Acanthamoeba Keratitis: A Contact-lens-associated Infection

There has been recent news coverage of Acanthamoeba Keratitis, a sight-threatening protozoal infection associated with contact lens wear. Consequently, contact lens manufacturers and those making contact lens care products have been implicated in the increasing incidence of the condition in recent years. This short article aims to give an overview of the condition, how it can be managed and how it differs from other contact-lens-associated conditions.

What is Acanthamoeba?

Acanthamoeba is a ubiquitous free-living amoeba found in soil, air and water. It has a life cycle consisting of a trophozoite (active, replicating) phase and cyst (dormant) phase. During the cyst phase it can survive adverse environments with varying pH, temperatures and osmolarities^{1,2}.

Several Acanthamoeba species are pathogenic; the most common are A. castellanii and A. polyphaga, though colonisation with the amoebae does not necessarily lead to disease, as 80% of the normal human population have antibodies to Acanthamoeba².

It can cause a devastating corneal infection (*Acanthamoeba* Keratitis, AK) in immunocompetent patients, with 85-88% of cases occurring in contact lens wearers. The incidence of AK among contact lens wearers is around 17-19 cases per million in the United Kingdom³.

Immunocompromised patients are at risk of developing granulomatous amoebic encephalitis, cutaneous lesions, pulmonary and renal disease².

Why Are Contact Lens Wearers at Risk of Developing Corneal Infection?

There are many reasons why contact lens wearers (CLW) are at risk of developing a microbial keratitis (MK); some are related to the physical and physiological changes to the cornea that occur with contact lens wear, while others are related to contact lens material and care products, in addition to which there is an association with the quality of lens care and hygiene^{4,5}.

Microbial invasion into the corneal stroma is achieved through changes in the tear film when lenses are worn and by damage to the glycocalyx of the corneal epithelium in the post lens environment (the area between lens and the anterior surface of the cornea). These can occur by direct trauma caused by the lenses or through changes in the binding and transport proteins in the cornea⁵.

There has been some conflicting research into how contact lens material can affect infection rates with those using Silicone Hydrogel lenses and re-usable soft contact lenses showing higher rates of vision loss following MK^{4, 11}.

Other areas of research include the possibility of multipurpose contact solutions having poor amoebicidal

activity^{7, 8}. A recent outbreak in America and Singapore led to the withdrawal of one multipurpose solution from the market^{9, 10}.

Prolonged contact lens wear and poor lens hygiene (washing lenses in tap water, swimming in contact lenses, not replacing lens cases or cleaning solutions frequently etc.) have been associated with higher rates of microbial keratitis and often have the worst clinical outcomes^{3, 4, 6}.

Clinical Presentation

Symptoms

If the diagnosis of AK is made within one month of the onset of symptoms, this is referred to as early disease. Misdiagnosis or delayed presentation can lead to more advanced clinical findings and poorer prognosis^{3, 12}.

Most patients present with unilateral pain, photophobia and tearing; bilateral disease is more common in CLW ¹⁵. Other symptoms include blurred vision, red eye and itchy eye. The pain is usually severe and classically described as disproportionate to the findings on slit lamp examination ¹⁴.

Clinical Features of

Acanthamoeba Keratitis

- Most cases occur in contact lens wearers
- Symptoms include red eye, tearing, itching and pain disproportionate to clinical findings
- Examination findings include epithelial defects, perineural infiltrates, limbitis

Risk factors for developing AK in non-contact-lens wearers include trauma or exposure to water or soil, which can occur with those employed in agriculture and exposure to contaminated tank-fed water¹⁶.

Signs

Early features of AK on slit lamp examination are^{3, 12-14}:

- Punctate Keratitis
- Corneal epithelial loss
- Limbitis
- Perineural

 infiltrates this is
 a pathognomonic
 feature of AK, which
 may represent the
 Acanthamoeba
 trophozoites clustering
 around the nerves
 (Image A)
- Pseudodendrites



Image A. Fluorescein staining demonstrating ring abscess in the corneal stroma

CPD

Severe findings in late disease ^{3, 12-14}:

- Abscess formation (Image B)
- Pus in anterior chamber (hypopyon)
- Corneal melt and
 perforation
- Cataract
- Glaucoma
- Posterior segment inflammation



pathognomic of Acanthamoeba Keratitis

Some of these findings in severe, prolonged AK are due to the topical treatments used for the condition, or due to a more general inflammatory response to the infection¹⁶. Spread of the infection beyond the cornea is extremely rare and has only been reported in a handful of cases^{3, 17}.

Management

Investigations

A diagnosis of AK can be made based on clinical features alone; however a definitive diagnosis requires at least one sample that is *Acanthamoeba*-positive on histology, culture or identification by DNA polymerase chain reaction^{3, 16}.

First-line investigations are corneal scrape biopsies and cultures, lens cultures and lens case cultures. Confocal microscopy is an optical imaging technique used in vivo that can aid in the diagnosis of AK but is only available in some centres¹⁸.

Treatment

The aim of treatment is to eradicate viable cysts and trophozoites and to dampen the inflammatory processes. The mainstays of treatment are topical agents such as polyhexamethylene biguanide (PHMB) and chlorhexidine; these are biguanide agents. Biguanides can be used alone or in combination with other drops like propamidine and hexamidine.

Initially, topical treatments are administered every hour (day and night) for 48 hours, which may require a hospital admission. Thereafter the treatment is weaned slowly over the course of months; average treatment course is six months in the UK. Treatment continues until there are no further clinical signs of *Acanthamoeba* infection. The treatment is often prolonged due to the ability of *Acanthamoeba* to become encysted and therefore more resistant to the medications^{19, 20}. If persistent inflammation is present on examination, then topical corticosteroids are indicated and sometimes systemic antifungals and steroids are used for the treatment of the extracorneal complications of AK^{21, 22}.

