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Streptococcus Mitis/Oralis Corneal Ulcer After Corneal Transplantation

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Abstract

Streptococcus mitis/oralis (S. mitis/oralis) corneal ulcer occurred in a case of corneal transplantation reducing vision to hand movements close to face in the right eye. Treatment with 5% vancomycin eye drops led to healing of corneal ulcer, followed by scar formation. Fresh corneal graft transplanted after three months resulted in clear graft well opposed to the host cornea accompanied with visual acquity of 6/24 and -2 170° refractive correction. While *viridans Streptococci* have been implicated in corneal infections, this is the first case of *S. mitis/oralis* corneal ulcer of its kind.

S. mitis/oralis is expanding in pathogenicity crossing the barriers of commensalism to cause opportunistic infection in susceptible hosts. It is difficult to identify and differentiate it to species level through conventional, molecular and mass spectrometry due to limitations of phenotypic expression, genotypic sequence and spectra databases. Both penicillin and high level gentamicin resistance has been reported. *S. mitis/oralis* can lead to permanent corneal scarring leading to loss of vision and consequent corneal transplantation thereby mandating a high index of suspicion and prudence in attributing causality to initiate early treatment to preserve vision in cases of corneal ulcers.

Keywords: *Streptococcus mitis/oralis*, emerging pathogen, corneal ulcer, corneal transplantation

Introduction

Streptococcus mitis/oralis (S. mitis/oralis) are α-hemolytic Streptococci of the viridans group constituting human oral and nasopharyngeal microflora. They are classified under the mitis group along with *S. pneumoniae* as well as several other oral Streptococci such as *S. cristatus, S. peroris, S. infantis, S. australis, S. oligofermentans, S. gordonii, S. sanguis, S. parasanguis, S. australis* and *S. sinensis. S. mitis* and *S. oralis* are clinically and biochemically indistinguishable isolates which are represented as *S. mitis/oralis*. They are expanding in pathogenicity crossing the barriers of commensalism to cause endocarditis, meningitis, bacteremia and septicemia (1).

Viridans group Streptococci have been implicated to cause corneal ulcers and keratitis due to predisposing conditions such as trauma, surgery, corneal transplantation, use of contact lens, ocular surface diseases, dry eye, keratoprosthesis, corneal ring segments and immunocompromised states. However report of *S. mitis/oralis* corneal ulcer, to the best of our knowledge, has not been described in the literature.

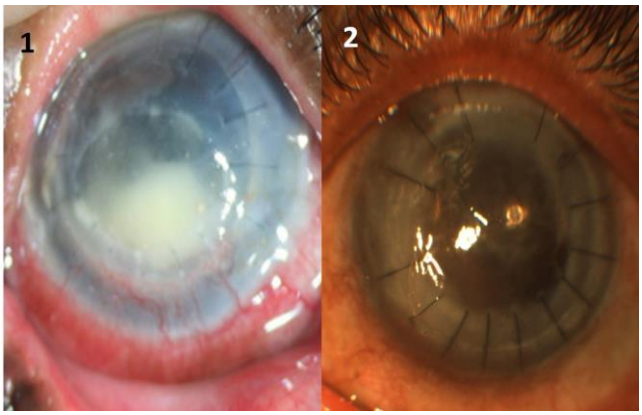

Fig. 1. 1) Corneal graft in situ with well localized yellowish white infiltrate of approximately 4 x 6 mm occupying the inferior part of cornea with surrounding edema and an overlying epithelial defect of about 7 x 6 mm. 2) Corneal re-transplantation with well apposed clear graft.

Case Report

A 60-year-old non-diabetic non-hypertensive male presented with redness, pain, watering, photophobia and diminished vision in the right eye of one month duration. He gave a history of having undergone corneal transplantation in the same eye about a year ago. Initial ocular examination revealed lid edema and conjunctival congestion. Vision was hand movements close to face. The graft in situ was well opposed to host cornea by multiple interrupted sutures. Slit lamp examination revealed a well localized yellowish white infiltrate of approximately 4 x 6 mm mainly occupying the inferior part of cornea involving the visual axis with surrounding edema and an overlying epithelial defect of about 7 x 6 mm. (Figure 1) Anterior chamber was well formed and pupil was

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central, circular and sluggishly reacting to light. Posterior chamber examination revealed lens in situ. Fundus was unremarkable. Intraocular pressure was 14 mm by applanation tonometry. Left eye examination was normal.

Direct smears of corneal scraping revealed 1-2 Gram positive cocci in few fields on Gram stain. Potassium hydroxide mount and Giemsa stains were not contributory. Viridans group Streptococci (*S. mitis/oralis*) were isolated from two consecutive corneal scrapings by both conventional and automated system. Small, dry, gray, α-hemolytic colonies on sheep blood agar yielded non-motile, nonsporing Gram positive cocci negative for catalase, resistant to optochin, bile insoluble, pyrollidonyl arylamidase negative and chemically inert. (Figure 2) VITEK 2 compact automated system (bioMérieux, France) identified *S. mitis/oralis* with 99% probability. Inhibition zones by Kirby-Bauer disk diffusion exhibited susceptibility only to vancomycin, ofloxacin, levofloxacin and linezolid.

