Bilateral nummular infiltrates: An uncommon presentation of Candida keratitis

Deena Dahshan
Charles D Francis
Maya S. Bitar

Follow this and additional works at: https://hsrc.himmelfarb.gwu.edu/smhs_ophthalm_facpubs

Part of the Ophthalmology Commons
Bilateral nummular infiltrates: An uncommon presentation of *Candida* keratitis

Deena Dahshan a,⁎, Charles D. Francis a, Maya S. Bitar b

a Joan C Edwards School of Medicine, Marshall University, 1600 Medical Center Dr, Huntington, WV, 25701, USA
b School of Medicine & Health Sciences, George Washington University, Ross Hall, 2300 Eye Street, NW, Washington, D.C., 20037, USA

ARTICLE INFO

Keywords:
Nummular keratitis
*Candida* albicans
Mycotic
Cornea

ABSTRACT

Purpose: We present a case of misdiagnosed fungal keratitis due to a bilateral nummular presentation.

Observations: A 41-year-old female patient, contact lens wearer, presented initially at an optometrist with acute bilateral blurred vision and photophobia. She was found on exam to have multiple round stromal infiltrates bilaterally. She did not have significant ocular surface issues prior and had no history of topical steroid use. Adenovirus testing was negative, and she was started on a topical antibiotic-steroid combination. She did not improve and was referred for further evaluation. We initially suspected a herpetic infection and began treatment with oral antivirals. Cultures came back positive for *Candida albicans* in the right eye. She was very photophobic and cultures were unable to adequately be obtained from the left eye. She was switched to topical voriconazole drop in both eyes and gradually improved with excellent visual outcome. Urogenital cultures were negative. Contact lens use was discontinued through the course of the treatment.

Conclusions: Bilateral *Candida* keratitis is rare and has not been reported in a nummular pattern and in a patient without significant ocular surface issues or chronic use of steroid drops. Differential diagnosis of nummular keratitis mostly includes viral and inflammatory conditions. This case highlights the need to stay alert to a possible fungal etiology and a potential risk of using topical steroids at initial presentation of nummular keratitis.

1. Introduction

Nummular keratitis consists of multiple anterior stromal infiltrates. It has been described associated with viral and inflammatory conditions, mostly adenovirus. We present a case of misdiagnosed fungal keratitis due to a bilateral nummular presentation. Fungal keratitis is rare and often a diagnostic challenge as it can present similarly to other types of keratitis. Topical steroids, while frequently prescribed on initial presentation of ocular inflammation, may contribute to further progression of infection.

2. Case report

A 41-year-old female presented to clinic for sudden onset of redness, swelling and mattering of both eyes with associated irritation, and photophobia occurring for five days. She worked in a bakery and wore soft contact lenses but denied sleeping or swimming in them. She was previously seen by three different doctors. She was initially diagnosed by her optometrist with adenoviral conjunctivitis and tested for it but was negative. She was then thought to have a chemical keratitis. She was started on a combination of loteprednol etabonate 0.5% and tobramycin 0.3% ophthalmic suspension (Zylet, Bausch and Lomb). As she was not improving, she was referred to our department for evaluation and management.

Her review of systems was positive for rhinorrhea and a productive cough for which she was treated with oral azithromycin and one intramuscular injection of steroid by her primary care physician. Her past medical history was significant for well controlled diabetes mellitus on insulin, mild lupus that did not necessitate any systemic medication and a history of right periorbital cellulitis 15 years prior. She was also a smoker and was allergic to penicillin, Bactrim and moxifloxacin.

On presentation, her best corrected visual acuity was 20/20 in both eyes. Slit lamp examination of the right eye was remarkable for mild conjunctival injection and six scattered small round cornea anterior stromal infiltrates and an epithelial defect over the largest infiltrate (Fig. 1). The left eye had more conjunctival injection and two round corneal anterior stromal infiltrates: a small paracentral one and a larger 1.2 mm denser peripheral one with overlying 1mm epithelial defect over...
the infiltrate (Fig. 1). Intraocular pressures were borderline: 22 mmHg in the right and 20 mmHg in the left eye. The rest of the eye exam was within normal limits. Corneal scraping specimens from the right cornea was sent for herpes simplex (HSV) PCR testing and for bacterial and fungal stains and cultures. The left eye was extremely photophobie and scraping was difficult to obtain. She was started on oral valacyclovir and doxycline. Zylet was stopped. She was instructed to use frequent lubricating drops, oral ibuprofen for pain, and to discontinue any contact lens wear. Close follow-up was required. Two days later, Candida albicans was isolated on bacterial culture from the right eye. HSV PCR was negative. She was thus started on a compounded drop of 1% voriconazole hourly in both eyes. On follow-up, the infiltrates of the right eye healed progressively while the larger peripheral infiltrate of the left eye was slower to respond and caused around twenty percent stromal thinning. It finally scarred down two months later (Fig. 2). Voriconazole was progressively tapered over a three-month period. There was no recurrence at the four month follow-up examination. Topical nonsteroidal drops were added for pain control. During the course of treatment, the patient also developed ocular hypertension that was controlled with dorzolamide drops. Her best corrected vision on last visit was 20/20 in both eyes.

