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Original Research Article

Fate of indeterminate microbial keratitis

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ABSTRACT

Background: Previous published literature has shown that there is no significant difference between outcomes of culture positive and culture negative infective keratitis. This study was done to find the outcome in cases of indeterminate keratitis in our institute. Purpose was to highlight the fate of indeterminate microbial keratitis.
Methods: Patients presenting to cornea services of ABVIMS and Dr. RML hospital from February 2017 to April 2021 were evaluated for demographic and microbiological assessment, clinical presentation and management.
Results: The 188 out of 310 cases were microbiologically positive. No organism could be detected in 122 cases. Clinical prognosis is worse in cases of indeterminate keratitis.
Conclusions: Cases with indeterminate microbial keratitis do not show timely and appropriate response which leads to spread of infection resulting in more complications and less CDVA.

Keywords: Microbial keratitis, Indeterminate, Fate

INTRODUCTION

Microbial keratitis is defined as the infective disease of the corneal stroma with defect of corneal epithelium caused by pathogens namely bacteria, fungi, protozoa.[3] It is a common potentially sight threatening ocular infection.[4] Clinically it presents with pain, congestion, corneal ulceration and stromal infiltration. Without aggressive and effective treatment corneal thinning leading to perforation and endophthalmitis or severe corneal scarring can complicate microbial keratitis.

As it is a potential sight threatening disorder, urgent eradication of the causative organism is needed to halt the disease process and limit the extent of scarring and loss of vision.

As the yield of microbiological assessment is usually between 50-60%, indeterminate cases pose diagnostic dilemma and therapeutic challenge.[5-7] A retrospective study was done to evaluate the fate of cases of indeterminate microbial keratitis.

METHODS

In a retrospective study, 310 cases of microbial keratitis presenting to the cornea services of Atal Bihari Vajpayee institute of medical sciences and Dr. Ram Manohar Lohia hospital between Feb 2017-April 2021 were evaluated for demographic and clinical features. The principles of Declaration of Helsinki were followed and informed consent was taken from all the patients. Ethical clearance was waived off as it was a retrospective study of patients routinely attending the cornea clinic.

Microbiological assessment was done in all the cases and depending on the result the cases were divided in group A (Positive microbiological result) and group B (Negative microbiological result). Detailed history including trauma, diabetes mellitus was taken in all the cases. Clinical examination was done with emphasis on corneal

sensation, extent of corneal ulcer and depth of infiltrate. Microbiological study guided the type of treatment given in each case.

For microbiological evaluation, corneal scraping was done on slit lamp with 15 number blades under topical anaesthesia. The base and edges were scraped after removing any loose mucous or debris. The material was directly transferred on glass slides for Gram's staining and KOH preparation. The material was also inoculated on Blood agar, chocolate agar, Mac-Conkey's medium and two Sabouraud's dextrose agar medium on 25 and 37 degree celsius. The yield was evaluated by a senior microbiologist.

Group A comprised of cases in which microbial yield was positive. Group B had cases in which no yield could be detected.

Targeted therapy was given in group A and empirical treatment was started depending on the clinical features in group B. After 48 hours repeat scraping was done in group B. In cases of negative yield or poor response to treatment, corneal biopsy which is a well-established diagnostic modality was carried out.[8] In cases of positive result or good response, the treatment was continued till the keratitis resolved.

In cases of no response but with smaller infiltrate, second line of drugs or antifungal therapy was initiated. Cases with very large infiltrate or infiltrate threatening limbus, therapeutic keratoplasty was done.

Antibacterial treatment given empirically included topical fortified cefazolin, fortified vancomycin, fortified tobramycin, moxifloxacin whereas antifungal drugs included systemic ketoconazole and topical natamycin, voriconazole.

The cases were regularly followed up till resolution and visual acuity stabilization.

Chi square test and Fischer exact test were used for statistical analysis.

RESULTS

The age and sex distribution in the two groups A and B is shown in Table 1.

Table 1: Age and sex distribution.

