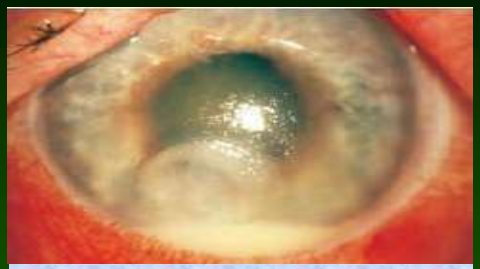
FUNGAL KERATITIS



AKRAM ELGAZZAR MD
Lecturer of Ophthalmology
AL-AZHAR UNIVERSITY
DAMIETTA

INTRODUCTION

- Fungal keratitis is a serious ocular infection with potentially catastrophic visual results.
- Worldwide, it is significant cause of ocular morbidity and unilateral blindness.
- Fungus may be a part of normal external ocular flora (3-28% of normal eyes).

•Fungi are ubiquitous in environment and gain access to cornea through epithelial defect.

•Loss of vision with fungal keratitis is quite disabling in terms of economic impact and social consequences.

DEFINITION

"Fungal keratitis is defined as discontinuation in normal epithelium of cornea associated with necrosis of surrounding corneal tissue"

➢It primarily affect the corneal epithelium and stroma, although the anterior chamber and endothelium of eye may get involved in more severe disease.

EPIDEMIOLOGY

•Its incidence is between **6%-20%** in all microbial keratitis cases depending on geographical location.

•Fungal keratitis is primarily seen in tropical climates and is rare in temperate areas.

•While tropical climate shows a preponderance of filamentous fungi, temperate climates show higher percentage of yeast infections.

MORPHOLOGICAL CLASSIFICATION OF FUNGI

Fungi are eukaryotic heterotrophic organisms and typically form reproductive spores.

Fungal keratitis may be caused by filamentous or non-filamentous fungi.

Filamentous fungi-

- Aspergilus flavus
- Aspergilus fumigatus
- Fusarium spp.
- Alternaria spp.

FUSARIUM OXYSPORUM

Filamentous fungi (contd.)

- Acremonium
- Curvularia

ASPERGILUS FLAVUS

Non- Filamentous fungi (Yeast)

- Candida

CANDIDA ALBICANS

PATHOGENESIS

➢Fungal keratitis caused by ***filamentous fungi*** typically occurs secondary to ocular trauma from vegetative material or contact lens wear or prior ocular surgery(lasik) in ***previously healthy eye***.

➢***Nonfilamentous*** yeasts(Candida sp.) typically cause keratitis in eyes with ***preexisting ocular surface disease*** or eyes that have been recently treated with topical steroids.

➢Fungi gain access to stroma through epithelial defect. In stroma, it cause tissue necrosis & host inflammatory reaction.

➢Fungi can penetrate through intact descemet membrane and into anterior chamber via proteolytic enzymes.

RISK FACTORS

1 Trauma (most common)

2.Contact lens use

3.Ocular surface disease- Herpes Simplex, Herpes Zoster, Vernal / allergic keratitis

4.Topical medications- steroid, anesthetic abuse, broad spectrum antibiotic

5.Corneal surgery-PRK,LASIK

6.Immunocompromised state- HIV, Leprosy

CLINICAL FEATURES

"Symptoms are much milder than clinical signs"

SYMPTOMS :

- ✓Foreign body sensation
- ✓Slow onset increasing pain
- ✓Blurry vision
- ✓Photophobia
- ✓Red eye
- ✓Tearing
- ✓Discharge

SIGNS:

Nonspecific- Ciliary congestion

Epithelial defect

Anterior chamber reaction

Specific-Dry looking ulcer (rough texture)

Elevated edge

Feathery margins

Satellite lesions

Specific signs (contd.)

