



Viral Keratitis

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Viral keratitis is a common cause for unilateral blindness in both developing and developed countries. The frequency of viral keratitis has become greater because of the role of newer antibiotics in eliminating the bacterial flora.

Even though both DNA and RNA viruses are responsible for keratitis, common corneal infections are caused by DNA viruses-(herpes group viruses- (Type I, Type II, Type III -VZV, Type IV-CMV, Type V-EBV) and adenoviruses).

Herpes Type I- and Type II (Fig. 1) cause labial infection and keratitis which are its commonest manifestations.



Fig. 1. Herpes virus

Prevalence

Studies show that 90 % of adults have positive herpes simplex antibodies but all are not symptomatic. Transmission occurs by direct contact with lesions, secretions or sub clinically.

After entry into the host and primary infection with viral replication within the end organ, HSV travels in a retrograde fashion to various sensory ganglia, most commonly the trigeminal ganglion and possibly the brain stem.

Clinical Manifestations

1) Congenital Ocular Herpes

Is rare and is acquired from genital herpes in the mother, during birth. Ocular lesions include lid lesions, conjunctivitis, epithelial and stromal keratitis and cataracts.

2) Primary Ocular Herpes

It is the first infection of a non immune patient. By the age of 5 years, 60 % population has been infected by HSV. But only 6 % of these develop clinical manifestations which typically affects perioral region rather than the eye. May present as typical epithelial lesions such as A/C follicular conjunctivitis, kerato conjunctivitis with pre auricular lymphadenopathy, punctate keratitis evolving into microdendrites etc. Condition is self limiting and the usual course of the disease is 10 days.

3) Recurrent Ocular Herpes

33 % of recurrence is reported within two years in patients with two prior infections.

A clinical manifestations of infectious keratitis and immunological disease can affect all levels of the cornea. Bilateral disease is noted in immuno compromised patients.

Whether primary infection is asymptomatic or symptomatic, all patients once infected with HSV at

any site become viral carriers with the virus residing in a latent stage in the sensory ganglia or cornea.

Trigger factors for reactivation-

Fever, systemic illness
 UV light
 Intra ocular surgery
 Ocular trauma
 Trigeminal ganglionectomy
 Laser treatment on the eye
 Topical steroids, latanoprost, etc.

Clinical types of recurrent ocular herpes

- 1) Infective epithelial keratitis
 - a) Corneal vesicles
 - b) Dendritic ulcers
 - c) Geographical ulcers
- 2) Non infective epithelial keratitis
 Neurotrophic keratopathy
- 3) Stromal keratitis
 - a) Necrotising stromal keratitis-Infective
 - b) Immune stromal (interstitial) keratitis-Non-infective
 - i) Antigen antibody complement mediated
 - ii) Lymphocyte mediated
- 4) Endothelitis
 - a) Disciform
 - b) Diffuse
 - c) Linear

1) Infective Epithelial Keratitis

Superficial Punctate Keratitis : Earliest manifestation of viral infection of cornea are corneal vesicles/superficial punctate keratitis with decreased corneal sensation (Fig. 2a & 2b).

Symptoms include pain photophobia, watering, decreased vision

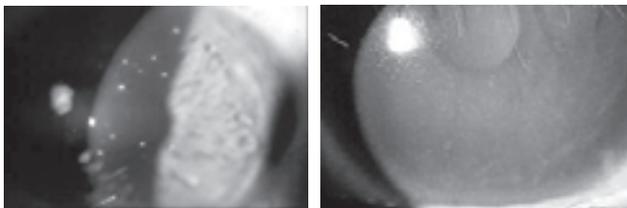


Fig. 2. Superficial punctate keratitis

S/L biomicroscopy shows multiple white sub epithelial non staining infiltrates

Dendritic ulcer

This is a common presentation. It is a branching linear lesion with terminal bulbs and swollen epithelial borders that contain live virus. It extends upto the basement membrane. Even after healing of the ulcer, the dendritic ulcer may result in abnormally appearing epithelium for several weeks. This epitheliopathy is dendritic in shape but is not ulcerated and does not require treatment (Fig. 3a & 3b).



