgical intervention.

In our series adequate therapeutic success with medical treatment alone was achieved in majority of patients. High index of clinical suspicion,repeat microbiological examinations, early and accurate diagnosis and execution of appropriate therapy with specific anti parasitic medications helped us achieving good therapeutic results in this otherwise blinding parasitic corneal infection.

Conclusion:

Diagnosis and management of acanthamoeba keratitis remains challenging for ophthalmologists worldwide. Till recently AK is considered as a rare cause for microbial keratitis in India. But current report suggest a rising trend and the high possibility of concurrent acanthamoeba infections in patients with fungal keratitis. High index of clinical suspicion and repeated microbiological evaluations in all non healing ulcers will help in identifying this causative organism. Polluted domestic water sources including wells and water storage tanks facilitates the growth of acanthamoebae. This fact highlight the importance of maintaining high water quality standards and proper environmental hygiene in order to prevent this devastating corneal infection.

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