Parasitic Keratitis

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Various parasitic infections are important causes of ophthalmic diseases worldwide. Most parasitic infections are spread by insect vectors or consuming or getting contact with contaminated water. There are fairly obvious reasons why parasitic diseases are found mainly in tropics:

- The warm climate encourages the growth and survival of the parasites
- The warm climate encourages the insect vectors
- Poor sanitation and poor water supply makes the food/water contaminated
- People live in close contact with domestic animals which are involved in the life cycle of some parasites

Various organisms producing keratitis are the following:

- Acanthamoeba
- Microsporidia
- Onchocerca
- Leishmania
- Trypanosoma brucii
- Echinococcus granulosus
- Crab louse –Marginal Keratitis (IJO 1976-Dr. Ittyerah)
- Other free living amoeba –Vahikampia/Hartmanella
- Acanthamoeba keratitis

The pathogenic species of Acanthamoeba known to produce keratitis are the following
1. A castellani
2. A polyphaga
3. A hatchetti
4. A culberstoni
5. A rhysodes
6. A griffina

Out of these castellani and polyphaga are commonly associated with keratitis whereas culberstoni is rarely encountered but highly virulent.

Life Cycle

The life cycle consists of 2 stages:

1. Trophozoite (14-40 μm in diameter)
2. Cyst (12-16 μm diameter & a double layered wall)

Fig. 1. Isophozotic and Cyst of Acanthamoeba

Acanthamoeba genus causes 3 clinical syndromes.
- Granulomatous amoebic encephalitis, Disseminated granulomatous amoebic disease (eg- skin, sinus, and pulmonary infection)
- Amoebic keratitis

Patients who develop the first two are usually immunocompromised whereas those who develop keratitis are immunocompetent.
Acanthamoeba was first established as a case of human disease in 1973. This vision threatening corneal disease was first recognized in contact lens wearers. There was a sharp increase in the recognition (and perhaps incidence) of this disease in the late 1980's. First case of Acanthamoeba keratitis from India was reported in 1987 from Aravind Eye Hospital, Madurai.

**Epidemiology**

Acanthamoeba are free living, ubiquitous pathogenic protozoa. They are isolated from soil, water (including natural and treated) air and dust. Most persons appear to have been exposed to this organism during their lifetime as 50-100% of healthy people have serum antibodies against acanthamoeba. Studies have also demonstrated that this amoeba can be cultured from nasopharynx of healthy individuals. Acanthamoeba cysts are very resistant to chlorine. It converts from trophozoites to more durable cyst form during unfavourable conditions, making the organism highly resistant to killing by desiccation, irradiation or chlorination. Acanthamoeba thrives in soil, ponds, swimming pools and contact lens solution. Despite widespread prevalence in nature, the incidence of keratitis is low because it is a weak pathogen and there is a high degree of innate host resistance. Trophozoites are probably more important than cysts in initiating keratitis.

The incidence of Acanthamoeba keratitis accounts for 1-4% of proved keratitis. Mud as a cause for corneal trauma resulting in Acanthamoeba keratitis is significantly more than any other material. Contact lens wear does not emerge as an important risk factor for the development of Acanthamoeba keratitis in our population.

**Pathophysiology**

The occurrence of infection is multifactorial. Keratitis occurs in patients with minor corneal trauma. Minor trauma in western countries is due to contact lens wear. Amoeba are introduced via contaminated solution or wearing lenses while swimming. All types of contact lens can predispose to this. In our country, people belonging to poor socio economic strata are affected (who are using unclean, contaminated water for washing eyes). 60% of cases in our country are due to ocular trauma. Humans come into contact with amoeba while swimming in lakes, pools, sea water and also on contact with mud and tap water. This direct exposure combined with minor trauma leads to corneal infection.

