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EDITORIAL

The diagnostic dilemma of fungal keratitis

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Fungal infections are an important cause of ocular morbidity and visual loss, especially in populations which are agrarian, in tropical humid climates, such as Nepal, Africa and India. The annual global incidence of culture-proven fungal keratitis (FK) exceeds 1.05 million cases and Asia has the lion's share of FK in the world [1]. Additional significant risks include various types of contact lens wear [2, 3]. In the Asia Cornea Society Infectious Keratitis Study (ACSIKS) that evaluated infectious keratitis in the Asia-Pacific region, fusarium species was found to be the commonest isolate from corneal scrapings in FK [4].

The diagnostic process in eyes with FK requires an early detection of the presence of a fungal pathogen and this can be present in 50% of cases. The early detection allows the prompt use of anti-fungals. Natamycin is the preferred agent in filamentous fungal infections, and is most effective when started early in the course of the disease, as it does not penetrate the corneal stroma appreciably.

Fungal cultures take time and speciation is sometimes difficult, but in the recent context of Pythium infections which can mimic fungal infections in early clinical presentation, do have a role [2, 5, 6]. The role of In Vivo Confocal Microscopy (IVCM) has been described in recent times, to detect the presence of in vivo corneal pathogens such as fungi and acanthamoeba, as an aid to routine microbiology [7]. While this modality may help in the diagnosis of non-responsive keratitis, the need for a relatively expensive device and expert interpretation has limited its routine clinical use.

Polymerase chain reaction (PCR) has the advantage of rapid diagnosis, with small amounts of specimen, but also suffers from limitations mentioned in the elegant study by Koay & Tuft in this issue [8]. Contamination from the environment and commensals can result in a positive result. The test is again relatively expensive, requires a diagnostic lab, and hence is also not a tool for routine clinical use, limited to large scale specialised and or tertiary institutions worldwide.

False-positive fungal culture or PCR can be caused by environmental contamination, non-pathogenic bystanders or colonisers [9]. The authors speculated the small number that received both culture and PCR tests was due to a low clinical suspicion for FK. Fungal PCR may not be readily available and institutions may only be able to provide culture or smear for the detection of fungus. Sabouraud agar is a common medium for fungal culture which requires incubation for 7–14 days. This would significantly delay a timely diagnosis [10]. Potassium hydroxide smears could hasten the diagnostic process, as it is both sensitive (80–99.3%) and specific (83.8–99.1%) in detecting fungal elements [11–13]. On the other hand, PCR is known for its high sensitivity and rapidity compared to cultures.10 From this study, the false-positive rate of culture was almost three-fold that of PCR. However, it was not possible to determine whether a combination of both tests could further reduce the false-positivity rate than PCR alone.

The sensitivities of fungal culture and PCR are dependent on multiple factors, such as the size of lesion, any pre-treatment with antimicrobials and the different primers used [14]. Kim et al. compared microbial culture and sequenced PCR and found that PCR matched the culture results in 29 out of 31 culture-proven FK [9]. Lau et al. also observed that 93.6% of culture-proven FK yielding a positive PCR, matching the pathogen to that identified by culture [15]. Kuo et al. evaluated a dot hybridisation assay which demonstrated twice the sensitivity and similar specificity to culture. As a result of high sensitivity, the number of false-negative cultures had outnumbered the false-positive by dot hybridisation which had a negative culture result [16].

A study by Upadhyay et al. [17]. indicated that early prophylaxis of traumatic corneal abrasions with 1% chloramphenicol ointment was able to prevent corneal infections in the majority of patients, and more recently, Matoba has reported the response of some fungal infections to Moxifloxacin [18]. Hence, in the absence of clinical information regarding the onset and stage of keratitis when the investigations were obtained, the interpretation of the results reported is harder.

While the availability of the data regarding the possible false positive rates of investigations such as cultures and PCR (the IVCM was negative in all eyes tested), is helpful, further information is required to fully assess the relevance of these investigations in the context of fungal keratitis. In contrast to specialised institutional practice, in countries where it is more prevalent such as India & China, the reliance is on expert interpretation of KOH smears to identify the fungus, as this provides a rapid, inexpensive, sensitive and specific diagnosis [13, 19].

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COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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