

## Microsporidial Keratitis in an Immunocompetent Patient

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### INITIAL PRESENTATION

**Chief Complaint:** Blurry vision of the right eye

#### History of Present Illness

A 55-year-old immunocompetent man was referred for 11-months of progressive blurry vision, burning, and photophobia in the setting of corneal edema and epithelial erosions in his right eye. These findings had persisted with unclear etiology despite a trial of prednisolone, Muro 128 drops, and oral valacyclovir. Two weeks prior to presentation, his exam was notable for mild conjunctival injection, patchy epithelial basement membrane dystrophy, and central corneal edema in the right eye. The left eye was unaffected.

#### Past Ocular History

- None

#### Past Medical History

- Herpes Zoster (shingles), two episodes without ocular involvement
- Hemolytic anemia

#### Medications

- Folic acid 1 mg q24h

#### Allergies

- No known allergies

#### Family History

- Non-contributory

#### Social History

- Non-contributory

#### Review of Systems

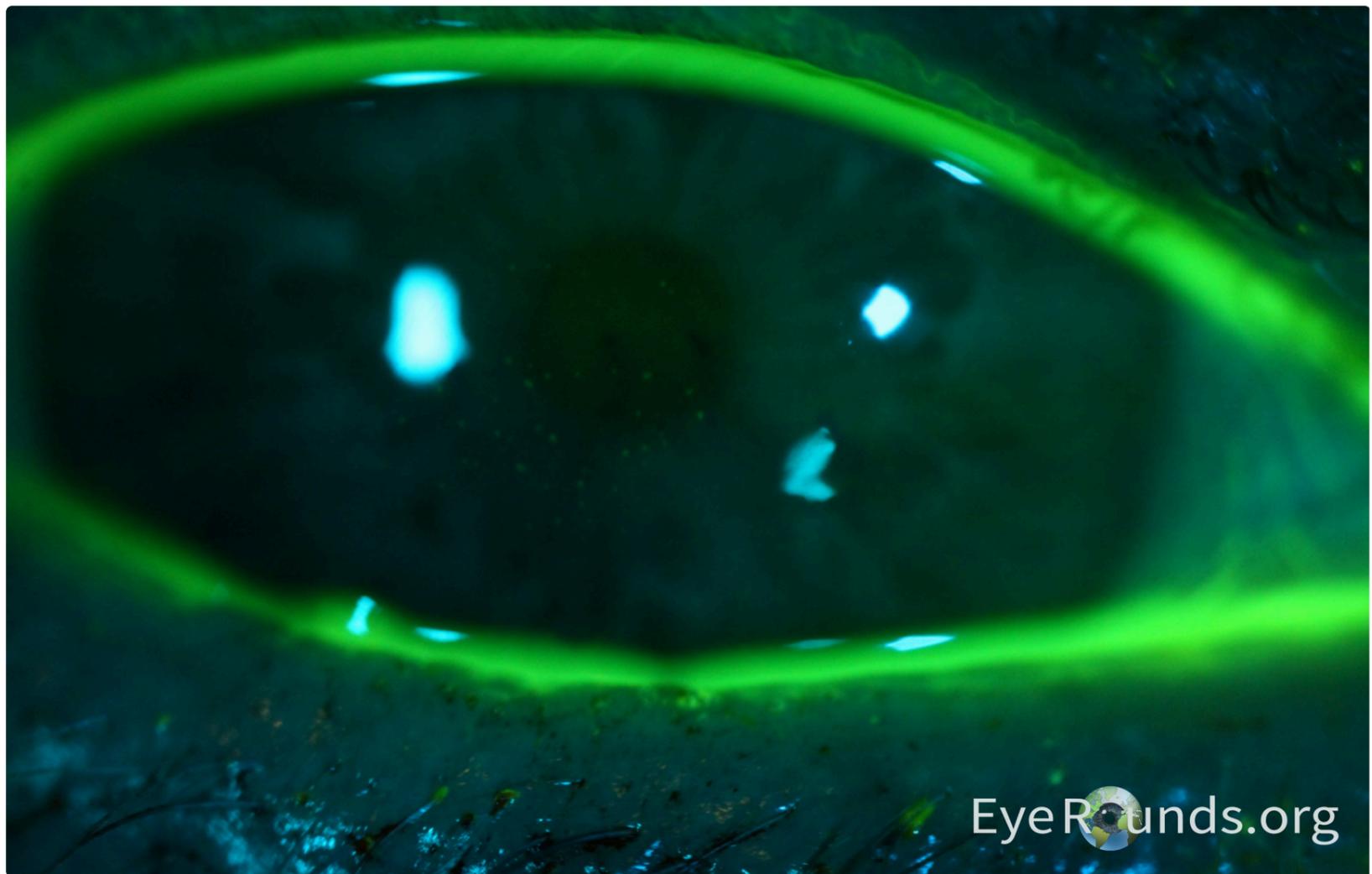
- Negative except for what is detailed in the history of present illness