Fig. 3. Dendritic keratitis

Geographic ulcer

This is a widened dendritic ulcer with swollen epithelial borders that contain live virus (Fig. 4a and 4b). It extends through the basement membrane and has scalloped borders. May be associated with previous use of steroids.

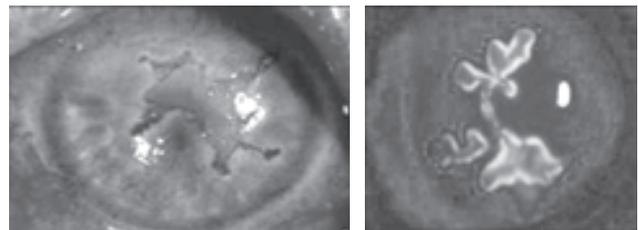


Fig 4. Geographic keratitis

Sequelae of Infective Epithelial keratitis

Infective epithelial Keratitis may resolve completely or may progress to stromal disease.

2) Neurotrophic keratopathy

Factors contributory:-

- a) Impaired corneal sensation
- b) Decreased tear secretion
- c) Excessive use of antivirals

Patients who have had epithelial disease are at risk to develop this entity. This is neither immune nor infectious. The epithelial defect is oval in shape with smooth borders and eventually leads to stromal ulceration (Fig. 5).



Fig. 5. Neurotrophic keratopathy

Complications are stromal scarring, corneal neovascularisation, secondary bacterial infection, necrosis and perforation of cornea.

3) Stromal Keratitis

Rare in primary infection. Stromal disease accounts for 20-48 % of recurrent ocular disease.

a) Necrotising stromal keratitis

The clinical findings are necrosis, ulceration and dense infiltration of the stroma with an overlying epithelial defect (Fig. 6). The combination of replicating virus and severe host inflammatory response leads to destructive intrastromal inflammation. The ulcer resembles microbial keratitis.

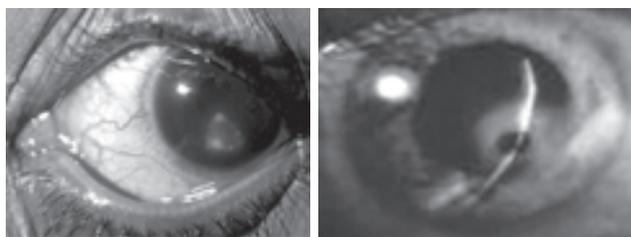


Fig. 6. Necrotising stromal keratitis

b) Immune stromal (interstitial) keratitis

i) Non infective antigen antibody complex mediated stromal keratitis which manifests as a recurrent disease (Fig 7).

Retained viral antigen within the stroma triggers an intrastromal inflammation. Punctate stromal

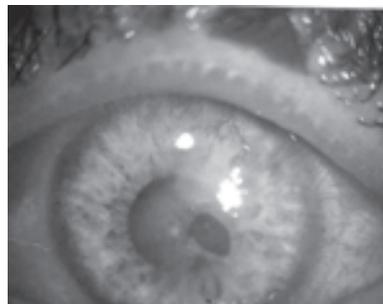


Fig. 7. Stromal interstitial keratitis

opacities with intact overlying epithelium is characteristic. The stromal infiltration may be focal, multifocal or diffuse accompanied by anterior chamber reaction and ciliary flush. It may lead to disciform keratitis at any level of the cornea. Stromal neovascularisation may occur.

ii) Wesseley ring

It is an immune phenomenon seen in the cornea due to deposition of immune complexes and inflammatory cells around the antigen.

iii) Limbal vasculitis

is often confused with staphylococcal marginal keratitis associated with infective blepharitis

Symptoms in limbal vasculitis are pronounced, neovascularisation is common. Corneal sensation is diminished and the lesions progress centrally, and can affect any meridian (Fig. 8).

