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Case Report Open Access

Contact-Lens Associated Simultaneous *Fusarium* and *Acanthamoebia* Keratitis Treated with Therapeutic Penetrating Keratoplasty

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Abstract

Purpose: To report concurrent *Fusarium* and *Acanthamoeba* keratitis associated with contact lens wear and treated with penetrating keratoplasty.

Methods: A 27 year old woman, presented with a 7 day history of pain, watering and foreign-body sensation in her left eye in the setting of monthly disposable contact lens wear and swimming with lenses in situ. She had been self-treating with combination dexamathasone 0.1% and tobramycin 0.3% drops (Tobradex®). Slit-lamp examination revealed a 1.0 x 1.0 millimetre corneal ulcer with underlying infiltration. Corneal scrapes were performed and hourly Ofloxacillin 0.3% drops commenced. Initially symptoms and signs improved but worsened a week later. The scrapings grew *Aspergillus fumigates* and she was then referred to the corneal service.

Results: At this stage a central stromal infiltrate was observed with surrounding satellite infiltrates. The cornea was re-scraped (as it was felt the *Aspergillus* culture was the result of a contaminant) and the patient was commenced on hourly Econazole 1% drops and systemic Voriconazole. Three days later, the second scrapings grew *Acanthamoeba polyphagia.* Intensive Brolene and Polihexamide drops were commenced, in addition to the systemic and topical anti-fungal treatment. Despite treatment, symptoms and signs of keratitis worsened, vision reduced to light perception and 4 weeks later she underwent a left therapeutic keratectomy. Histological examination of the corneal button revealed fungal hyphae and culture grew *Fusarium*. Topical anti-protozoal and antifugal therapy and systemic Vorconazole were continued for 8 weeks. Six months following keratoplasty the corneal graft remains clear on a reducing dosage of topical dexamethasone 0.1% with a best corrected visual acuity of 20/30.

Conclusion: Concurrent *Fusarium* and *Acanthamoeba* keratitis may occur in the setting of contact lens wear and their misuse. Despite intensive appropriate topical and systemic therapy the condition worsened but remained central in location and following therapeutic penetrating keratoplasty resolved.

Keywords: Acanthamoeba; Fusarium; Cornea; Contact lens

Introduction

Microbial keratitis is a rare but potentially devastating complication of contact lens wear [1]. Natural protective physiological mechanisms can be disrupted by lens wear especially if they are misused or over-worn [2]. Contact lenses interfere with the wiping action of the lids, create tear stagnation, reduce corneal epithelial thickness, cell turnover and desquamation, create epithelial hypoxia, produce breaks (erosions and abrasion) in the epithelial barrier, reduce corneal sensitivity and provide a surface for microbial adhesion; all of which increase the chances micro-organisms invading and infecting the cornea.

Incidence rates for contact lens related microbial keratitis have been reported at approximately 1 in 5000 for rigid lenses, 1 in 2500-5000 daily-wear soft lenses and 1 in 500-800 for extended-wear soft lenses per annum [3-4]. Pseudomonas aeruginosa and staphylococci are the most common organisms isolated [5]. Whilst infection with atypical organisms is uncommon, there has over recent years been an increase in their incidence, in particular of Acanthamoeba and Fusarium [6,7]. The rise in these infections appears to be related to the use of certain contact lens solutions, namely Advanced Medical Optics Complete MoisturePlus (AMO, Santa Ana, California, USA) and ReNu with MoistureLoc (Bausch and Lomb, Rochester, New York, USA) respectively [6,8-10]. Contact lens solutions generally are more effective against bacteria rather than fungi or Acanthamoeba and in "real life conditions" where cleaning protocols may not be strictly adhered to, some "multipurpose" and "no rub" solutions may have diminished antimicrobial activity, especially against protozoa and fungi. Interestingly, the recall of these solutions whilst resulting in a decline in the incidence of Fusarium keratitis has not seen a similar response with Acanthamoeba [6-11].