### OCULAR EXAMINATION

- **Visual Acuity without correction (*Snellen*)**
  - Right eye (OD): 20/20 -2 without correction
  - Left eye (OS): 20/20 -3 without correction

- **Ocular Motility/Alignment**
  - Full in both eyes (OU)
- **Intraocular Pressure (IOP) (Tonopen)**
  - OD: 22 mmHg
  - OS: 21 mmHg
- **Pupils**
  - OD: 4 mm in dark, 3 mm in light, no relative afferent pupillary defect (RAPD)
  - OS: 4 mm in dark, 3 mm in light, no RAPD
- **Confrontation visual fields (Counting fingers)**
  - Full OU
- **Gonioscopy**
  - No peripheral anterior synechiae, angles deep and open OU
- **External**
  - Normal
- **Slit lamp examination**

	<b>OD</b>	<b>OS</b>
<b>Lids/lashes</b>	Very long lashes with corneal touch without staining at baseline	Very long lashes with corneal touch without staining at baseline; one distichiotic lash without cornea touch
<b>Conjunctiva/sclera</b>	Clear	Clear
<b>Cornea</b>	Bandage contact lens in place; epithelial multifocal punctate raised coarse lesions staining with fluorescein centrally; on sclerotic scatter, patch of edema centrally; no keratic precipitates	clear
<b>Anterior Chamber</b>	Deep and quiet	Deep and quiet
<b>Iris</b>	Normal architecture, no atrophy or transillumination defects	Normal architecture
<b>Lens</b>	Clear	Clear
<b>Anterior Vitreous</b>	No cell or flare	No cell or flare



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**Figure 1:** Fluorescein staining of the right eye demonstrating multifocal epithelial punctate raised lesions.

• **Dilated fundus examination (DFE)**

	OD	OS
<b>Disc</b>	Normal	Normal
<b>Macula</b>	Normal	Normal
<b>Vessels</b>	Normal	Normal
<b>Periphery</b>	Normal	Normal

• **Additional Testing**

- Anterior Segment Optical Coherence Tomography (AS-OCT)
  - OD: Moderate stromal edema, EBMD on pachymetry/epithelial mapping
- Corneal Tomography
  - OD: Significant edema, mild posterior flattening superiorly and inferiorly. Densitometry 60.2, central cornea thickness 542, Kmean 46.
  - OS: Densitometry 44.3, central corneal thickness 489, Kmean 47.
- Aerobic culture (cornea scrapings OD): No organisms or polymorphonuclear leukocytes (PMNs).
- Potassium hydroxide fungal stain with calcofluor white (corneal epithelium OD): No fungal elements observed.

**DIFFERENTIAL DIAGNOSIS:**

- [Adenovirus keratitis](#)
- [Thygeson keratitis](#)
- [Bacterial keratitis](#)
- [Fungal keratitis](#)
- [Herpetic keratitis](#)

## CLINICAL COURSE

This patient was initially evaluated in the cornea clinic as a referral from outside hospital with approximately 1 year of irritation and edema OD refractory to a completed trial of topical steroid treatment. Ocular exam was notable for diffuse conjunctival injection, corneal edema, borderline elevated intraocular pressure OD (22 mmHg), and patchy EBMD OD. Imaging obtained at initial evaluation, including OCT anterior segment imaging and corneal topography, confirmed stromal edema with EBMD and mild posterior flattening of the cornea. The patient had bandage contact lens placed OD and was prescribed moxifloxacin, artificial tear solution, and allergy drops QID, in addition to brimonidine. Prednisolone was held.