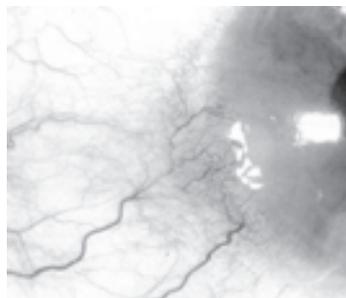


Fig. 8. Limbal vasculitis

ii) Non infective lymphocyte mediated limbal vasculitis (Fig. 9)

Endothelitis

Many patients with HSV disease develop stromal oedema without stromal infiltration. They present with

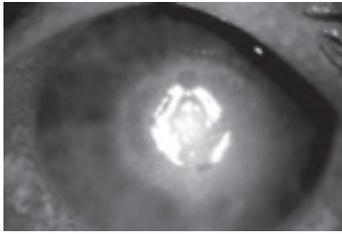


Fig. 9. Viral endothelitis

KPs, overlying stromal and epithelial oedema and iritis. Disciform keratitis is actually an endothelitis as the inflammatory reaction is not a reaction of stroma but at the level of the endothelium. May clinically present as disciform, diffuse or linear lesions (Fig. 10).

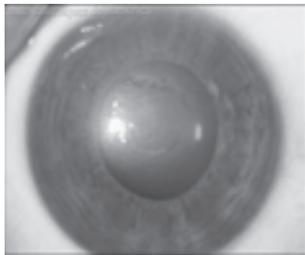


Fig. 10. Disciform endothelitis

Iridocyclitis

It may develop concomitantly or subsequently with HSV infection. A trabeculitis is a common accompaniment leading to secondary glaucoma, iris atrophy, corneal decompensation etc. (Fig. 11)



Fig. 11. Zoster ophthalmicus

DIAGNOSIS OF VIRAL KERATITIS

- 1) Clinical presentation
- 2) Decreased or absent corneal sensation-in herpetic keratitis
- 3) Exam of infected samples cytology for inclusion bodies

- 4) Electron microscopy
- 5) Growth of virus in tissue culture
- 6) Detection of viral antigen
- 7) Serological tests
- 8) PCR-Specific but costly

Treatment of IEK (Infective epithelial keratitis)

- 1) Debridement of the involved epithelium with a sterile applicator followed by local antiviral treatment- 3 % Acyclovir eye ointment 5 times daily for 2 weeks
- 2) In recurrent cases oral ACV 200mg 5 times daily for 2-3 weeks

Occasional patients develop more than 2-3 recurrence/year.

Such patients require oral Acyclovir 400mg bid 6 months to 2 years or newer antiviral drugs like Famcyclovir (Famvir) 500 mg 3 times a day or Valacyclovir (valtrex) 500mg 3 times a day are also effective and more convenient.

In the absence of stromal disease corticosteroids are contraindicated in infective epithelial keratitis

In Epithelial trophic ulcers(meta herpetic ulcers) structural damage occurs in basement epithelium and anterior stroma due to recurrent scarring and loss of sensation which results in persistent sterile ulceration. Damaged basement membrane takes atleast 12-15 weeks to heal.

Management of trophic ulcers

Antiviral therapy is not indicated in patients with trophic ulcers.

Cauterization can worsen the condition by further damaging the basement membrane

Lubrication with artificial tears, patching, therapeutic contact lenses can be tried.

Tissue adhesive with soft contact lenses till the epithelial healing closes the defect may help.

Conjunctival transplantaion, tarsorrhaphy, conjunctival flapping or KP are the other therapeutic options.

Cyclopentolate is avoided since this drug tend to attract polymorphs

Treatment of herpetic immune stromal / endothelial disease

- 1) Artificial tears if disease is mild and not involving the visual axis.
- 2) Cylcoplegics atropine/homatropine
- 3) Topical steroids 0.1% dexamethasone or 1% prednisolone eye drops every 3 hours for severe disease to 0.12% prednisolone eye drops daily QID for less severe cases and tapered slowly.
- 4) Topical antibiotic prophylaxis at higher steroid dosage
- 5) Topical Acyclovir 5 times if steroids are used more than 2 times/day.
- 6) If the epithelium is ulcerated topical steroids are replaced by 1% medroxy progesterone
- 7) Antiglaucoma therapy as and when needed
- 8) Consider systemic Acyclovir 400mg bid in place of topical ACV in recurrence IEK.
- 9) "Kerato plasty SHOULD BE DEFERRED"-until the eye has been quiet on little or no steroid treatment for several months. HSV – IK is the commonest form of ocular herpes to recur in a new graft.