Initially he was started on broad spectrum antimicrobials eye drops such as 5% cefazolin and ciprofloxacin hourly. Susceptibility guided treatment by 5% Vancomycin eye drops lead to healing of epithelial defect, disappearance of corneal infiltrate followed by scar formation. Fresh corneal graft was transplanted after three months. The graft remained clear, well opposed to the host cornea with visual acuity of 6/24 and -2 170° refractive correction at the end of six month status post-regrafting.

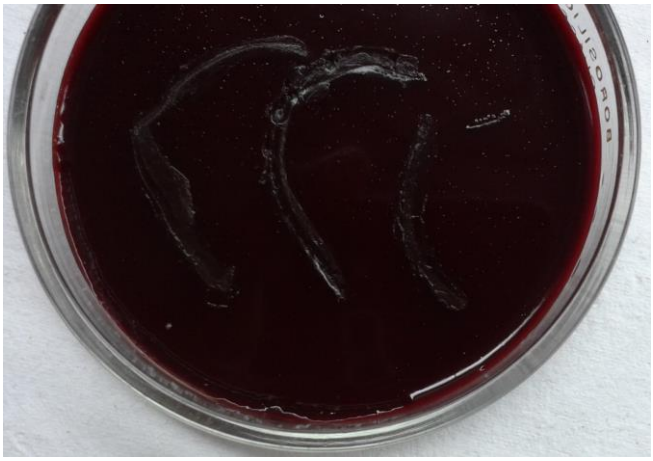

Fig. 2. Small, dry, gray, α-hemolytic colonies of *Streptococcus mitis/oralis* from corneal scraping on sheep blood agar (bioMérieux, France).

Discussion

S. mitis/oralis, along with other viridans Streptococci may present diagnostic and therapeutic challenges. Differentiation of *S. pneumoniae* from other viridans group Streptococci and further species level identification is challenging in clinical laboratories by standard diagnostic techniques. *S. mitis/oralis* may also be confused with Gp C and G small colony variants. Identification by automated systems such as Vitek 2 compact may require disambiguation through molecular techniques such as polymerase chain reaction (PCR), arbitrarily primed PCR, DND-DNA hybridization and sequencing of rnpB, soda, tuf and groEL genes which are resource intensive and available in research laboratories (2-4). DNA fingerprinting is useful to identify strains such as *S. oralis* subsp *corona* and *S. oralis* subsp *mitior* (5). Automated systems expedite rapid identification which can help institute early susceptibility guided therapy (6, 7). Molecular techniques are limited by pre-designed markers, sophisticated infrastructure and standardization. Matrix assisted laser desorption ionization Time of Flight (MALDI-TOF) Mass Spectrometry can also be used. However, the differentiation of *S. mitis* and *S. oralis* is difficult even with the best methods owing to limitations of phenotypic expression, genotypic sequence and spectra databases.

S. mitis/oralis has been reported resistant to penicillin (Minimal inhibitory concentration/MIC 16-32 µg/ml). High level gentamicin resistance (MIC >2000 µg/ml) through chromosomally integrated gene coding gentamicin resistance similar to *Enterococcus faecalis* and *E. faecium* has been reported (8). Commensal Streptococci may serve as a reservoir of β-lactam resistance genes in *S pneumoniae* (9). *S. mitis/oralis* exists in both non-capsulate and capsulate forms, which may alter susceptibility to human antimicrobial peptides (10). *S. mitis/oralis* also enhances the adhesion and biofilm formation of *Pseudomonas aeruginosa* (11).

While immunization against *Pseudomonas aeruginosa*, *Serratia marcescens*, *Staphylococcus epidermidis* and *Staphylococcus aureus* have been found to be protective against keratitis, active immunization against pneumolysin or polysaccharide capsule was not found protective against *S. pneumoniae* keratitis. However, passive immunization with pneumolysin antiserum was found to be protective (12, 13).

Streptococcal corneal ulcers and infectious crystalline keratopathies caused by viridans Streptococci, *S. pneumoniae*, *S. bovis*, *S. abiotrophia defectiva* requiring corneal transplantation have been reported (14-16). However, this is the first case of *S. mitis/oralis* corneal ulcer of its kind, to the best of our knowledge. The presence of Gram positive cocci in direct smears coupled with isolation of *S. mitis/oralis* on consecutive cultures in the setting of graft infection post-corneal transplantation establishes its pathogenicity. Reduction in local immunity post corneal transplantation surgery on the backdrop of avascular cornea renders the surface susceptible for opportunistic infections.

Both corneal ulcer and keratitis can lead to permanent corneal scarring leading to loss of vision and consequent corneal transplantation. Clinical suspicion and prudence in attributing causality of viridans Streptococci in the etiology of corneal ulcers should be maintained while considering contamination as commensal microflora. An early identification and susceptibility testing is mandatory to institute targeted therapy to reduce corneal inflammation, preserve vision and reduce further complications.

Conclusion

S. mitis/oralis corneal ulcer post corneal transplantation represents crossing of the commensalism barrier to emerge as an opportunistic pathogen. Clinical intuition and microbiological expertise is required to diagnose, differentiate and treat corneal infections caused by *S. mitis/oralis* to preserve vision and improve outcome in corneal transplantation.

Conflicts of Interest: None

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