Approximately 2 weeks later, the patient returned to clinic for a corneal scraping OD. Repeat ocular examination was significant for decreased intraocular pressure OD of 13 mmHg compared to initial visit, in addition to the presence of staining central epithelial punctate lesions OD. Corneal scraping specimens were analyzed via potassium hydroxide preparation and aerobic culture, with no fungal elements observed and no organisms or PMNs, respectively. Differential diagnosis was updated to reflect high suspicion for microsporidia keratitis given the year-long chronic irritation refractory to initial treatment in an immunocompetent patient, stromal edema, and pattern of central punctate epithelial lesions. The possibility of adenoviral keratitis was also considered. Brimonidine was stopped and the patient was restarted on prednisolone acetate taper, in addition to continuing moxifloxacin and artificial tears. The patient was also prescribed albendazole 400 mg PO BID, but the patient was not able to take this medication due to lack of insurance coverage. PCR was considered as a potential next step for formal diagnosis of microsporidia keratitis. Patient clinically improved on medication regimen over the next month with less tearing and irritation. Approximately six months after initial evaluation, the patient's foreign body sensation with accompanying irritation had resolved with no superficial keratitis or edema visualized on exam.

## DISCUSSION

Microsporidia species, recently classified as fungi, are a rare cause of infectious keratitis.<sup>(1)</sup> Despite this reclassification, microsporidia keratitis is a separate entity from fungal keratitis. Microsporidia are unicellular obligate parasites that have been implicated in various organ system infections with a predilection for the gastrointestinal system. The involvement of the eye was initially described in the early 1970s after exposure to goats, with spores observed in the deep stroma of the cornea on histopathology. Ocular infections did not gain widespread recognition among ophthalmologists until the 1990s, coinciding with infections observed in individuals with human immunodeficiency virus (HIV). However, an escalating incidence of microsporidiosis has been observed in immunocompetent patients since the beginning of the century.<sup>(2)</sup> While the global prevalence of microsporidia keratitis is not well described, a study of 4822 microbial keratitis cases in India found that 0.4% were confirmed to be due to microsporidia.<sup>(3)</sup> Some risk factors associated with the development of microsporidia keratitis include systemic immunosuppression, local immunosuppression, trauma, soil exposure, and contact lens usage.<sup>(4)</sup> Numerous outbreaks in various Asian countries have been linked to contaminated soil and water exposure with increased prevalence of infections during periods of heavy rain and floods.<sup>(4-8)</sup> A study in the United States corroborates these findings with over 50% of infected patients having a history of exposure to specific lakes or swamps.<sup>(9)</sup> These studies highlight the importance of geographic location and environmental factors in disease acquisition. Additionally, zoonotic transmission has been suggested as a possible cause for infection.<sup>(10)</sup>

### Presentation

There are two main forms of microsporidia keratitis: keratoconjunctivitis, seen more commonly in the immunosuppressed, and stromal keratitis, which is predominant in the immunocompetent. Keratoconjunctivitis is more common; however, there has been an increase in confirmed cases of microsporidia stromal keratitis even in the United States.<sup>(11)</sup> Microsporidia keratitis presents non-specifically with injection, tearing, decreased visual acuity, pain, foreign body sensation, and photophobia. Patients may have a history of exposure to contaminated water or soil.

In the keratoconjunctivitis form, ophthalmic examination will uncover conjunctival injection alongside multiple coarse corneal punctate lesions that stain with fluorescein and vary in size and distribution.<sup>(12, 13)</sup> These findings can look like adenovirus keratitis. In cases of stromal keratitis, examination reveals conjunctival injection accompanied by stromal edema and opaque mid to deep stromal infiltrates. Features of disciform keratitis can be seen as well. Disease progression can result in stromal thinning, vascularization, and scarring.<sup>(14, 15)</sup> Suppuration is not a feature of either form of microsporidia keratitis and should prompt consideration of alternative causes of keratitis. A study has reported interstitial keratitis thought to be due to an immune reaction to microsporidial antigens and presenting with nummular corneal lesions and stromal edema.<sup>(16)</sup>