Given that our patient did not have significant risk factors for Candida albicans keratitis and given the bilateral occurrence, it was decided to test for a urogenital source of infection, and the culture result was negative. Contact lenses were not obtained for cultures and the patient was advised to discontinue contact lens use through the course of treatment.

3. Discussion

Nummular keratitis, first described in 1905,1 is a corneal sign, rather than a specific disease.2 Corneal structure is disrupted with fine granular coin-shaped opacities causing extreme patient discomfort and possible loss of vision.3 This is predominantly seen with viral keratoconjunctivitis, due to adenovirus or herpes zoster infections. Adenovirus strains produce an infection of corneal epithelial cells, with superficial punctate keratitis followed by nummular subepithelial infiltrates.7 Other causes of corneal subepithelial infiltrates reported in literature include brucellosis, acanthamoeba, Lyme disease, adult inclusion conjunctivitis, Epstein Barr virus, Herpes Simplex, and hyperimmunoglobulin D disease.2,3 It has not been reported associated with Candida keratitis as in this report. Reported distinctions made from adenovirus nummular keratitis include unilateral presentations, deeper infiltrates, accompanying systemic disease, and unusual persistence of lesions.8 In our case, the most common etiology for nummular keratitis were ruled out as adenovirus and herpes virus testing were negative. Acanthamoeba was important to consider given contact lens wear, but our patient denied any exposure to contaminated water and it is unlikely to present bilaterally.9 She had no exposures suggestive of brucellosis or Lyme disease. Concerning an inflammatory etiology, the patient did have a history of lupus, but she was otherwise asymptomatic for it and was not requiring any immunosuppressive treatment. While topical steroids may be considered for treatment of different etiologies of nummular keratitis, it would be detrimental in a case of fungal keratitis, hence the importance to keep this diagnosis in mind.1 Fungal keratitis is not as common as bacterial or viral etiologies, as it accounts for less than 10% of all corneal infection.7 It is often difficult to differentiate from other causes of corneal ulcers. A retrospective review by Sun et al. showed that only two of twenty-nine cases of Candida were diagnosed at initial presentation.5

Knowing predisposing factors and typical signs of Candida keratitis on examination allows for a high index of suspicion. A case series of patients with Candida keratitis found that all patients had a combination of two or more risk factors, with ocular surface disease and steroid use being the most prevalent.7 Our patient did not have any obvious risk factors except corrective contact lens wear, associated with only four of the twenty-one patients in the case series. Interestingly, our patient works as a professional baker using yeast while wearing contact lenses, which raised the question about occupational exposure. However, baker’s yeast is a different species called Saccharomyces cerevisiae. Theoretically, the bakery environment may have been the source of Candida, with various growth mediums for yeast, that can extend to contact lens via contamination and biofilm formation.8

Literature reports describe fungal infections progressing with an indolent course, with less conjunctival injection than bacterial infections.9 Yeast driven ulcers are described as superficial, white, raised colonies or satellite lesions with distinct borders, and corneal infiltrates with feathery edges and intact epithelium with deep stromal involvement.9,10 The presentation of Candida keratitis in our case was acute and its corneal pattern is to be differentiated from the typical satellite lesions by a more scattered pattern and absence of plaque like aspect. Other indications to suspect fungal etiology include presentations worsening with steroids and lack of improvement with antibiotics.10 Our case of Candida keratitis was also atypical due to the simultaneous bilateral presentation. There are rare case reports of bilateral Candida keratitis, presenting in a sequential fashion.11 A recent report suggested a urogenital source for the eye infection. Our patient was tested for a urogenital source, and her culture was negative. The patient in that article also turned out to be HIV positive.11 HIV has been implicated in other cases of fungal keratitis as well.12 Our case presented recent negative testing and deferred repeat testing for HIV. Definitive diagnosis of a fungal ulcer is made from corneal scraping and cultures prior to initiating antifungal treatment.

Amphotericin B has been considered the mainstay for treatment of Candida infection.1 We elected to use voriconazole, a newer antifungal, due to its better bioavailability and it worked very well for our patient.

