Commentary: A retrospective multifactorial analysis of Pythium keratitis and review of the literature

The emerging corneal pathogen, *Pythium insidiosum* is an oomycete, a eukaryote (has true nuclei) with filamentous, coenocytic (nonseptate threads lacking cross-walls) cell growth. Owing to its, typical filamentous-like growth resembling fungi, it commonly tends to get misdiagnosed as mycotic keratitis. However, the cell wall is not composed of chitin as in true fungi but composed of cellulose and β-1, 3 glucan.[1-4] Pythium keratitis has gained increasing importance in recent years due to the difficulty in diagnosis as a result of the lack of clinical suspicion and poor awareness about this organism by both corneal specialists and microbiologists. The morphology and lifecycle of this oomycete are similar to fungi while the molecular and phylogenetic studies reveal a significant difference.[4] This review article[5] provides a comprehensive overview on the typical clinical features to facilitate early identification, microbiological characteristics differentiating pythium from fungi, and the proposed treatment protocols, which would result in a better prognosis on management. This review comprehensively elaborates the various important clinical aspects of Pythium keratitis reported hitherto in literature. Confocal features of Pythium keratitis have also been proposed to aid the diagnosis and treatment.[4] In confocal, hyphae are observed as multiple, linear hyper-reflective, well-delineated structures with 4 μm width and 350 μm length,

seen in all the layers of the cornea with occasional branching and intersecting pattern. This can be considered as a rapid diagnostic modality before the growth of Pythium in culture.

Diagnosis of Pythium keratitis commences with clinical suspicion by the treating corneal physician, with a high degree of competency to recognize the clinical features. The typical clinical presentation comprises of subepithelial/superficial stromal infiltrates with radiating reticular or tentacle-like extensions, and surrounding dot infiltrates.[6] The peripheral furrowing that develops with progression, encircling the ulcer, has been described as a characteristic feature. Hypopyon may also be associated as reported by several clinical series. In this study, 46.6% of the patients had thick endothelial and anterior chamber exudates associated with rapid progression of the ulcer, and perforation occurring in 13.3% of the cases. These pointers serve to aid in the identification of the organism based on clinical suspicion and help the microbiologist to observe typical growth patterns of pythium. Furthermore, KOH 10% wet mount, reveals a long slender hyaline sparsely or aseptate hyphae with perpendicular lateral branches. The size of the filaments can be 3–10 μm or even larger. Culture detection of flat, feathery, colorless, nonsporulating colonies on 5% sheep blood agar aids in the early diagnosis of this organism.[1,7] The pythium identification is confirmed with the incubated carnation leaf method for zoospore formation.

Notably, Pythium shows *in vitro* susceptibility to tigecyclin, linezolid, and minocyclin. Tetracyclin and doxycyclin may also be effective in treating this organism.[8,9] The key finding in this review[5] is the proposal of medical management based on the size and depth of the ulcer. Early identification with infiltrating size less than 4 × 4 mm, involving less than 1/3 depth of the stroma, enabling early institution of treatment with topical linezolid monotherapy saw good healing with a corneal scar in 72.7% of the cases. Pythium keratitis of large size infiltration, more than 4 × 4 mm size involving mid-deep stroma with peripheral furrowing and approaching the limbus was managed with topical linezolid 0.2% and azithromycin 1%. Medical therapy for pythium was started only after the positive culture results were obtained in all cases in this series. Early initiation of appropriate antimicrobial therapy in Pythium keratitis plays a crucial role in optimal healing, which otherwise remains difficult to contain with medical and surgical management. Hence, early commencement of therapy on clinical suspicion may be worth considering in the scenario of Pythium keratitis, which tends to mimic mycotic keratitis but behave like bacterial keratitis with rapid progression and deterioration. With the recognition of the typical clinical features and smear results, antimicrobial therapy can be initiated to avoid the devastating ensuing complications with rapid progression leading to endophthalmitis and evisceration. Another salient aspect noted in this study was early therapeutic keratoplasty intervention (63.3%) performed at a mean duration of 11 ± 1.4 days resulting in salvaging of 90% of the eyes. Recurrence of infection in the graft was seen in 20% necessitating repeat keratoplasty to control the infection. This study compared with others has a high success rate with medical treatment, even though the sample size is low.

In conclusion, a high index of clinical suspicion by the treating corneal surgeon along with the assistance from the ocular microbiologist can identify the Pythium microbes in the corneal infection with either typical clinical presentation or with a nonhealing ulcer. Prompt institution of appropriate medical therapy, close follow-up, and early surgical intervention remain the key to success in management for a better prognosis in Pythium keratitis.

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