**Clinical features**

Patients will have similar symptoms as with other forms of keratitis, but pain will be out of proportion to the findings. **Clinical signs** are discussed in three stages:

1. **Early stage** Epithelial defects, epithelial haze, pseudodendrites
2. **Late stage** Epithelial defects, stromal infiltrates, nummular keratitis
3. **Advanced stage** Ring infiltrate, satellite lesions, stromal abscess (Fig. 2 a-d)

**Other features**

- Severe anterior and posterior uveitis
- Nodular or Diffuse scleritis
- Corneal stromal infiltrates (single, multiple, ring shape)
- Anterior uveitis (transient hypopyon)
- Radial keratoneuritis
- Disciform keratitis

Fig. 2. Clinical findings in acanthamoeba keratitis (a) epithelial haze (b) pseudo dendrites (c) Ring infiltrate (d) stromal abscess
Clinical characteristics that help to distinguish Acanthamoeba keratitis from other keratitis include the following:

1. Ring infiltrate
2. Elevated epithelial lesion
3. Relative lack of vascularisation even in chronic and severe cases

**Clinical Diagnosis**

Acanthamoeba keratitis poses a diagnostic challenge because of its similarity to fungal and viral keratitis. Most often Acanthamoeba keratitis in early stage is misdiagnosed as herpes simplex keratitis, and in late stage as fungal keratitis. There will be a history of trauma with soiled water, organic matter, and rarely contact lenses. Adults engaged in outdoor work are affected mainly. Suspect when the response to antiviral or antibiotic drugs is poor or absent. Patient might have had several consultations with different Ophthalmologists before a proper diagnosis is established.

**Laboratory Diagnosis**

Acanthamoeba trophozoites or cysts can be demonstrated in corneal scrapings or a biopsy sample via wet mount, stains, histopathologic examination or culture.

**10% KOH wet mount** is used routinely as an initial procedure to identify cysts and to exclude fungi. Sensitivity of this test is almost equal to Calcoflour white. Motile trophozoites may be seen in a wet mount preparation.

Stains commonly used are:

- **Geimsa**
  - Cysts & Trophozoites stain purple
- **Lactophenol cottonblue**
  - Cyst wall stains green/
  - Trophozoite red
- **Gram**
  - Cysts show as multisided gram positive crystals
- **Calcoflour white**
  - Cyst wall stains green/
  - Trophozoite red
- **PAS**

**Other diagnostic options**:

Indirect fluorescent antibody staining

**Confocal microscopy**: This provides in vivo views of the cornea and delineates both trophozoites and cysts. The double walled cysts are particularly prominent and radial keratoneuritis can be appreciated. This can also be used to monitor the patient on treatment. Equipment is costly and is available only in specialized centres. If corneal specimens are unremarkable consider culturing contact lens or cleansing solution for amoeba

**Culture** Acanthomeba could be isolated by inoculating the specimen on non nutrient agar with E.coli overlay. The plate should be incubated for more than a week. Acanthamoeba feed off the bacteria, leaving linear tracks(migration tracks/snail tracks) in the plates.

Tissue specimens, corneal smears, contact lenses and swabs may be kept in Page’s saline (phosphate buffered saline) and sent to lab, if materials for culturing are not available (fig 7)

![Fig. 7. Acanthomeba in culture on non nutrient agar with E. Coli overlay](image)

An alternative to non nutrient agar has also been described. Corneal scrapings may be inoculated in tissue culture flask containing suspension of E.coli in ¼ Ringer solution. The flask is incubated at 37ºC and examined daily for trophozoites using an inverted microscope.

Superinfecting bacteria can complicate the diagnosis and isolation of bacterial pathogen does not exclude Acanthamoeba as the cause for keratitis

**Treatment**

There is no consensus on treatment. Various regimens are described. Treatment is required for 6-12 months. Prolonged medication results in corneal vascularisation and toxic keratitis.
Drugs used are:

1. Aromatic diamidines - Propamidine isethionate 0.1 %
   Dibromopropamidine ointment 0.15 %
   (Brolene eye ointment, not available in India)

2. Aminoglycosides - Neomycin

3. Imidazole & Triazole antifungals

4. Polymyxins

5. Cationic antiseptics - Polyhexamethylene biguanide (PHMB) 0.02 %
   Chlorhexidine 0.02 %

Primary agents used are biguanides as they are both trophocidal and cysticidal and also less toxic to cornea than aminoglycosides and antifungals.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Trophicidal</th>
<th>Cysticidal</th>
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<tbody>
<tr>
<td>Chlorhexidine</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>PHMB 0.025%</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Propamidine 0.1%</td>
<td>+</td>
<td>-</td>
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<tr>
<td>Neomycin</td>
<td>+</td>
<td>-</td>
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<tr>
<td>Clotrimazole</td>
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Initial approach can be -

1. Cationic antiseptics in combination with neomycin and propamidine.

2. A combination of topical biguanide and diamidine therapy.

(Pentamidine is not available in India)

Treatment is divided into three phases

1. Loading dose - On days 1 to 3. The patient is given chlorhexidine or PHMB and propamidine with or without neomycin. Each drug is given hourly.