![Fig. 1. Nummular keratitis seen on slit lamp exam on initial presentation of right eye and left eye. A, Slit lamp picture of the right eye showing conjunctival injection and scattered small round corneal superficial stromal infiltrates labeled with asterisks (*). B, Slit lamp picture of the left eye showing conjunctival injection and two round corneal anterior stromal infiltrates marked with asterisks (*). One infiltrate had an overlying epithelial defect stained with fluorescein. The patient was very photophobic hence it was difficult to obtain pictures of the full cornea.](image-url)
Previous reports also showed good efficacy of topical voriconazole on Candida ulcers.\(^7\) Our patient’s largest infiltrate initially progressed, causing mild thinning of the cornea, before it started responding to treatment after few days. This is likely due to a larger and deeper yeast load that required more time to be sterilized, although Peponis et al. speculate that initial worsening could be due to abrupt disruption of topical steroid in misdiagnosed fungal resulting in acute rebound inflammatory reaction.\(^9\)

With limited treatment options and delayed diagnosis, fungal ulcers have reportedly poor outcomes and often require surgical intervention.\(^10\) Sun et al. determined that a third of patients in their case series of Candida keratitis required a keratoplasty and two out of 26 had to be enucleated or eviscerated.\(^7\) Qiao et al. reported even worse outcomes with 76% requiring surgical intervention and three out of 21 requiring enucleation.\(^7\) Our patient had a very favorable outcome likely due to the absence of chronic ocular disease that is often present in other cases of Candida keratitis. She was able to maintain her presenting best corrected visual acuity of 20/20. Presenting visual acuity and the presence of a corneal graft seem to be prognostic factors in candida keratitis.\(^9\)

Patients with misdiagnosed fungal keratitis often present on a combination of topical steroids and antibiotics. A recent retrospective chart review of fungal keratitis in a South Korean hospital found prior topical steroid use with worse disease progression, treatment failure, and more commonly necessitating surgical intervention.\(^9\) Cessation of prior topical steroid use in misdiagnosed fungal keratitis presents with its own dilemma as it can further contribute to worsening inflammation and corneal necrosis.\(^9\) Our case further emphasizes risks associated with topical steroid use in atypical cases of keratitis.

**4. Conclusion**

Bilateral nummular keratitis due to mycotic etiology is exceedingly rare. This case uniquely details the clinical presentation of bilateral Candida albicans nummular keratitis associated with contact lens use and possible occupational exposure. Corneal scraping is essential for ambiguous corneal infiltrates to diagnose fungal infections. Our patient was treated with an antibiotic and topical steroid regimen prior to diagnosis of fungal keratitis which could have worsened the prognosis. Monotherapy with topical voriconazole was sufficient for resolving our patient’s infection and led to a favorable outcome.

**Patient consent**

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

**Funding**

No funding or grant support received for this work.

**Authorship**

All authors attest that they meet the current ICMJE criteria for Authorship.

**Declaration of competing interest**

There is no conflict of interest regarding publication of this paper. The following authors have no financial disclosures: DD, CF, MB.

**Acknowledgements**

None.

**References**

1. Dimmer F. Nummular keratitis and its related corneal inflammation. Zschr Augenh. 1995;13:621–635.
2. Rao SK, Srinivas SP, Nair AK. Nummular keratitis – a modern-day conundrum. TNOA J Ophthalmic Sci Res. 2019;57:308–310.
3. Reinhard T, Schilgen G, Steinert M, Hacker J, Sundmacher R. Nummular infiltrates in Acanthamoeba keratitis. Acta Ophthalmol Scand. 2003;81(5):541–543.
4. Peponis V, Herz JB, Kaufman HE. The role of corticosteroids in fungal keratitis: a different view. Br J Ophthalmol. 2004 Sep;88(9):1227.
5. Farahani M, Patel R, Dwarakanathan S. Infectious corneal ulcers. Dis Mon. 2017 Feb; 63(2):33–37.
6. Sun RL, Jones DB, Wilhelmsen KR. Clinical characteristics and outcome of Candida keratitis. Am J Ophthalmol. 2007;143(6):1043–1045.
7. Qiao GL, Ling J, Wong T, Yeung SN, Lovieno A. Candida keratitis: epidemiology, management, and clinical outcomes. Cornea. 2020;39(7):801–805.
8. Zara G, Budroni M, Mazzuza F, Fancelli F, Zara S. Yeast biofilm in food realms: occurrence and control. World J Microbiol Biotechnol. 2020;36(9):134.
9. Thomas PA, Kaliamurthy J. Mycotic keratitis: epidemiology, diagnosis and management. Clin Microbiol Infect. 2013 Mar;19(3):210–220.
10. Bourcier T, Sauer A, Dory A, Denis J, Sabou M. Fungal keratitis. J Fr Ophthalomol. 2017;40(9):e307–e313. ISSN 0181-5512.
11. Aranga S, Kwaga T, Leck A, Hu VH, Burton MJ. Bilateral Candida keratitis in an HIV patient with asymptomatic genitourinary candidiasis in Uganda. Med Mycol Case Rep. 2018 Dec;22:14–17.
12. Kitterand DC, Seedor JA, Shah MK, Koplin RS, McCormick SA. Fungal keratitis at the New York eye and ear infirmary. Cornea. 2006;25(3):264–267.
13. Lee SJ, Lee JJ, Kim SD. Topical and oral voriconazole in the treatment of fungal keratitis. Kor J Ophthalmol. 2009;23(1):46–48.
14. Cho CH, Lee SB. Clinical analysis of microbiologically proven fungal keratitis according to prior topical steroid use: a retrospective study in South Korea. BMC Ophthalmol. 2019;19(207).