Compared to bacterial keratitis infection with atypical organisms such as acanthamoeba and fungi, tend to follow a more insidious course, often with a delay in diagnosis. Diagnostic delay and resistance to treatment often result in a poor outcome and the need for surgical intervention [12]. We report an unusual case of severe contact lens related keratitis in the setting of monthly disposable contact lens wear and swimming with contact lenses in situ due to concurrent *Fusarium* and *Acanthamoeba* keratitis. The case is presented in relation to its possible causation, presentation, clinical course, histopathology and medical and surgical management. A review of the few reported cases within the literature is presented and discussed with regards to the present case.

Case History

A 27 year old woman, presented to our Emergency Ophthalmic

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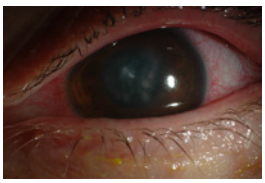

Figure 1: Photographs of left cornea showing a central stromal infiltrate surrounded by deep stromal satellite lesions.

Figure 2: Photograph of left cornea showing confluence of deep stromal infiltrates despite intensive anti-microbial of fungal therapy.

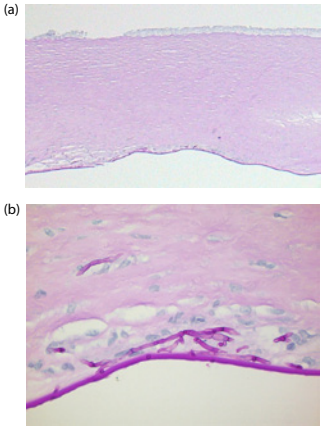

Figure 3a and 3b: Histological cross-section of corneal button, showing fungal hyphae stained with Periodic acid-Schiff adjacent to Descemet's membrane below ulcer with clear zone in the periphery of the button.

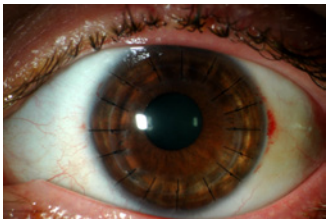

Figure 4: Picture of left cornea six months following therapeutic keratoplasty. The graft remains clear with sutures still in situ with a best corrected visual acuity of 20/30.

Clinic with a 7 day history of pain, watering and foreign-body sensation in her left eye. She was a low myope who usually wore monthly-disposable contact lenses (Air Optix®, Ciba Vision, Novartis). She did not sleep in her lenses and took them out and cleaned them each night with an "all in one", "no-rub" solution (SOLO-care AQUA®, Ciba Vision, Novartis). She gave a history of swimming with her lenses in situ while on holiday in Hungary in a pool, the water of which was apparently supplied by a natural spring, a few days before her symptoms commenced. She had been self-treating with combination dexamathasone 0.1% and tobramycin 0.3% drops (Tobradex®) which initially improved symptoms but only for a few days. On presentation, best corrected visual acuity (BCVA) was 20/20. Slit-lamp examination revealed a 1.0 x 1.0 millimetre corneal ulcer close to the visual axis with underlying corneal infiltration. Corneal scrapes were performed, sent for microbiology and the patient commenced on hourly Ofloxacillin 0.3% drops and the Tobradex® stopped. Initially symptoms and signs improved with closure of the ulcer and some resolution of the underlying stromal infiltrate. However, symptoms worsened at seven days following presentation at which time it was reported that the corneal scrapings had grown *Aspergillus fumigates*. She was then referred to the corneal service at our hospital.