Penetrating Keratoplasty should be considered when there is corneal perforation that cannot be treated with other modalities, especially in the presence of a central stromal scar.

PK helps to eliminate the corneal antigenic materials responsible for immune mediated keratitis.

Post operatively Acyclovir 400mg bid for 1 year is given along with frequent topical steroids to improve graft survival. (12-19% recurrence)

Herpes Zoster Keratitis

Varicella zoster virus is also known as Herpes virus III differs clinically and antigenically from herpes simplex. Chicken pox and zoster are different entities caused by the same virus.

Aetiopathogenesis-Chicken pox represents primary infection after exposure of a non immune person to varicellazoster virus. This virus then becomes latent in the cells of dorsal root ganglion through out the body. Reactivation may occur resulting in characteristic dermatological eruption of the herpes zoster, common in older age group. Herpes Zoster in younger age indicates immunosuppression.

Commonly involves ophthalmic division of 5th cranial nerve. Nasociliary involvement in herpes zoster ophthalmicus is associated with 76% chance of ocular complications. Herpes Zoster virus lies latent in trigeminal ganglion, reactivation is preceded by a prodrome of malaise, fever and head ache which represents viremia.

HUTCHINSON's sign describes vesicles at the side and tip of nose. It indicates ocular involvement which occurs in 50% cases (Fig. 12).

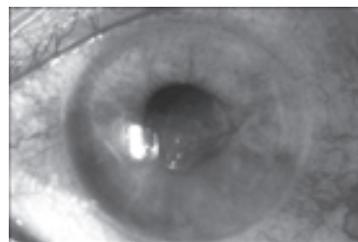


Fig. 12. Pseudo dendritic ulcers

Clinical manifestations are variable. These include punctate epithelial keratitis, associated with follicular conjunctivitis, pseudodendritic keratitis, anterior stromal infiltrates or nummular keratitis, kerato uveitis, endothelitis, serpiginous ulceration, sclerokeratitis, corneal mucous plaques, disciform keratitis, neurotrophic keratopathy, exposure keratopathy and interstitial keratitis

Pseudo dendrites-are broader, more plaque like and without central ulceration. Varicella Zoster Virus is present in these lesions.

Nummular keratitis

Represent stromal reaction to soluble viral antigen diffusing into the anterior stroma/or direct viral toxicity. These lesions appear as hazy granular infiltrate just under the Bowmans membrane, they are markers of previous Herpes zoster virus inflammation (Fig. 13).

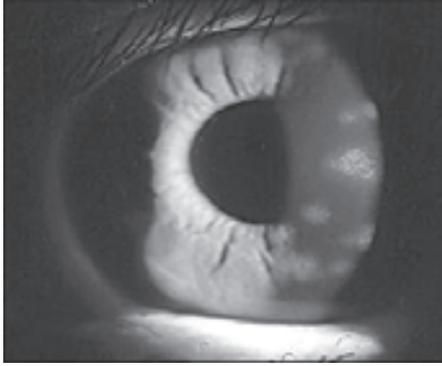


Fig. 13. HZ nummular keratitis

Management

To prevent-severe ocular hazards and promote healing of skin lesions as the crust formation leads to severe trigeminal neuralgia.

- high doses of oral Acyclovir 800mg 5 times/day 10 days started within 72 hours of onset of disease
- For severe cases parenteral Acyclovir 5-10 mg/Kg IV 8th hourly for 8-10 days
- Topical antibiotic to skin lesion

Nummular keratitis, disciform keratitis, sclero keratitis all respond to topical steroids. 1% prednisolone acetate eyedrops 6th hourly along with cycloplegics and antibiotic cover is given.

