Clinical and demographic study of microsporidial keratoconjunctivitis in South India: a 3-year study (2013–2015)

Rohan Agashe,[1] Naveen Radhakrishnan,[1] Sayali Pradhan,[1] Muthiah Srinivasan,[1] Venkatesh N Prajna,[1] Prajna Lalitha[2]

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[1]Department of Cornea and Refractive Services, Aravind Eye Hospital, Madurai, Tamil Nadu, India
[2]Department of Ocular Microbiology, Aravind Eye Hospital, Madurai, Tamil Nadu, India

Correspondence to
Dr Prajna Lalitha, Department of Ocular Microbiology, Aravind Eye Hospital, 1, Anna Nagar, Madurai 625020, Tamil Nadu, India; lalitha@aravind.org

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ABSTRACT

Aim To study the demographic profile, clinical features, treatment outcome and ocular morbidity of smear-positive microsporidial keratoconjunctivitis.

Methods Retrospective case series of all patients with clinical features of microsporidial keratoconjunctivitis and who were smear positive for the same on Gram stain from January 2013 to December 2015. Demographic data, predisposing factors, microbiological investigations, clinical course and visual outcome were analysed.

Results Of the 10 655 patients with conjunctivitis, 550 (5.2%) patients were positive for microsporidia on Gram stain during this time period. The disease was prevalent throughout the year with an increased incidence from July to December. Bilateral involvement was seen in 27 (4.9%) patients. There was no predisposing risk factor in 428 (77.8%) patients. 384 (69.1%) patients had received prior treatment before presentation to us with the most common drug being antibiotic in 285 (49.4%) patients. All the patients underwent diagnostic corneal debridement and received topical 0.3% fluconazole eye drops four times a day. Of the 296 patients who followed-up, 187 (63.1%) patients had complete resolution without sequelae. 68 (22.9%) had persistent superficial punctate keratopathy, 30 (10.1%) developed subepithelial nummular keratitis. No significant change in visual acuity was seen in 255 (80.7%) eyes, two or more line improvement was seen in 48 (15.2%) eyes, while two or more line worsening was seen in 13 (4.1%) eyes.

Conclusions Microsporidial keratoconjunctivitis is prevalent in South India throughout the year. The characteristic clinical signs and simple microbiological investigation help us to differentiate it from adenoviral keratoconjunctivitis. The visual prognosis is good.

INTRODUCTION

Microsporidia are a diverse group of obligate spore-forming intracellular eukaryotes that are closely related to fungi, causing keratoconjunctivitis and stromal keratitis.[1] The awareness of keratoconjunctivitis caused by microsporidia is increasing and more cases are being reported in the last decade.[2] Recent large volume case series have reported microsporidial keratoconjunctivitis in healthy individuals, which differs from the early reports of microsporidiosis in immune-compromised individuals.[3–7] Previous reports also show a seasonal trend in the occurrence with the majority of keratoconjunctivitis occurring during the monsoon.[8]

Several observational case reports have studied the effects of topical antimicrobial agents like chlorhexidine,[3] ciprofloxacin,[3] moxifloxacin,[9] voriconazole,[10] polyhexamethylene biguanide (PHMB),[8] fumagillin,[11] oral albendazole,[12 13] oral itraconazole[14 15] and procedures like repeated corneal swabbing[16] for the treatment of microsporidial keratoconjunctivitis. Microsporidial keratoconjunctivitis although more prevalent, is often misdiagnosed as adenoviral keratoconjunctivitis and is under-reported due to the lack of literature.[8] The aim of our study was to analyse the demographic profile, clinical features, treatment outcome and ocular morbidity of smear-proven microsporidial keratoconjunctivitis in South India.

MATERIALS AND METHODS

The retrospective retrieval of patient data was performed after obtaining permission of the Institutional Review Board of Aravind Eye Hospital, Madurai. The records of patients with clinical features of keratoconjunctivitis who presented to Aravind Eye Hospital, Madurai between January 2013 and December 2015 and who were positive on Gram smear for microsporidiosis were reviewed to assess the demographic data, predisposing factors, clinical course, treatment and visual outcomes. The number of cases occurring each month was also recorded.