- Stromal infiltrate
- Endothelial plaque (fig.2)

Fig.2

- Grey/ Brown pigmentation

- Hypopyon (sterile/non sterile, thick, immobile)
- Immune ring of wesseley-due to deposition of immune complexes and inflammatory cells.(fig 3

Fig.3

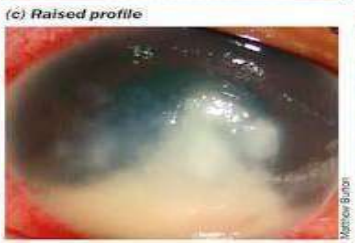
Grading of corneal ulcers

features	Mild	Moderate	Severe
Size	< 2 mm	2-5 mm	> 5 mm
Depth of ulcer	< 20%	20-50%	> 50%
Stromal infiltrate	Dense Superficial	Dense upto mid stroma	Dense deep stromal
Scleral involvement	-	-	present

DIFFERENTIAL DIAGNOSIS

- Bacterial keratitis
- Acanthamoeba keratitis
- Herpes simplex virus keratitis
- Atypical mycobacterial keratitis
- Sterile corneal ulcer
- Retained foreign body
- Marginal ulcer

Fungal keratitis Vs Bacterial keratitis



MANAGEMENT

❖**HISTORY**

- History of recent ocular trauma (specially with vegetative material)
- Contact lens wear
- Use of ocular medications
- Recent ocular surgery

❖SLIT LAMP EXAMINATION

- Stain with Fluorescein to assess for epithelial defect
- Assess for corneal infiltrate
- Assess for anterior chamber reaction (cells and flare)
- Evert upper eyelid to check for retained foreign body
- Hypopyon
- Check intraocular pressure (IOP)- digitally

▪**CORNEAL ULCER:- A description**

1.Location- should be marked schematically on diagram.

May be central, paracentral, peripheral or total.

Central ulcers have poor vision with poor visual prognosis

2.Shape of ulcer no definite shape in fungal keratitis

3.Margins irregular, rolled out, feathery margin

4.Size of ulcer- important for follow up visits and monitor progress

5.Epithelial defect- epithelial defect and size of infiltration should be measured separately in two largest meridians.

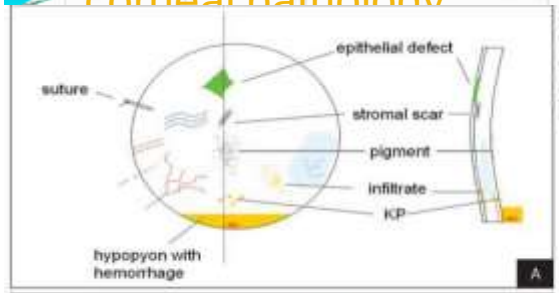
•Staining (fluorescein or rose bengal) may be used whenever necessary.

•Epithelial edema if present should be noted.

6..***Infiltration***- May be single or multiple. Depth, size, density of infiltration should be noted.

7.***Corneal sensations-*** either with a cotton whisp or esthesiometer

Color coding of general corneal pathology



❖LABORATORY EVALUATION

- Obtain corneal scrapings for microscopy and culture
- Scrape deep into ulcer margin and base to obtain adequate material

➢**Microscopy** should ideally include :

- **Smear** Potassium hydroxide (KOH) preparation(10%)

❑KOH wet mount is simple , inexpensive and rapid test that is easy to interpret. So it is preferred in resource poor areas.

KOH preparation technique-

1. Place corneal scraping on clean slide.
2. Add a drop of 10% KOH to the specimen.

3.Cover specimen with cover slip, avoid air bubble entrapment

4.Incubate for 5-10 min at room temperature.

