ABSTRACT... dar_asad@hotmail.com. This article presents patients with unilateral painful red eye refractory to recommended standard treatment regimes in which staining, culture and sensitivity reports were inconclusive. On ocular examination hazy cornea with central corneal abscess was common in all cases. Corneal biopsy was reserved for cases with inconclusive laboratory reports as well as poor response to standard treatment regime. The former revealed fungal hyphae in all cases. Patients mentioned had general predisposition e.g. diabetes mellitus, hot climate (Multan) as well as predisposing factors such as contact lenses, dry eye syndrome, poor ocular hygiene, agricultural background were more prone to fungal keratitis, hence better diagnosed and confirmed early by contemplating corneal biopsy.

Key Words: Painful red eye, Refractory keratitis, uncontrolled diabetes mellitus, contact lens use, dry eye syndrome, corneal biopsy.

INTRODUCTION

Infective keratitis is common cause of ocular morbidity. A significant proportion of cases have potentially modifiable risk factors e.g. uncontrolled diabetes mellitus, contact lens use, dry eye syndrome were associated with refractory keratitis and poorer visual outcomes. Many cases of severe keratitis might be avoided, or their severity reduced, by appropriate education of patients and ophthalmologists.

CASE EXAMPLE: 01

A 70 years old lady reported with right painful red eye and reduced visual acuity of 40 days duration. It was associated with headache, mild discharge and photophobia. She was having diabetes mellitus for last 10 years, for which she was taking injection insulin (70:30) 35+20 units twice daily. There was no history of trauma, surgery, contact lens use, floaters, flashes of light, fever, rash, joint pain, urinary complaints or past
history of hypertension. On general physical examination she was a lady of average built with poor personal hygiene but without any obvious pallor, edema, jaundice, rash and palpable lymph nodes. She had a full volume pulse with blood pressure of 130/80 mm of Hg.

Ocular examination revealed that visual acuity was perception of light in right eye and 6/18 in left eye. Anterior segment examination of right eye showed swollen lids, congested conjunctiva, hazy edematous cornea with central abscess and hypopyon (1.5mm in width & 7.5mm in height initially which eliminated later).

Investigations revealed raised blood glucose level, corneal scrapings for culture and sensitivity showed no organism growth and ultrasonography B scan was within normal limit. A diagnosis of right keratitis with hypopyon was made.

A multidisciplinary approach was adopted to manage the patient by involving the medical specialist. The patient was put on Inj. Insulin, oral hypoglycemic drugs, topical antibacterial (fortified eye drops), antiviral, antifungal and cycloplegics along with broad-spectrum systemic antibiotics. During the course of treatment sub. conjunctival injections of antibiotics were also given. But the patient did not respond well even after two weeks of continuous treatment and monitoring which was also associated with poor (fluctuating blood glucose levels daily) diabetic control. Then corneal biopsy was performed which showed necrotic corneal tissue with fungal hyphae. Then specific treatment for filamentary fungal keratitis (with strict diabetic control) was started to which patient responded well by improving symptoms and signs both.

**CASE EXAMPLE: 02**
A 25 years old lady reported with left painful red eye and...
reduced visual acuity of 03 days duration. It was associated with headache, mild discharge and photophobia. She was having history of contact lens use for last two years. There was no history of trauma, surgery, floaters, flashes of light, fever, rash, joint pain, urinary complaints or past history of hypertension and diabetes mellitus.

On general physical examination she was a lady of average built with poor personal hygiene but without any obvious pallor, edema, jaundice, rash and palpable lymph nodes. She had a full volume pulse with blood pressure of 110/80 mm of Hg.

Ocular examination revealed that visual acuity was 6/60 in left eye and 6/18 in right eye without glasses and 6/60 in left eye and 6/6 in right eye with glasses. Anterior segment examination of left eye showed swollen lids, congested conjunctiva, hazy edematous cornea with central abscess. Pupil, iris, lens and posterior segment examination was not possible due to hazy view. Examination of right eye revealed no abnormality

Corneal scrapings for culture and sensitivity showed no organism growth and ultrasonography B scan was within normal limit. A diagnosis of left keratitis was made.

The patient was put on topical antibacterial (fortified eye drops), antifungal and cycloplegics along with broad-spectrum systemic antibiotics. But the patient did not responded well even after two weeks of continuous treatment and monitoring. Then corneal biopsy was performed which showed necrotic corneal tissue with fungal hyphae. Then specific treatment for filamentary fungal keratitis was started to which patient responded well by improving symptoms and signs both.

CASE EXAMPLE: 03
A 65 years old gentleman reported with right painful red eye and reduced visual acuity of 07 days duration. It was associated with headache, mild discharge and photophobia He was having history of dry eye syndrome for which he was using lubricating eye drops for last three years. There was no history of trauma, surgery, floaters, flashes of light, contact lens use, fever, rash, joint pain, urinary complaints or past history of hypertension and diabetes mellitus.

On general physical examination he was a gentleman of average built with poor personal hygiene but without any obvious pallor, edema, jaundice, rash and palpable lymph nodes. He had a full volume pulse with blood pressure of 130/70 mm of Hg.