Age (Years)	Group A		Group B	
	Male	Female	Male	Female
<20	9	6	3	3
20-40	57	33	40	25
40-60	43	17	22	23
>60	13	10	2	4

In group A out of 188 cases, 5 cases needed TPK, one was eviscerated and one case became phthisical. In group B of indeterminate keratitis, out of 122 cases, 93 cases were started on antibacterial and 29 on antifungal therapy. 12 cases underwent TPK, 2 needed evisceration and 6 became phthisical.

Group A and Group B were evaluated on the basis of size of corneal ulcers as shown in Table 2.

Table 2: Size of corneal ulcer.

Size of ulcer	Group A	Group B
<5	86	26
5-8	54	36
>8	48	60
Total	188	122

The size of corneal ulceration was significantly more in cases of indeterminate keratitis (X^2=24.18; p<0.001). On assessing both the groups in cases of ulcer size of >8 mm, Fisher exact test statistic value was '0', the result was significant at p<0.05.

On comparing group A and B on the basis of depth of infiltrate (Table 3), the depth of infiltrate was statistically more in indeterminate cases (X^2=18.75, p<0.05).

Table 3: Depth of infiltration.

Variables	Group A	Group B
Superficial stromal	70	20
Mid stromal	67	46
Deep stromal	51	56
Total	188	122

On relating both the groups in cases of depth of infiltrate reaching to deep stromal level, Fischer exact test statistic value was 0.0009, the result being significant at p<0.05.

Corrected distant visual acuity (CDVA) in both the groups is shown in Table 4.

Table 4: Final corrected distant visual acuity.

Variables	Group A	Group B
6/6-6/12	75	19
6/18-6/36	48	25
6/60-3/60	30	35
<3/60-PL+	28	23
Total	181	102

The CDVA was significantly better in group A (X^2=21.24, p<0.005). When final visual acuity of 6/6-6/12 was compared in both the groups, Fisher exact test statistic value was 0.0001, the result being significant at p<0.05.

DISCUSSION

Microbial keratitis is a common cause of sight threatening disease in developing countries. These cases are more prevalent among low socio economic groups and in rural settings.[9] At the same time a lack of specialized services and a good microbiological backup in these areas often leads to incorrect diagnosis.[10] The poor prognosis in such cases may be compounded by use of cocktail therapy where the patient is simultaneously started on multiple therapy.[11] We conducted a study to determine the fate of such cases wherein no microbial diagnosis could be established because of varied reasons.

Out of 310 patients included in our study, a microbiological diagnosis was established in 188 patients (61%) while no organism could be detected in 122 cases. This positivity rate was similar to that found by Bourcier et al.[11] These cases where no causative organism could be established were treated on the basis of clinical features and the patients were carefully monitored. The therapy was switched when there was no clinical response. These patients were often on multiple drug regimen which may cause partial resolution and hence difficulty in isolation of any organism. The prognosis and the final visual acuity was found to be poorer in these cases as compared to group A. There could be multiple reasons for the same. It could be due to patient presenting in advanced stages of infiltrate and hence warranting surgical intervention. Co-existent factors like uncontrolled glaucoma or vitreous seeding often led to poorer prognosis even after surgical intervention. The cases with indeterminate microbial keratitis did not show timely and appropriate response which led to spread of infection resulting in more complications and less CDVA. Indiscriminate self-medication, antibiotic resistance, injudicious use of steroids can also be a reason for indeterminate keratitis and poor results on treatment.[13] This is in contrast to the conclusion made by Bhadange et al and Duarte et al in their study.[1,2]

Tools for newer frontier in therapy of infectious keratitis may emerge from microbial genomics and proteomics.[14] Such tools will hopefully identify newer targets for intervention to prevent corneal destruction as a result of infective keratitis.

Limitation

The socio-economic status and the literacy status of the patients in a government hospital is often poor which could account for the delayed presentation and hence poor response of therapy in these patients. Also, this being a retrospective study only routine microbiological work up was done in these patients.

CONCLUSION

Microbial keratitis is a challenging situation for every ophthalmologist. The challenge lies in not only curing the infection but also managing the complications and visually rehabilitating the patient. This difficulty is compounded when a microbiological diagnosis cannot be established as targeted therapy may not be delivered. Our article aims to highlight the poor prognosis in such cases and the need to find better and faster tools.

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