

BRIEF COMMUNICATION



False positive fungus results from investigation of microbial keratitis

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Eye (2023) 37:574–575; <https://doi.org/10.1038/s41433-022-02201-4>**INTRODUCTION**

The diagnosis of fungal keratitis is normally based on the presence of characteristic clinical signs and a positive result from investigations such as corneal culture, polymerase chain reaction (PCR), and in vivo confocal microscopy (IVCM) [1, 2]. Antifungal treatment may then be initiated, continued, or modified. However, if a positive investigation does not correlate with the clinical signs, the result may be considered a false positive with no change in management. Although the range of positive investigations for fungal keratitis is 25–68% for culture and 37–93% for PCR [1], there is little information as to whether these figures represent true or false positive results. This study aims to contribute to an estimate of the proportion of fungal culture or PCR results that may be false positives.

METHODS

We searched electronic records from July 2013 to December 2019 for patients investigated for microbial keratitis (MK) who had a positive culture or PCR test for fungus. We defined a false positive result as a case in which fungus was identified, with a result considered by the laboratory to be significant, which resolved with no antifungal prescription (e.g., natamycin, chlorhexidine, amphotericin, or voriconazole). The clinical records of these cases were reviewed. The methodology for culture and PCR has been described previously [1].

RESULTS

We identified thirty (2.0%) of 1488 cultures and seventeen (0.7%) of 2371 PCR tests from eyes that met the inclusion criteria. Both tests were not performed in the majority, which may reflect an overall low level of clinical suspicion of fungal infection, but in two of fifty-six eyes where both tests were performed they were both positive; one reported *Aspergillus spp.* from both, whilst in the second *Penicillium spp.* was identified from culture and *Cladosporium spp.* was identified by PCR and 18S rRNA gene sequencing. None of the eyes examined with IVCM showed fungal elements. All the cultured fungi were potential corneal pathogens.

Notably, the spectrum of fungi identified from culture differed from that identified by 18S rRNA gene sequencing (Tables 1 and 2), which indicates a lack of concordance between the two methods [1]. Reasons for not treating these cases included the decision that the result was inconsistent with the clinical signs, or that healing had already occurred without therapy by the time the positive result was available.

DISCUSSION

To the best of our knowledge, this is the first report to estimate false positive fungal culture and PCR results following the standard investigation of MK. The aetiology of the positive results may be commensals in the tear film, a self-limiting infection, or identification of a fungus of uncertain pathogenicity (e.g., *Phoma spp.*, *Microdochium spp.*). Of relevance, fungi can be detected by culture or PCR from the cornea or conjunctiva of healthy eyes [3, 4]. Our conclusion is that whilst culture and PCR are helpful in

Table 1. Details of the 32 fungi isolated from culture from 30 cases considered as false positive results, with speciation where available.

Genus	Species	Number
Alternaria	spp	2
Aspergillus	spp ^a	7
Candida	spp ^b	6
Fusarium	spp	14
Penicillium	terverticillate	1
Phoma	spp	1
Rhodotorula	mucilaginoso	1


^aA. flavus 2 cases, A. fumigatus 1 case, A. niger 4 cases.

^bC. albicans 2 cases, C. lipolytica 1 case, C. parapsilosis 3 cases.

Table 2. Details of the nineteen fungi identified by polymerase chain reaction and 18S rRNA sequencing from seventeen cases considered to be false positives, with speciation where available.

Genus	Species	Number
Alternaria	spp ^a	7
Ascomycota	spp	1
Aspergillus	spp	1
Cladosporium	spp	6
Microdochium	nivale	1
Naganishia	spp	1
Pithomyces	spp	1
Pleosporaceae	chartarum	1

^aA. infectoria 1 case, A. tenuissima 1 case.

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guiding the management of MK, there are some instances when a microbiologically significant laboratory result is not consistent with infection and this may represent a false positive. This study provides a lower limit for the proportion of false positive fungal results from the standard investigation of suspected MK and helps refine estimates of the accuracy of these techniques. The upper limit, i.e., the proportion of investigation-positive case treated with an antifungal that are false positives, is unknown.

DATA AVAILABILITY

To maintain patient anonymity the data will not be placed on a public repository.

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AUTHOR CONTRIBUTIONS

ST and S-YK conceived the study and ST wrote the first draft of the manuscript. ST and S-YK performed the literature search. S-YK performed the data analysis. Both authors were responsible for the interpretation of the data, reviewed and approved the final manuscript, and had responsibility for the decision to submit for publication.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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