2. Intensive treatment - On days 4 to 7. Above regimen is repeated, 2hrly during day and 4hrly at night.

3. Maintenance phase. From day 8 onwards for atleast 4 months-chlorhexidine or PHMB with or without propamidine 6hrly.

A regimen which can be advocated here is as follows:

PHMB 0.02% hrly for 1week, 2 hrly for 2 weeks, 4 hrly upto 8 weeks.

If no toxicity, continue 4-6 hrly till it heals, which may require nearly 1 year.

(Prolonged use of PHMB promotes corneal vascularistion which is reversible when drug is tapered/withdrawn)

Combine Adjuvant therapy

Topical steroids is controversial as it will foster conversion of cyst to trophozoite

Systemic therapy

Itraconazole/ketaconazole 600mg/day orally

Pentamidine IV in recalcitrant cases 4 mg/kg/d i/v. After first 3 doses reduce to 3mg/kg/d to minimise toxicity

Surgical treatment

Epithelial debridement: Effective in early phase in combination with antimicrobials.

This will improve penetration of the drug and facilitates removal of pathogen

Penetrating keratoplasty: Timing of surgery is critical. It is unwise to perform keratoplasty before infection is controlled or organism is fully eradicated, otherwise graft recurrence will occur. But if impending perforation is seen, keratoplasty may be done, with risk. Optical graft may be done after complete resolution of infection.

In general, treatment of Acanthamoeba keratitis has been disappointing, partly because the infection is frequently well advanced before diagnosis and partly because the available treatment is suboptimal. Successful treatment requires early diagnosis and aggressive medical and surgical management.

Conclusion

Acanthomeba keratitis is a challenging disease to Ophthalmologists. Prevention is the only method till we get a specific drug. Contaminated water is the source of infection in our region hence prevention is a difficult task.
Microsporidiosis

Microsporidians are obligate intracellular parasites and are omnipresent (fig 8)

Microsporial keratitis was first described in 1973

Three species are known to cause keratitis
Encephalitozoon hellum Imuno compromised cases
Nosema corneum Immunocompetent cases
Nosema ocularum Immunocompetent

10 mg/ml suspension of fumagillin can be applied hourly for 24 hrs and then tapered. Complete resolution of symptoms has been reported in a period of 3 days.

Onchocerciasis (River blindness)

The causative organism is a filarial nematode Onchocerca volvulus which is transmitted by the Simulium black fly. There is transplacental transmission also

Eye disease is related with inflammatory response generated by nematodes, which can be found in the conjunctival epithelium, corneal stroma, iris, ciliary body, sclera, extra ocular muscles and optic nerve sheath

Manifestations

Inter palpebral marginal keratitis, Sub epithelial opacities, Stromal oedema due intrastromal worm are some of its clinical manifestations. Cornea may contain large numbers of living microfilaria. Worms are visualized in the slit lamp on retro illumination. Calcific band keratopathy and both anterior and posterior uveitis may be associated with river blindness.

Microfilaria may be observed in the anterior chamber especially in the inferior angle on gonioscopy, or seen as moving shadows against red background with ophthalmoscope.

Diagnosis Based upon the identification of the worm from skin snips

Diagnosis is also confirmed by Mazzoti test: 30 minutes after oral administration of diethyl carbamazepine patient develops pruritis, erythema, flu like symptoms. After the drug administration microfilaria can be recovered from urine and blood.

Treatment

The mainstay of treatment is oral Ivermectin as single dose (150 μgm/kg) and repeated every 6 months to 1 year.

Because of the more complex scenario as well as wide variety of pathological manifestations, each ocular disease has to be addressed individually, including epidemiology, pathogenesis, diagnosis and treatment.