Neurotrophic keratitis is managed conservatively using lubricants, patching, therapeutic contact lens, tarsorrhaphy and conjunctival flapping

Corneal mucous plaques requires the use of topical steroids supported by lubricants and mucolytic agents like acetyl cysteine 10%

Penetrating Keratoplasty has a poor success rate and hence a period of 1 year after the disease become quiescent is advised. Healthy donor tissue, postoperative protection of epithelium with lubricants, and tarsorrhaphy increase the rate of success of penetrating keratoplasty.

Live attenuated varicella zoster vaccine is used in the prevention of varicella zoster infections.

Adenoviral Keratitis

This is commonly associated with fever and upper respiratory infection

Keratitis is seen associated with pharyngo conjunctival fever caused by type 3,4,7 adenoviruses. (30 %), or more commonly with epidemic keratoconjunctival fever (80 %)

Clinical Manifestation

Stage I - punctate epithelial erosions (7-10 days)

Self limiting in 2 weeks. Antivirals are not useful.

Stage II - focal white subepithelial opacities which represent an immune response to the virus (Fig. 14).

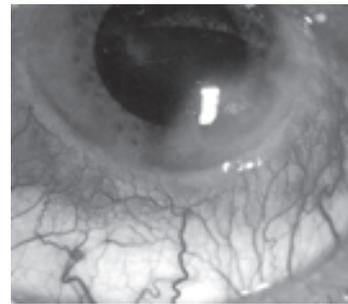


Fig. 14. Focal white subepithelial opacities in adenoviral keratitis which probably represents an immune response to the virus

Stage III - anterior stromal infiltrates which fade over months or years.

These are associated with preauricular lymphadenopathy.

This needs supportive and symptomatic treatment. Steroids suppress inflammation but lesions can recur on tapering steroids.

Epstein Barr virus-infection can produce infectious epithelial keratitis, microdendritic ulcers, stromal keratitis etc. Epithelial keratitis responds to topical Acyclovir or trifluoro thymidine while stromal keratitis needs topical steroids as in herpes disease.

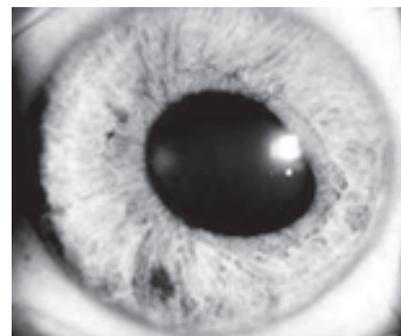


Fig. 15. Post trabeculitis iris atrophy

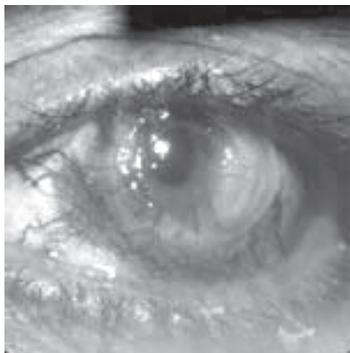


Fig. 16. Herpetic keratitis graft recurrence

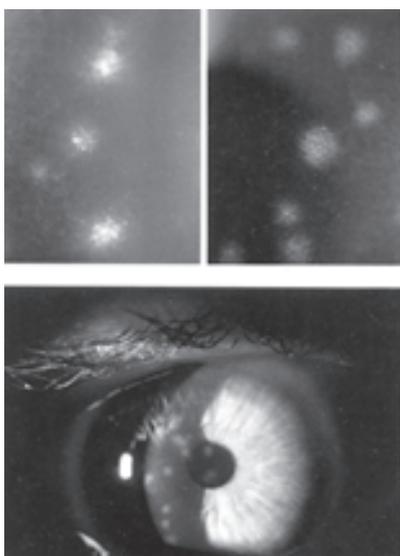


Fig. 17. Adenoviral keratitis

In case of **Molluscum Contagiosum** (pox viruses) the umbilicated wart like growths along the lid margins are associated with punctate keratitis as a result of virus shed into the tear film. Untreated patients develop pannus. Therapy is surgical removal of growths by excision, chemical cautery or cryotherapy. HIV patients are particularly affected by this virus.