5.Examine saline wet mount with 10x and 40x

- Stains- Gram stain
  Giemsa stain
  Gomori methamine silver stain

- **Fluorescent microscopy-**
  Calcufluor white stain
  Acridine orange

➢ **Culture media:-** Corneal scrapings should be sent for culture in all suspected cases. Culture media should be same for general infectious keratitis workup

- Sheep Blood Agar
- Chocolate Agar
- Sabourauds Dextrose Agar (SDA)
- Brain heart infusion broth

❑ **Positive culture** expected in **90%** cases,
within 72 hrs in 83% cases
within 1 week in 97% cases

✓ Increasing humidity of medium by placing inoculated agar plates in plastic bags enhance fungal growth

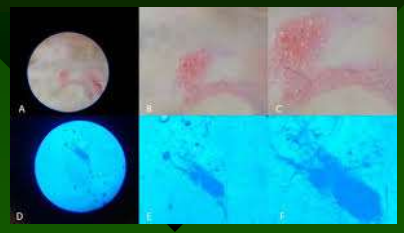
❑ If cultures are negative but have high clinical suspicion consider **corneal biopsy**.

➢ **Newer methods of detection**

- *Confocal microscopy*- identification of fungal hyphae in vivo within cornea.
- *Anterior segment OCT*- mycotic keratitis presents early localized or diffuse necrotic stromal cystic space.
- *Polymerase chain reaction*
- *Genotyping*
- *Antifungal susceptibility testing*
- *Smartphone based digital imaging*

Smartphone-based digital imaging

Recently Agarwal *et al*. have reported on the use of smartphone-based digital imaging in diagnosis and follow-up of keratitis.Tissue samples obtained by conventional corneal scraping were stained and imaged using a smartphone coupled with a compact pocket magnifier and integrated light-emitting diode assembly. Photographs of multiple sections of slides were viewed using smartphone screen and pinch-to-zoom function.



TREATMENT

➢ **Aim of treatment** :

•Resolution of infectious process as rapidly as possible

•Decrease in adverse outcome such as the need for a therapeutic keratoplasty or loss of the eyes.

➢ **General concerns during treatment:**

•Fungal keratitis is difficult to treat and often has long protracted course, may take weeks or month to resolve

•Daily exams are required until clinical improvement or stabilization is observed

•Close follow up is essential and hospital admission may be necessary.

•Corneal transplant may be required for severe or recalcitrant cases

MEDICAL MANAGEMENT

❖**SPECIFIC TREATMENT-Antifungal drugs**

The mainstay of treatment of fungal keratitis are topical antifungal agents.

❑***Topical antifungal*** - Natamycin(5%), Amphoterecin B(0.15%), Fluconazole(0.2%),Voriconazole(10%),Nystatin (3.5%)

❑***Intracameral***-Amphoterecin B(15mcg/0.1ml),Miconazole(5mg/0.5ml)

❑***Intravitreal***-Voriconazole(50mcg/0.1ml), Amphoterecin B(5mcg/0.1ml)

❑***Oral***- Ketoconazole(200-400mg/daily), fluconazole(100-400mg/d),Itraconazole(200-400mg/d), Voriconazole(200mg, BD), Posaconazole(200mg ,TDS)

❑***Intravenous***-Amphoterecin B(0.5mg/kg), Fluconazole(200-400mg/d), Itraconazole (200mg/d)

➢**Natamycin** (5% topical solution)-initially q1-2h, then tapered over 6-8wks .

▪FDA approved drug for fungal keratitis ; available as ophthalmic drops.

▪Drug of choice for filamentous fungi

▪Poor penetration limits use in deep or severe infections

➢**Amphoterecin B** (0.15% topical solution) initially q1-2h then tapered over 4-6wks

▪Good activity against Aspergillus and Candida

▪Not available as a topical solution, must be compounded from intravenous formulation.(50mg of Amphoterecin B is diluted in sterile water = 0.15%)

▪Can be used via topical, subconjunctival, intracameral, intravitreal or intravenous route.

➢**Voriconazole** (1%) q1h, then tapered over 6-8wks .