All patients with keratoconjunctivitis underwent a comprehensive slit lamp examination by a cornea specialist. After documenting the clinical characteristics, all eyes with typical clinical features of microsporidial keratoconjunctivitis like coarse superficial punctate epithelial keratitis (figure 1) were subjected to corneal scraping for Gram stain. Under topical anaesthesia with 0.5% proparacaine, corneal scrapings were obtained using sterile cotton tipped swab and the material was smeared on a glass slide and was subjected to Gram stain. In patients with bilateral involvement, the eye with more significant involvement was scraped. Patients who were positive on smear for microsporidiosis were treated with topical 0.3% fluconazole eye drops (Zocon, FDC, India) four times a day till the resolution of the disease.

Statistical analysis was done using statistical software STATA V.11.0, USA. Continuous variable were expressed as mean (SD) and categorical variable were expressed as frequency (percentage).

RESULTS

Of the 10 655 patients with conjunctivitis, corneal swabbing was done in 915 (8.6%) patients with clinical suspicion of microsporidial keratoconjunctivitis,

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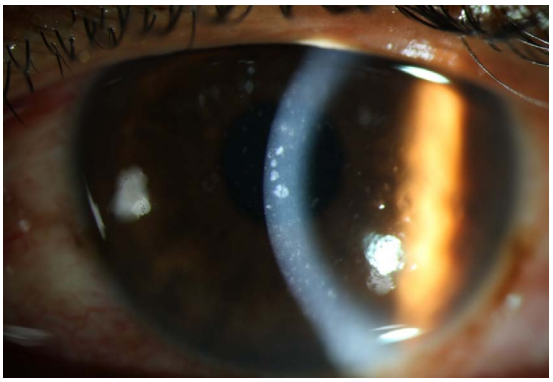

Figure 1 Slit lamp image showing the coarse superficial punctate keratitis typically seen in microsporidial keratoconjunctivitis.

of which 550 (60.1%) patients tested positive for microsporidia on Gram smear and were included in this study. The smear positivity rate was 60.1%. Bilateral involvement was seen in 27 (4.9%) patients. The age of the patients ranged from 6 to 85 years (mean±SD: 36.14±15.79) with a slight male preponderance (305, 55.5%). The temporal distribution of prevalence is shown in figure 2 with a peak in the month of November (71, 12.9%), which is the period for the north-west monsoon in this geographical area. There was significant increase in the occurrence of microsporidial keratoconjunctivitis in the last 6 months of all 3 years (2013: p=0.0001, 2014: p=0.0001, 2015: p=0.0003; table 1). Further analysis of the incidence of smear-positive microsporidial keratoconjunctivitis for the last 10 years was done, which showed a statistically significant steep increase in the incidence of smear-positive microsporidial keratoconjunctivitis with stabilisation over 2012–2015 (p=0.0001; see table 2 and online supplementary figure S1).

The mean time to presentation from the onset of symptoms was 6.5 days (1–30 days). Most of the patients did not have recall of any risk factors (428; 77.8%). History of risk factor was present in 83 patients, of which fall of dust was seen in 70 (12.7%) patients and fall of insect in 13 (2.4%) patients (table 3). None of the patients used contact lens. Of the 550 patients, 166 (28.8%) did not receive any prior treatment, 285 (49.4%) had received topical antibiotics, the most common being chloramphenicol (72, 25.4%), 69 (12%) had received topical steroids, 43 (7.5%) had received topical antiviral medications and 71 (12.3%) were treated with lubricants. Presenting symptoms included redness, irritation, watering, eye pain, lid swelling, foreign body sensation and decrease in vision. All patients presented with greyish white coarse diffuse superficial punctate keratitis, which could be removed with a sterile cotton tipped swab.

Table 1 Comparison of the occurrence of smear-positive microsporidial keratoconjunctivitis between the first and second 6 months of 2013–2015

Year	Microsporidial keratoconjunctivitis, n (%)		Total	p Value*
	January–June	July–December		
2013	60 (34.3)	115 (65.7)	175 (100.0)	<0.0001
2014	62 (31.2)	137 (68.8)	199 (100.0)	<0.0001
2015	64 (36.4)	112 (63.6)	176 (100.0)	0.0003

*One sample proportion test.