At referral stage, visual acuity was 20/40, central stromal infiltrates were observed with surrounding satellite infiltrates and underlying endothelial deposits (Figures 1A and 1B), consistent with fungal keratitis. The cornea was re-scraped, as it was felt the *Aspergillus* culture might be the result of a contaminant. The patient was commenced on hourly Econazole 1% drops and systemic Voriconazole 400mg bd for 24 hours and 200mg bd thereafter. Three days later, the second scrapings grew *Acanthamoeba* (subsequently identified as *Acanthamoeba polyphagia*). The patient was then commenced on hourly Brolene 0.1% and Polihexamide 1% drops. In addition the systemic and topical anti-fungal treatments were continued, as although fungus was not isolated from the second scrapings clinically the features were suspicious of fungal keratitis. Initially symptoms and signs improved and 10 days after commencing intensive anti-fungal and anti-protozoal treatment BCVA remained at 20/40. However, over the next two weeks, despite treatment, symptoms and signs of her keratitis worsened (Figure 2). Vision reduced to light perception, the stromal infiltrates increased in density and a small hypopyon appeared. As the keratitis remained central, a decision was made to perform a therapeutic penetrating keratoplasty. This procedure was performed, 6 weeks after presentation. Surgery was uncomplicated. The host trephine was 7.75mm. This size was selected as it was 0.5-1.00mm larger for 360 degrees than the central area of keratitis seen on slit lamp examination. The donor trephine was 8.00mm and 16 10/0 nylon interrupted sutures were used. The anterior chamber was thoroughly irrigated with balanced saline at the time of surgery.

Histological examination of the corneal button reported a week after surgery revealed extensive fungal hyphae (Figures 3a and 3b) and microbiological culture grew *Fusarium*. Amphotericin 1% and Chlorhexadine 0.02% drops and systemic Vorconazole 200mg bd were prescribed on a reducing dosage over 8 weeks. As the original microbiological diagnosis was than of acanthamoeba keratitis and removal of the infected area with a clear surrounding zone of 0.5-1.00mm had been achieved, topical Dexamethazone 0.1% eye drops were prescribed immediately following penetrating keratoplasty. A week later when *Fusarium* had been isolated and histological examination confirmed concurrent fungal keratitis, a decision was made to continue the topical steroids as the graft remained clear with no signs of recurrent infection.

Six months following keratoplasty the corneal graft remains clear with sutures still in situ on a reducing dosage of topical dexamethasone 0.1% and with a best corrected visual acuity of 20/30 (Figure 4).

Discussion

We present an unusual case of combined Fusarium and Acanthamoeba keratitis in the setting of monthly-disposable contact lens wear. Occam's razor or "lex parsimoniae" (law of parsimony),

attributed to the 14th-century English logician and Franciscan friar William of Ockham who wrote "entities must not be multiplied beyond necessity", recommends selecting the competing hypothesis that makes the fewest new assumptions. Applying this theory in medicine, and in our case infective keratitis, proposes that it is far more likely that one organism is responsible for the infection rather than two or more. Whilst this is generally correct, exceptions can obviously occur. It is not entirely unrealistic to consider that multiple micro-organisms can invade and infect the cornea if biological protective mechanisms have been compromised, such as in our case as a result of contact lens wear. Interference with lid action, tear stagnation, reduced sensation and corneal epithelial trauma and hypoxia in the presence of lens microbial contamination can all provide conditions for infection with bacteria, fungi or amoeba [2]. In cases, where despite the isolation of an infective micro-organism, the response to appropriate anti-microbial therapy is poor, poly-infection should be considered. Further specimens for culture and sensitivity and/or imaging with con-focal microscopy, which is useful for identification of Acanthamoeba cysts and fungal hyphae [13]. Should be undertaken.

Whilst unusual, ours is not an isolated case. Within the literature there are 10 previously reported eyes with combined Acanthamoeba and Fusarium keratitis [14-22]. In the majority of these cases, as in ours, contact lenses were implicated. Our patient, in similarity to a previous report, was wearing a silicone hydrogel monthly disposable contact lens [22]. Such extended-wear soft contact lenses have significantly reported high rates of microbial keratitis, especially if worn over-night, than daily disposable soft lenses: 1 in 2500-5000 for daily-wear compared to 1 in 500-800 for extended-wear lenses per annum [3,4]. Individuals wearing such lenses must be carefully educated to adhere to strict hygiene protocols. If they cannot achieve them, then cessation of wear of such lenses should be considered.

Typically in the reported cases, Acanthamoeba was discovered and treated with anti-protozoal therapy before Furarium was identified and anti-fungal treatment commenced. Indeed in similarity to our case, fungal keratitis was often only diagnosed following therapeutic keratoplasty and histological examination of the corneal button [14-22]. It has been postulated that, this may represent the faster progression of Acanthamoeba keratitis with the fungi serving as a nutrient for the amoebae [21,22].