Patients are reviewed frequently in the outpatient setting to ensure improvement in treatment and will require dose adjustments accordingly.

In some persistent cases surgical treatment may be indicated. This can range from epithelial debridement to corneal graft surgery, and even enucleation in the most severe cases²³.

Given the potential devastating consequences of AK, there is a growing body of research on why the incidence of the infection is increasing and whether it is purely related to increasing contact lens use. Nonetheless it is important that cases are identified and treated promptly in order to optimise prognosis and reduce complication rates.



Summary

- Acanthamoeba Keratitis is a sight-threatening infection of the eye
- · Contact lens wearers with poor lens hygiene are at greatest risk of developing the condition
- Persistent contact-lens-associated infections require urgent review by ophthalmologists
- · It requires intensive topical treatment with frequent, prolonged follow-up
- Prognosis improves with early diagnosis and treatment

CPD

References

- 1. Siddiqui R, Khan N. Biology and Pathogenesis of Acanthamoeba. Parasites and Vectors (2012); 5:6
- Trabelsi H, et al. Pathogenic Free-Living Amoebae: Epidemiology and Clinical Review. Pathologie Biologie (2012); 60(6): 399-405
- Dart J, Saw V, Kilvington S. Acanthamoeba Keratitis: Diagnosis and Treatment Update 2009. American Journal of Ophthalmology (2009); 148(4): 487-494
- 4. Dart J, Radford C, et al. Risk Factors for Microbial Keratitis with Contemporary Contact Lenses: A Case Control Study. American Academy of Ophthalmology (2008); 115(10): 1647-1654
- 5. Shovlin JP (moderator). Ocular Surface Health with Contact Lens Wear. Contact Lens and Anterior Eye (2013); 36(s1): S14-S21
- Seal D, Kirkness CM, Bennett H, Peterson M, Keratitis Study Group. Acanthamoeba Keratitis in Scotland: Risk Factors for Contact Lens Wearers. Contact Lens and Anterior Eye (1999); 22(2): 58-68
- Johnston SP, et al. Resistance of Acanthamoeba Cysts to Disinfection in Multipurpose Contact Lens Solutions. Journal of Clinical Microbiology (2009); 47:2040-2045
- Kilvington S, et al. Encystment of Acanthamoeba During Incubation in Multipurpose Contact Lens Disinfectant Solutions and Experimental Formulations. Eye and Contact Lens: Science and Clinical Practice (2008); 34: 133-139
- Por YM, et al. Acanthamoeba Keratitis Associated with Contact Lens Wear in Singapore. American Journal of Ophthalmology (2009); 148: 7-12
- Joslin CE, et al. Association of Contact Lens Solution use and Acanthamoeba Keratitis. American Journal of Ophthalmology (2007); 144:169-180
- 11. Wilcox MD. Microbial adhesion to silicone hydrogel lenses: a review. Eye & Contact Lens: Science & Clinical Practice (2013); 31: 60-65

- 12. Tu Ey, et al. Prognostic Factors Affecting Visual Outcome in Acanthamoeba Keratitis. Ophthalmology (2008); 115: 1998-2003
- 13. Bacon AS, et al. A Review of 72 Consecutive Cases of Acanthamoeba Keratitis, 1984-1992. Eye (1993); 7: 719-725
- 14. Illingworth CD, Cook SD. Acanthamoeba Keratitis. Survey of Ophthalmology (1998); 42: 493-508
- Radford CF, Minassian DC, Dart J. Acanthamoeba Keratitis in England and Wales: Incidence, Outcome and Risk Factors. British Journal of Ophthalmology (2002); 86: 536-542
- 16. Sharma S, Garg P, Rao GN. Patient Characteristics, Diagnosis and Treatment of Non-Contact Lens Related Acanthamoeba Keratitis. British Journal of Ophthalmology (2000); 84: 1103- 1108
- Davis M, et al. Acanthamoeba Endophthalmitis Following 17. Penetrating Keratoplasty for Acanthamoeba Keratitis. Archives of Ophthalmology (2010); 128: 505-506
- Vadavalli P, et al. The Role of Confocal Microscopy in the Diagnosis of Fungal and Acanthamoeba Keratitis. Ophthalmology (2011); 118(1): 29-35
- 19. Clarke B, et al. Advances in the Diagnosis and Treatment of Acanthamoeba Keratitis. Journal of Ophthalmology (2012); 2012: 848892
- 20. Oldenburg C, et al. Microbiological Cure Times in Acanthamoeba Keratitis. Eye (2011); 25: 1155-1160
- McClellan K, et al. Effect of Steroids on Acanthamoeba Cysts and Trophozoites. Investigative Ophthalmology and Visual Science (2001); 42: 2885-2893
- 22. Park DH, et al. The Role of Topical Corticosteroids in the Management of Acanthamoeba Keratitis. Cornea (1997); 16: 277-2
- 23. Bouheraoua N, et al. Prognostic Factors Associated with the Need for Surgical Treatments in Acanthamoeba Keratitis. Cornea (2013); 32(2): 130-136



Haneen Jasim

Haneen is a Clinical Teaching Fellow at Musgrove Park Hospital Email: hjasim@doctors.org.uk

Derek Tole

Derek is a Consultant at Bristol Eye Hospital Email: derek.tole@uhbristol.nhs.uk



Mohan Mundasad

Mohan is an Associate Specialist at Bristol Eye Hospital Email: mohan.mundasad@uhbristol.nhs.uk