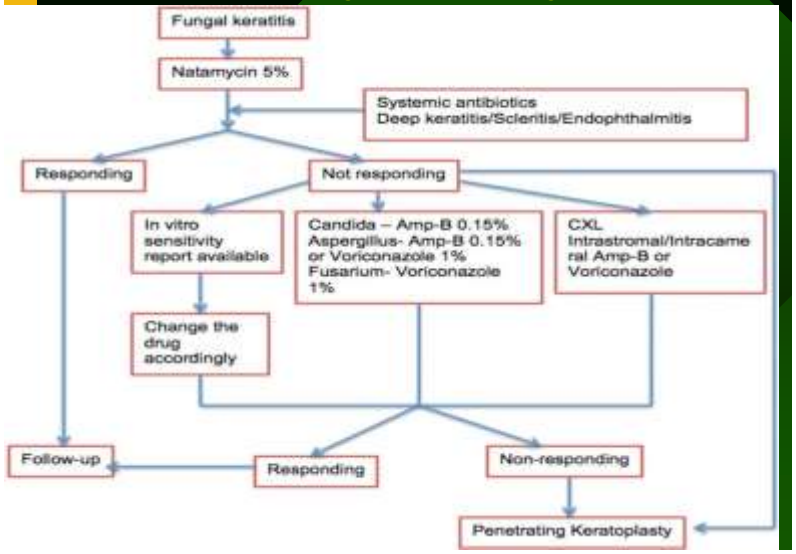
▪Broad spectrum of activity against Candida, Aspergillus, Fusarium, Scedosporium.

▪Difficult to obtain as topical - need to be compounded

➢**Econazole** (1% topical solution is available in India)
Found to be equivalent to Natamycin 5% in randomized control trial by Prajna etal

➢**Clotrimazole** (1% topical solution is available in India)
Not ideal as monotherapy

Flowchart for management of fungal keratitis



Indication for systemic antifungal

(Voriconazole 1st choice)

- Severe deep keratitis
- Scleritis
- Endopthalmitis
- Virulent fungus
- Prophylactic treatment after penetrating keratoplasty

Nonspecific treatment

- Add a cycloplegic (1% atropine, TDS)
- Systemic analgesic and anti-inflammatory to relieve pain and decrease edema.
- Multivitamins to improve immunity and help in healing
- Systemic ascorbic acid to accelerate corneal remodeling and healing
- Antiglaucoma medication

- Currently the use of corneal collagen crosslinking is being evaluated. A recent study found collagen cross-linking not to be beneficial as an adjuvant in deep stromal recalcitrant smear-positive fungal keratitis.
- Inflammatory response from topical toxicity may be confused with persistent inflammation.

Surgical management

- Epithelial debridement- done every 24- 48 hrs under topical anesthesia with surgical blade.
  - It can be done under operating microscope or in slit lamp view.
  - It debulks necrotic material and organisms
  - Enhances penetration of topical drops

- Cyanoacrylate tissue adhesive and bandage contact lens may be used in management of perforation or impending perforation
- .Conjunctival flap
- Lamellar Graft
- Therapeutic Penetrating Keratoplasty

CONCLUSION

✓Most common causative organism is Aspergillus worldwide.

✓Trauma with vegetative material, contact lens use, indiscriminate use of topical steroids, preexisting ocular surface disease are most common risk factors.

- Prolonged and aggressive therapy with antifungal medications and repeated debridement is necessary to treat infection.

✓Corneal perforation and endopthalmitis is common in fungal keratitis and it often require surgical intervention.

Management of fungal keratitis remains a challenge to cornea specialists. Emerging fungal pathogens and resistance to existing antifungal drugs have further added to the reasons for poor prognosis in fungal keratitis. Newer investigative tools, such as PCR and IVCM, can help in reducing the time gap between clinical suspicion and microbiological diagnosis.

Newer antifungal agents and newer methods of targeted drug delivery system can be helpful in treating recalcitrant cases. Nanoparticles and AMPs have shown promise in experimental studies and offer hope for improving prognosis in cases of fungal keratitis in future.


Thank
you!