Ocular examination revealed that visual acuity was 6/24 in left eye and hand movements in right eye without glasses and 6/12 in left eye and no improvement in right eye with glasses. Anterior segment examination of right eye showed swollen lids, congested conjunctiva, hazy edematous cornea with central abscess. Pupil, iris, lens and posterior segment examination was not possible due to hazy view. Examination of left eye revealed no abnormality except lenticular opacity.

Corneal scrapings for culture and sensitivity showed no organism growth and ultrasonography B scan was within normal limit. A diagnosis of right keratitis was made.

The patient was put on topical antibacterial (fortified eye drops), antifungal and cycloplegics along with broad-spectrum systemic antibiotics. During the course of treatment sub. conjunctival injections of antibiotics were also given. But the patient did not responded well even after two weeks of continuous treatment and monitoring. Then corneal biopsy was performed which showed necrotic corneal tissue with fungal hyphae. Then specific treatment for filamentary fungal keratitis was started to which patient responded well by improving symptoms and signs both.

DISCUSSION
The eye is subject to infections, among which the infection of the cornea is an important chapter of modern ophthalmology. The cornea may present with suppurative keratitis due to virus, bacteria, parasites and fungi. Fungi are not the most frequent etiologic agents of
infective keratitis. Even if they are not the most frequent type, the diversity of the clinical presentations and difficulty of treatment annually lead to several publications which enrich knowledge about this issue. Normal conjunctival micro-biota usually does not consist of fungi. In some special situations of life or work, individuals exposed to corneal trauma are more prone to develop mycotic infection.

Any situation that promotes loss of corneal epithelium integrity is considered a risk factor for keratitis in general. Mycotic keratitis refers to the corneal infection caused by either filamentous fungi (moulds) or yeast. There are important epidemiological and clinical differences between these two forms. The most important risk factors related to fungal keratitis include trauma (generally with plant material), chronic ocular surface diseases, contact lens usage, surgery, corneal anesthetic abuse, and immunodeficiencies. Interestingly, fungal keratitis is a condition related to warm climates. The patient presents with foreign body sensation, photophobia, blurred vision, and discharge. Red eye and ocular pain are associated features. Ocular examination shows fine or coarse granular infiltrate within epithelium and anterior stroma. Gray-white color, dry, and rough corneal surface that may appear elevated. Typical irregular feathery-edged infiltrate with white ring in the cornea and satellite lesions near the edge of the primary focus of the infection. In advance cases suppurative stromal keratitis associated with conjunctival hyperemia, anterior chamber inflammation, hypopyon, iritis, endothelial plaque or possible corneal perforation.

Histopathologically the lesions typically advance into the deep stroma of the cornea and contain hyphae that are 3-4 um in diameter with some swollen cells. The fungus usually develops throughout the entire depth of the cornea. It is not uncommon for hyphae to be only in the middle and deeper layers. Early in the disease, there is an acute suppurative inflammatory process accompanied by coagulative necrosis. Hyphae are typically aligned parallel to the lamellae of the cornea.

The diagnosis of mycotic keratitis must include the demonstration of the fungus in corneal scrapings and the recovery of a compatible fungus.

Clinical material can be mounted in 10% anoles or stained by the Gram, PAS, GMS, Giemsa or calcofluor techniques. Fungi are usually deep within the corneal structure, not on the surface. Extensive debridement may be necessary to obtain satisfactory clinical material. Swabs are unsatisfactory. If corneal smears and culture are not conclusive then corneal biopsy should be performed to confirm the diagnosis.

Fungal keratitis is a serious condition that requires prolonged treatment and close follow-up. Natamycin appears to be the drug of choice and amphotericin B a second alternative. Chlorhexidine has emerged as a potential inexpensive option but current data are limited. Systemic therapy with azoles, particularly fluconazole should be considered when yeasts are involved.

Surgery may be necessary, depending upon the degree of damage to the eye. Interventions range from simple scraping of ulcerative lesions to superficial or lamellar keratectomy. Animal models suggest that excimer laser may have a role in the future. Anecdotal experience with liposomal preparations of amphotericin B have suggested their potential role in refractory cases.

FACTORS RESPONSIBLE FOR POOR RESPONSE IN INFECTIVE KERATITIS.

Local
1. poor ocular hygiene
2. contact lens use
3. dry eye syndrome.

Systemic
Uncontrolled diabetes mellitus.

Others
1. Hot climate
2. Poor compliance
3. Low efficacy of drugs (improper storage and poor dispensing techniques.)

CONCLUSION
The experience of our cases is that if the patient of keratitis is having history of ocular trauma with vegetable matter (plants), uncontrolled diabetes mellitus (1st case), contact lens use (2nd case), dry eye syndrome (3rd case), living in hot climates (all cases), or/and poor personal hygiene (all cases) and any of these or more factors associated with no response to standard topical antibiotics and antiviral (all cases) then the most likely diagnosis should be of fungal keratitis. Corneal biopsy should be mastered and performed early.

Delay in diagnosis and treatment due to staining or culture and sensitivity in a patient who had already used topical antibiotics and antiviral therapy with no response for two to three weeks be avoided. Corneal biopsy should be the investigation of choice for confirmation of diagnosis if staining or/and culture and sensitivity both are negative.

REFERENCES
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