Of the 550 patients, 296 (53.8%) came for follow-up. Mean follow-up period was 3 weeks (range: 2 days to 16 weeks). Of the 296 patients who followed-up, 187 (63.1%) patients resolved completely without any sequelae. Of the patients who did not resolve, 68 (22.9%) had persistent superficial punctate keratopathy, 30 (10.1%) developed subepithelial nummular keratitis, 22 (7.4%) had persistent conjunctivitis, 3 (1%) developed uveitis and 3 (1%) patients had subsequent other eye involvement. Patients with uveitis were treated with topical prednisolone acetate 1% eye drops and cycloplegics along with 0.3% fluconazole eye drops. Steroids were tapered based on clinical resolution. Patients with persistent superficial punctate keratopathy and persistent conjunctivitis were continued on topical 0.3% fluconazole eye drops. The symptoms abated slightly with treatment but did not resolve completely. These patients were subsequently lost to follow-up.

Of the 316 eyes of 296 patients who followed-up, the visual acuity by Snellen chart at 4 weeks was 6/9 or better in 221 (69.9%) eyes, 6/12–6/18 in 64 (20.3%), 6/24–6/60 in 24 (7.6%) and <6/60 in 7 (2.2%) eyes. Among patients who followed-up, no significant change in visual acuity (±1 line change) was seen in 255 (80.7%) eyes, two or more line improvement was seen in 48 (15.2%) eyes, while two or more line worsening of visual acuity was seen in 13 (4.1%) eyes.

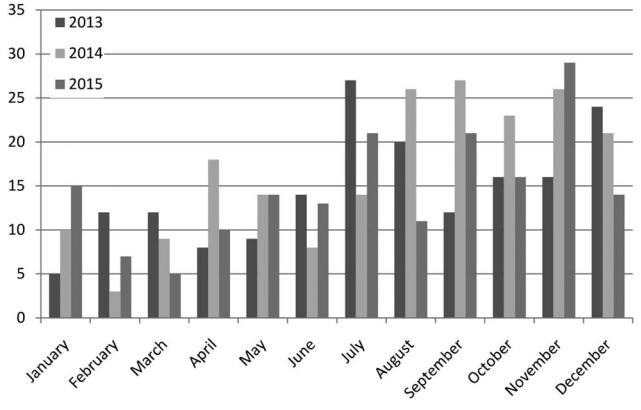

Figure 2 Monthly distribution of smear-proven microsporidial keratoconjunctivitis showing a significant increase in the number of cases in the second half of the year.

Table 2 Incidence of smear-positive microsporidial keratoconjunctivitis from 2006 to 2015

Year	Microsporidial keratoconjunctivitis	Total number of conjunctivitis cases	Percentage
2006	1	1963	0.05
2007	0	1527	0
2008	1	2038	0.05
2009	1	2334	0.04
2010	1	2504	0.04
2011	50	2525	2.0
2012	175	2808	6.2
2013	175	3212	5.4
2014	199	3963	5.0
2015	176	3480	5.1

p=−0.0001 by χ^2 test for trend.

Table 3 Demographic profile of smear-positive microsporidial keratoconjunctivitis

Variable	n (577 eyes of 550 patients)	Per cent
Gender		
Male	305	55.5
Laterality		
Bilateral	27	4.9
Risk factors		
No risk factor	428	77.8
Fall of dust	70	12.7
Fall of insect	13	2.4
Exposure to contaminated water	9	1.6
Others	30	5.5
Previous treatment		
No treatment	166	28.8
Antibiotic	285	49.4
Lubricant	71	12.3
Steroid	69	12.0
Unknown	68	11.8
Antiviral	43	7.5
Native medication	9	1.6
Treatment outcome		
Patients with follow-up	296	53.8
Resolved lesions	187	63.1

DISCUSSION

The prevalence of microsporidial keratoconjunctivitis is on the rise worldwide due to the recent increase in the awareness of the disease.[8] Still, a majority of the disease goes underdiagnosed or misdiagnosed as atypical adenoviral keratoconjunctivitis.[3 8] Our study is the single largest study of smear-proven microsporidial keratoconjunctivitis described so far to the best of our knowledge. The disease was unilateral, with a male preponderance and affected all ages with an increased incidence in the middle-aged adults in our study, similar to the existing reports.[3] Previous reports by Das *et al*[8] and Loh *et al*[2] have documented the occurrence of microsporidial keratoconjunctivitis during the rainy season. In our study, microsporidial keratoconjunctivitis was prevalent throughout the year with an increased incidence in the second half of the year.