Cytomegalovirus infection is the most common virus transmitted in utero. In AIDS patients it causes opportunistic infection of retina. Corneal manifestations include linear stellate endothelial deposits in reticular pattern most often in inferior cornea. These do not resolve even after effective treatment for CMV retinitis. Most of the RNA viruses like mumps, measles viruses produce only minimal epithelial keratitis most of which are insensitive to acyclovir. They need only symptomatic and supportive treatment.

Conclusion

Keratitis is the most serious manifestation of viral infection of the eye especially due to herpetic viruses. All layers of cornea can be involved by the acute or relapsing forms of the disease.

Now specific antiviral drugs are available with less toxic effects on the normal cells.

Long term therapy seems to be beneficial in chronic cases. Only herpes group virus respond to most of the antivirals.

Topical antiviral therapy can be stopped in two weeks. Topical corticosteroids are beneficial for inflammatory components like moderate to severe stromal keratitis, uveitis, trabeculitis, endothelitis etc. than infective epithelial disease. Once you start the patient on topical steroids prolonged maintenance dose may be required.

Role of systemic steroids are controversial. But oral antivirals combined with oral steroids relieves pain more than oral antiviral alone in severe form of the disease.

Severe corneal scarring requiring keratoplasty may be undertaken if there is no active disease and under cover of prophylactic oral antivirals for a minimum of one year with initial frequent steroid drops to reduce inflammation.

Reactivation of viral keratitis can be initiated by any type of laser treatment, antiglaucoma drugs like latanoprost, topical steroid therapy, exposure to uv light, intraocular surgeries etc. So a proper history and thorough examination is mandatory to rule out pre existing viral disease prior to any invasive procedure on the eye.

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In a lighter vein

.....By Degrees

RRV

There was a trilogy of Malayalam movies featuring two job seekers – turned – C.I.D.s. One of them boasts that he had a 'first class in B.Com.', while the other says that 'pre-degree is not a bad degree at all'. They mockingly reflect the mentality of our society, where the number of alphabets suffixing your name is given too much importance. The more, the better, it seems.

When I came out of the Medical College in the second half of seventies, post-graduates were not as common as was later. But people who had passed B.Sc. used to add that too before the M.B.,B.S. I had a class-mate who used to put B.Sc.(Spl.), because he had passed 'Special' B.Sc., with two main subjects (totally irrelevant to his profession). But that is nothing compared to another veteran whose qualifications, M.A.(Hum.), M.B.,B.S., used to puzzle me every time I passed his clinic. When I got to know him better, I asked him about the M.A.(Hum.) part. It was M.A. in Humanities from Aligarh Muslim University! In the early eighties, when P.G. degree was becoming more and more desirable (nee essential), lots of 'Academies' and 'Colleges' cashed in on that. Many are the G.Ps who still add F.I.C.A. (Fellow of International College of Angiology, nothing less) to their name.

You know, they are not to be blamed. The general public associates more degrees with more expertise. In our hospital we used to have a physician who had taken M.R.C.P from Edinburgh and Glasgow, and wrote both with an (E) and (G) suffixing them. Once I heard a patient comment to another. "Dr. Menon has passed M.R.C.P from England and 'Germany'".

I used to think that this affinity was peculiar to our society. But one of my class-mates who has returned from 'States' recently gave a notification in the Kerala Government Gazette about the change in his signature wherein he had added "MBBS" at the end. He says it is the custom there to add 'MD' to ones signature.

I had a relative who has passed M.Sc. and M.A. and went on to get an M.B.A. and later added L.L.B. and L.L.M. to them. While working on his doctoral thesis, he fell ill and died. They say he killed himself by degrees!

Tail piece: My eccentric friend says he is planning to start an **A**cademy of **M**edically and **O**phthalmologically **U**seful **S**pecialties. For five thousand rupees, he says he will make me a 'fellow' and then I can add **F.A.M.O.U.S.** to my suffixes. Tempting, isn't it?