### Diagnosis

The small size of microsporidia poses a diagnostic challenge, yet various methods have proven successful at detecting spores. Visualization of polar tubules on tissue biopsy with transmission electron microscopy remains the gold standard for microbiological diagnosis and species identification, but this is expensive, time consuming, and not routinely available.<sup>(17)</sup> Notably, routine corneal cultures are often negative as microsporidia are obligate intracellular organisms. Corneal scrapings, however, can

be analyzed with specialized stains under light microscopy, which reveal non-budding uniform oval spores. The modified trichome stains the spore's cell wall pink, disclosing a horizontal stripe, depicting the polar tubule, within the spore's interior. Other stains have been used with calcofluor white and modified Ziehl-Neelsen (1% H<sub>2</sub>SO<sub>4</sub>) among the more reliable options for corneal samples.(18, 19) Immunofluorescent assays directed against spore wall or polar tubes have been used to identify *E. hellem* from corneal tissues and conjunctival scrapings.(20) More recently, polymerase chain reaction assays targeting species-specific rRNA coding sequences have successfully identified several microsporidia species from corneal scrapings with approximately 80% sensitivity.(21) Non-invasive methods using anterior segment optical coherence tomography can assist in the diagnosis. Imaging typically shows hyper-reflective epithelial lesions, like those seen in adenoviral keratitis, though larger in size.(22) Continued efforts are being made to enhance detection of ocular microsporidia.

## **Treatment**

While there are no established guidelines for the treatment of microsporidia, partly due to the lack of research comparing the efficacies of different regimens, various treatments have been described anecdotally. This is especially true with microsporidia keratoconjunctivitis. Systemic Albendazole 400 mg BID, an anti-helminthic that inhibits tubulin polymerization, demonstrated efficacy in the resolution of microsporidia keratoconjunctivitis.(12, 23, 24) Others have reported success with topical antibiotics: fumagillin and fluoroquinolones. Fumagillin inhibits an enzyme involved in post translation modification of proteins. It is mixed in a saline solution and well-tolerated. In one study, microsporidia keratitis completely resolved without symptom recurrence, while another study necessitated maintenance therapy due to recurrent symptoms.(25, 26) There was one case where topical fumagillin eradicated microsporidia in stromal keratitis; however, the patient ultimately underwent a penetrating keratoplasty due to the development of bacterial keratitis.(11) A retrospective study in Singapore showed that 101 of 102 patients with superficial keratitis were successfully treated with topical fluoroquinolone monotherapy with only three cases of recurrent infection.(4) The fluoroquinolones used include ciprofloxacin 0.3%, gatifloxacin 0.5%, levofloxacin 0.5%, moxifloxacin 0.5% or norfloxacin 0.3% and treatment duration was individually tailored to the clinical response of each patient. Topical antifungals, specifically voriconazole, also have a role in treatment. Application of 1-2% topical voriconazole every two hours over several weeks has treated several cases of microsporidia keratoconjunctivitis without recurrence or treatment complications.(9, 27)

In contrast to superficial infections, stromal keratitis has limited pharmacologic options. Few cases have been successfully treated with medication using some combination of oral albendazole, topical voriconazole, polyhexamethylene biguanide, and chlorhexidine. An overwhelming majority of patients with stromal keratitis required surgery.(11, 28, 29) Penetrating keratoplasty is the surgery of choice, as lamellar keratoplasty is ineffective at preventing recurrence.(30)

## **DIAGNOSIS: Microsporidia Keratitis**

<p><b>EPIDEMIOLOGY OR ETIOLOGY</b></p> <ul style="list-style-type: none"> <li>• 1000-1500 microsporidian species. Microsporidia keratitis prevalence unknown</li> <li>• More common in men, usually unilateral</li> <li>• Risk factors <ul style="list-style-type: none"> <li>◦ Systemic immunosuppression (HIV, organ transplant)</li> <li>◦ Local immunosuppression (topical steroids)</li> <li>◦ Trauma</li> <li>◦ Soil and water exposure</li> <li>◦ Contact lens usage</li> </ul> </li> </ul>	<p><b>SIGNS</b></p> <ul style="list-style-type: none"> <li>• <b>Keratoconjunctivitis:</b> Conjunctival injection with multiple coarse corneal punctate lesions that stain with fluorescein.</li> <li>• <b>Stromal Keratitis:</b> Conjunctival injection with stromal infiltrates and edema. Can also have features of stromal thinning, vascularization, scarring, and disciform keratitis.</li> <li>• Suppuration is not observed in either form.</li> <li>• Diagnosis <ul style="list-style-type: none"> <li>◦ Transmission electron microscopy: Gold standard; visualization of polar tubules on tissue biopsy</li> <li>◦ Histopathology: Modified trichome stain shows ovoid spore with pinkish cell wall and interior horizontal stripe representing the polar tubule. Additional stains display non-budding uniform ovoid spores</li> <li>◦ Immunofluorescent assay: antibodies that target spore walls or polar tubules</li> <li>◦ Molecular analysis: detect species-specific rRNA sequences from samples</li> </ul> </li> </ul>
<p><b>SYMPTOMS</b></p> <ul style="list-style-type: none"> <li>• Slowly progressive</li> <li>• Non-specific symptoms: injection, blurry vision, pain, tearing, photophobia, and foreign body sensation</li> </ul>	<p><b>MANAGEMENT</b></p> <ul style="list-style-type: none"> <li>• No consensus nor guidelines regarding treatment</li> <li>• Medical management options of microsporidia keratoconjunctivitis includes systemic albendazole, topicals (fumagillin, fluoroquinolones, voriconazole)</li> <li>• Penetrating keratoplasty is preferred for microsporidia stromal keratitis</li> </ul>