In most reported cases, the keratitis was initially misdiagnosed as bacterial or viral [14-16,19-22]. Similarly, our case was initially diagnosed in the Emergency Ophthalmic clinic as a bacterial keratitis with the patient commenced on hourly Ofloxacillin 0.3% drops. Initial cultures reported a scanty growth of *Aspergillus fumigate*, which was thought by the microbiological service to be a contaminant. When referred to the corneal service, features of an atypical keratitis suggestive of fungal infection, with satellite lesions and endothelial deposits were noted. Although considered, it was somewhat surprising when the second scrapings grew Acanthamoeba and not fungi. Fusarium was not identified until therapeutic keratoplasty had been performed, because of worsening keratitis. Therapeutic keratoplasty has been required in the majority of previously reported eyes [1-17,20,22]. This is not surprising given the typical delays in diagnosis, the resistance of these organisms to antimicrobial therapy and the toxicity of this therapy. Thankfully, in our case following keratoplasty, recurrent infection has not occurred, the graft remains clear and visual outcome thus far is good.

One recently reported case high-lighted concerns associated with the use of topical corticosteriods in such cases. Our patient was self-treating with combination dexamathasone 0.1% and tobramycin 0.3% drops (Tobradex®) before presentation. Topical corticosteroids have the potential to adversely affect the outcome of infectious keratitis, if used before diagnosis and the instigation of appropriate anti-microbial therapy [23]. Whilst they can reduce inflammation and pain and limit corneal damage form proteolytic enzymes and bacterial toxins, they should only be considered once the infecting organism has been identified appropriate therapy instigated and a definite clinical improvement documented. In our case topical corticosteroids, were only introduced following penetrating keratoplasty once the infected tissue had been removed and in order to prevent graft rejection. They were continued when a week after surgery concurrent fugal keratitis with *Fusarium* was confirmed, as the graft remained clear with no evidence of recurrent infection. Had a definite diagnosis of fungal keratitis been made prior to surgery, then our practice is to only introduce topical steroids if there are no signs of recurrent infection at 2 weeks. We agree with previous authors that if the keratitis is showing a poor response to anti-microbial therapy, the diagnosis should be reconsidered and re-culture or con-focal imaging contemplated [22].

In recent years an increase in the incidence of *Acanthamoeba* and *Fusarium* contact lens related keratitis has been documented [6,7] and attributed to the use of certain "one-step", "no-rub" contact lens solutions, namely Advanced Medical Optics Complete MoisturePlus (AMO, Santa Ana, California, USA) and ReNu with MoistureLoc (Bausch and Lomb, Rochester, New York, USA) respectively [6,8-10]. Our patient was using an all in one", "no-rub" solution, SOLO-care AQUA® (Ciba Vision, Novartis). This has not been implicated in such infections. However, in view of recent problems individuals when using such solutions must be fully educated and urged to strictly adhere to cleaning protocols so that the antimicrobial activity of these "no rub" solutions are not diminished. The recall of the implicated solutions has resulted in a decline in the incidence of Fusarium keratitis but, not in cases associated with Acanthamoeba [6-11]. Interestingly, whilst Fusarium is a mandatory test organism for such solutions, Acanthamoeba currently is not.

Our patient reported a history of swimming, a few days before her symptoms commenced, with her lenses in situ, while on holiday in Hungary in a pool, the water of which was apparently supplied by a natural spring. Contamination of her lenses whilst swimming might be a significant contributory factor to her subsequent atypical keratitis. Acanthamoeba and Fusarium species have been isolated from both the water and surrounding surfaces in indoor swimming pools, spas and springs [24-28]. Indeed, in a recent study, Fusarium was the most frequently encountered organism recovered from swimming pool decking [24,25]. Both these organisms have been cultured from facilities which have been "adequately" halogenated [26]. Such evidence suggests that indiviuduals should not swim or bath in such facilities with their lenses in situ because of the possible risk of adhesion of micro-organism on contact lens surfaces and subsequent sight-threatening keratitis.

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