Reports by Theng *et al*,[17] Chan *et al*[18] and Kwok *et al*[9] have identified contact lens use, exposure to foreign body and soil as risk factors for microsporidial keratoconjunctivitis. Contrary to previous reports, majority of the patients in our study did not have any predisposing risk factor. Exposure to dust, insect and contaminated water were noted in a small group of patients. None of the patients in our study used contact lens or had exposure to swimming pool. Majority of the patients were misdiagnosed as viral keratoconjunctivitis and had received prior topical medications before presenting to us namely antibiotic, steroid or antiviral medications. The symptoms were persistent in spite of prior treatment and the average time for presentation from the onset of the symptoms was 1 week. Chan *et al*[18] and Lewis *et al*[19] have reported the persistence of microsporidial infection with the use of topical steroids.

All the patients presented to us with greyish white coarse multifocal raised superficial punctate epithelial keratitis, which were larger than the punctate keratitis of viral keratoconjunctivitis. As reported earlier by Fan *et al*,[16] the lesions could be removed by debridement leaving behind pits in the epithelium unlike the punctate keratitis of adenoviral keratoconjunctivitis. Ovoid microsporidial spores can be seen on Gram stain, 1% acid-fast stain and on Calcoflour white stain under fluorescent microscopy.[8] Das *et al*[8] reported a sensitivity of 90% for Gram stain in detecting microsporidial spores.

Various drugs have been reported to be useful in the treatment of microsporidial keratitis namely PHMB, fumagillin, itraconazole, voriconazole, fluoroquinolones and albendazole.[9–16] Das *et al*[20] compared the time to heal and time to cure between PHMB and placebo in a randomised controlled trial and concluded that PHMB did not offer any advantage over placebo. In another randomised controlled trial by Das *et al*,[21] corneal debridement did not have a significant advantage in terms of resolution of the corneal lesions and final visual outcome in clinically diagnosed microsporidial keratoconjunctivitis.

Due to persistence of the disease even with prior medications, the prolonged duration of the disease before presentation and the pathogen being closely related to fungi, we preferred an antifungal agent for the treatment of microsporidial keratoconjunctivitis and 0.3% fluconazole eye drops was used. We also noticed a good clinical response with topical 0.3% fluconazole eye drops and thus we have continued using it. In an ideal world, treatment regimen should be initiated in close conjunction with the clinical features and in vitro drug susceptibility results. In the absence of an established protocol for testing the drug susceptibility of microsporidia, fluconazole was used based on clinical experience. The visual prognosis of microsporidial keratoconjunctivitis is good as the disease resolves with no or visually insignificant corneal scars.[2] Among the patients who followed-up, >95% of patients had no decrease in the final visual acuity in our study.

The limiting factor in our study was that diagnostic corneal scraping was done in only those patients with clinical suspicion of microsporidial keratoconjunctivitis, and not all patients with conjunctivitis.

To conclude, microsporidial keratoconjunctivitis is a frequent form of keratoconjunctivitis in South India. The characteristic clinical features help us to differentiate microsporidial keratoconjunctivitis from other forms of keratoconjunctivitis, which can be confirmed by Gram stain.

Contributors Conception or design of the work; or the acquisition, analysis or interpretation of data for the work—RA, NR, SP, MS, NVP, PL. Drafting the work or revising it critically for important intellectual content—RA, NR, SP, MS, NVP, PL. Final approval of the version to be published—RA, NR, SP, MS, NVP, PL. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved—RA, NR, SP, MS, NVP, PL.

Competing interests None declared.

Ethics approval Institutional Review Board, Aravind Eye Hospital, Madurai.

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