Related Tutorial: [Cornea Culture](#)

## References

1. Lee SC, Corradi N, Byrnes EJ, 3rd, Torres-Martinez S, Dietrich FS, Keeling PJ, Heitman J. Microsporidia evolved from ancestral sexual fungi. *Curr Biol* 2008;18(21):1675-1679. [PMID 18976912]
2. Sharma S, Das S, Joseph J, Vemuganti GK, Murthy S. Microsporidial keratitis: need for increased awareness. *Surv Ophthalmol* 2011;56(1):1-22. [PMID 21071051]
3. Joseph J, Sridhar MS, Murthy S, Sharma S. Clinical and microbiological profile of microsporidial keratoconjunctivitis in southern India. *Ophthalmology* 2006;113(4):531-537. [PMID 16488011]
4. Loh RS, Chan CM, Ti SE, Lim L, Chan KS, Tan DT. Emerging prevalence of microsporidial keratitis in Singapore: epidemiology, clinical features, and management. *Ophthalmology* 2009;116(12):2348-2353. [PMID 19815287]
5. Fan NW, Wu CC, Chen TL, Yu WK, Chen CP, Lee SM, Lin PY. Microsporidial keratitis in patients with hot springs exposure. *J Clin Microbiol* 2012;50(2):414-418. [PMID 22116156]
6. Kwok AK, Tong JM, Tang BS, Poon RW, Li WW, Yuen KY. Outbreak of microsporidial keratoconjunctivitis with rugby sport due to soil exposure. *Eye (Lond)* 2013;27(6):747-754. [PMID 23598669]
7. Malik S, Ishaq M, Nayyar S, Humayun S. Microsporidial Keratitis - First Case Series of a Rare Pathogen in the Wake of Flood Disasters of 2022 in Pakistan. *J Coll Physicians Surg Pak* 2022;32(12):SS165-SS167. [PMID 36597327]
8. Uematsu M, Mohamed YH, Kusano M, Inoue D, Harada K, Tang D, Kitaoka T, Yagita K. Microsporidial keratoconjunctivitis - first outbreak in Japan. *BMC Infect Dis* 2023;23(1):752. [PMID 37915107]
9. Huang AS, Cho JS, Bertram BA. Microsporidial Keratitis Related to Water Exposure: A Case Series. *Cureus* 2021;13(6):e15760. [PMID 34164251]

10. Mathis A, Weber R, Deplazes P. Zoonotic potential of the microsporidia. *Clin Microbiol Rev* 2005;18(3):423-445. [PMID 16020683]
11. Matoba A, Goosey J, Chevez-Barrios P. Microsporidial Stromal Keratitis: Epidemiological Features, Slit-Lamp Biomicroscopic Characteristics, and Therapy. *Cornea* 2021;40(12):1532-1540. [PMID 33782266]
12. Chan CM, Theng JT, Li L, Tan DT. Microsporidial keratoconjunctivitis in healthy individuals: a case series. *Ophthalmology* 2003;110(7):1420-1425. [PMID 12867402]
13. Friedberg DN, Stenson SM, Orenstein JM, Tierno PM, Charles NC. Microsporidial keratoconjunctivitis in acquired immunodeficiency syndrome. *Arch Ophthalmol* 1990;108(4):504-508. [PMID 2108656]
14. Font RL, Su GW, Matoba AY. Microsporidial stromal keratitis. *Arch Ophthalmol* 2003;121(7):1045-1047. [PMID 12860813]
15. Rauz S, Tuft S, Dart JKG, Bonshek R, Luthert P, Curry A. Ultrastructural examination of two cases of stromal microsporidial keratitis. *J Med Microbiol* 2004;53(Pt 8):775-781. [PMID 15272065]
16. Mohanty A, Behera HS, Barik MR, Kaur A, Sharma S, Das S, Fernandes M, Panda S, Sahu SK. Microsporidia-induced stromal keratitis: a new cause of presumed immune stromal (interstitial) keratitis. *Br J Ophthalmol* 2023;107(5):607-613. [PMID 34937694]
17. DPDx - Laboratory Identification of Parasites of Public Health Concern. Centers for Disease Control and Prevention: Centers for Disease Control and Prevention, 2019. [rev. 5/29/2019; Accessed on 12/3/2023, <https://www.cdc.gov/dpdx/microsporidiosis/index.html>] <https://www.cdc.gov/dpdx/microsporidiosis/index.html>.
18. Garcia LS. Laboratory identification of the microsporidia. *J Clin Microbiol* 2002;40(6):1892-1901. [PMID 12037040]
19. Joseph J, Murthy S, Garg P, Sharma S. Use of different stains for microscopic evaluation of corneal scrapings for diagnosis of microsporidial keratitis. *J Clin Microbiol* 2006;44(2):583-585. [PMID 16455916]
20. Schwartz DA, Visvesvara GS, Diesenhouse MC, Weber R, Font RL, Wilson LA, Corrent G, Serdarevic ON, Rosberger DF, Keenan PC, et al. Pathologic features and immunofluorescent antibody demonstration of ocular microsporidiosis (*Encephalitozoon hellem*) in seven patients with acquired immunodeficiency syndrome. *Am J Ophthalmol* 1993;115(3):285-292. [PMID 8095123]
21. Joseph J, Sharma S, Murthy SI, Krishna PV, Garg P, Nutheti R, Kenneth J, Balasubramanian D. Microsporidial keratitis in India: 16S rRNA gene-based PCR assay for diagnosis and species identification of microsporidia in clinical samples. *Invest Ophthalmol Vis Sci* 2006;47(10):4468-4473. [PMID 17003441]
22. Sridhar MS, Shaik B. Anterior segment optical coherence tomography of microsporidial keratoconjunctivitis. *Indian J Ophthalmol* 2018;66(5):691-692. [PMID 29676317]
23. Gajdatsy AD, Tay-Kearney ML. Microsporidial keratoconjunctivitis after HAART. *Clin Exp Ophthalmol* 2001;29(5):327-329. [PMID 11720161]
24. Gritz DC, Holsclaw DS, Neger RE, Witcher JP, Jr., Margolis TP. Ocular and sinus microsporidial infection cured with systemic albendazole. *Am J Ophthalmol* 1997;124(2):241-243. [PMID 9262551]
25. Diesenhouse MC, Wilson LA, Corrent GF, Visvesvara GS, Grossniklaus HE, Bryan RT. Treatment of microsporidial keratoconjunctivitis with topical fumagillin. *Am J Ophthalmol* 1993;115(3):293-298. [PMID 8117342]
26. Rosberger DF, Serdarevic ON, Erlandson RA, Bryan RT, Schwartz DA, Visvesvara GS, Keenan PC. Successful treatment of microsporidial keratoconjunctivitis with topical fumagillin in a patient with AIDS. *Cornea* 1993;12(3):261-265. [PMID 8500340]
27. Khandelwal SS, Woodward MA, Hall T, Grossniklaus HE, Stulting RD. Treatment of microsporidia keratitis with topical voriconazole monotherapy. *Arch Ophthalmol* 2011;129(4):509-510. [PMID 21482878]
28. Donovan CP, Margo CE, Espana EM. Stromal microsporidial keratitis successfully treated with medical therapy. *Am J Ophthalmol Case Rep* 2021;23:101178. [PMID 34368500]
29. Sabhapandit S, Murthy SI, Garg P, Korwar V, Vemuganti GK, Sharma S. Microsporidial Stromal Keratitis: Clinical Features, Unique Diagnostic Criteria, and Treatment Outcomes in a Large Case Series. *Cornea* 2016;35(12):1569-1574. [PMID 27467044]
30. Font RL, Samaha AN, Keener MJ, Chevez-Barrios P, Goosey JD. Corneal microsporidiosis. Report of case, including electron microscopic observations. *Ophthalmology* 2000;107(9):1769-1775. [PMID 10964843]

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