Ophthalmology

Dr.Imad H. Sachit- MD,CABO,FICO,Consultant Ophthalmologist

Learning objectives:

At the end of lecture, students should be able to:

1. Understand the basic knowledge regarding anatomy and histology of cornea.

2. Evaluate & interpret the clinical signs of various corneal diseases according to its layers and differentiate between them.

3. Focusing on risk of microbial keratitis regarding causes, how to diagnose the underlying pathogens by taking culture & sensitivity and finally how to treat.

4. Detailed viral keratitis types explained & should be careful for treating by topical steroid in these situations.

The cornea

Gross Anatomy:

The cornea is the anterior continuation of the sclera. It is a transparent structure, its function is to focus the light rays on the retina, it represents the most important refractive power with forty-three (43) diopter.

Applied anatomy:

The cornea consists of the five following layers: (from anterior to posterior)

1- The epithelium: is stratified (multiple cell layers), squamous and non-keratinized when if damaged, it regenerates without any scarring .

2- Bowman's layer:

Is the Acellular superficial layer of the stroma which scars when damaged.

3- The stroma: makes up 90% of the corneal thickness. It is composed of regularly oriented layers of collagen fibrils whose spacing is maintained by glycosaminoglycan ground substance.

4- Descemet's membrane: it is composed of a fine latticework of collagen fibrils. It is the basement membrane of the endothelial cells.

5- The endothelium:
It consists of a single layer of hexagonal cells. It plays a vital role in maintaining corneal transparency & deturgescence , as water composes 70% of cornea that makes it relatively dehydrated as in other body tissue the water composes 98% of them, so active pump mechanism that removes the fluid that leaks to stroma. With age, the number of endothelial cells decreases and they are non-regenerative cells, therefore the neighboring cells enlarge to fill the space.

The cornea is transparent for the following reasons:
1- The epithelium is not keratinized.
2- The stroma is regularly oriented.
3- The endothelium has active pump, it pushes the fluid into aqueous and it acts as barrier to prevent entrance of aqueous inside the cornea.
4- The corneal nerves are unmylinated.
5- It contains NO blood vessels.
6- It contains NO pigments (as melanin).

Signs of corneal diseases:

1- Epithelial signs:

a- Punctate epithelial erosions (PEE):
Are tiny, slightly depressed, epithelial defects (micro-ulcers seen by slit-lamp), which stain with fluorescein.
e.g.(causes): vernal keratoconjunctivitis, poorly fitting contact lens, dry eyes, decreases corneal sensation (as in trigeminal nerve palsy or after herpes simplex viral keratitis), exposure to ultraviolet (during welding, *do not treat pain by xylocaine as it is toxic to the eye), corneal exposure, toxicity from drops (as those of aminoglycosides).

b- Punctate epithelial keratitis (PEK):
Is the hallmark of viral infections, it is characterized by granular, opalescent, swollen epithelial cells .

c- Epithelial oedema:
It is a sign of endothelial decompensation or **severe and acute or sudden** elevation of intraocular pressure (as that occurring in glaucoma as IOP is raised leading to oedema that affects the vision).

d- Filaments:
Small, comma-shaped mucus strands lined with epithelium (one end attached to the epithelial cornea and the other is free).
Causes:
Keratoconjunctivitis sicca (dry eye), recurrent erosion syndrome, eye patching, corneal exposure, diminished corneal sensation and herpes zoster ophtrhalmicus.
e- Pannus:
Is an inflammatory or degenerative sub-epithelial in growth of fibrovascular tissue from limbus.

2- Stromal signs:
a- Stromal infiltration:
Focal areas of active stromal inflammation composed of accumulations leucocytes and cellular debris. These focal areas are granular, gray-white opacities within the stroma.
Causes:
i- Non-infectious (Antigen sensitivity): e.g. contact lens wear and marginal keratitis.
ii- Infectious keratitis: e.g. bacteria, viruses, fungi and protozoa.
b- Stromal oedema:
Causing disturbance of regularly arranged collagen fibers (or fibrils) that affects eye vision by disturbance of corneal transparency .
Causes:
Keratoconus (bulging of the cornea making the cornea have conical shape, causing stretching descemet's membrane leading to rupture it and influx of the aqueous inside the stroma) and surgical damage to the corneal endothelium.
c- Vascularization:
Causes: Wide variety of corneal disorders, e.g. microbial keratitis, chemical burns, trauma, TB, syphilis and autoimmune keratoconjunctivitis (cicatricial pemphigoid and stevens-johnson syndrome).

3- Descemet's membrane signs:
a- Breaks:
Causes: Corneal enlargement, birth trauma, keratoconus and glaucoma (in children). It leads to influx of aqueous causing stromal oedema.
b- Folds (Striate keratopathy):
Causes: Surgical trauma, ocular hypotony, stromal inflammation and oedema.
***** Normal IOP is 10-21mmHg, if it is less than 6 then it is hypotony, while if it is more than 21 it is ocular hypertension.

Microbial keratitis

1- Bacterial Keratitis:

Predisposing factors:

- Bacteria capable of penetrating intact epithelium include Neisseria gonorrhoea and H. influenzae.
- Other bacteria are capable of producing keratitis only after compromisation of epithelial integrity with the following factors:

a- Contact lens wear: is the most common predisposing factor in patients with previously normal eye therefore meticulous lens hygiene therefore vital.

b- Pre-existing corneal disease: such as trauma (usually after surgery of cataract), exposure keratopathy and diminished corneal sensation.

c- Other factors: chronic blepharoconjunctivitis, chronic dacryocystitis, dry eyes, topical steroid therapy and hypavitaminosis A.

Clinical Features:

Symptoms:

Foreign body sensation, photophobia, blurring of vision, pain, eyelid oedema and discharge.

Signs:

- Conjunctival and circumcorneal injection (almost always with severe anterior uveitis).
- Epithelial defects associated with an infiltrate around the margin and base.
- Enlargement of the infiltrate associated with stromal oedema.
- Secondary sterile anterior uveitis with hypopyon.
- Progressive ulceration may lead to corneal perforation and bacterial endophthalmitis (involvement of all intraocular tissues).

Differential diagnosis of bacterial keratitis:

a- Fungal keratitis.

b- Acanthamoeba keratitis.

c- Stromal necrotic herpes simplex keratitis..

d- Sterile inflammatory corneal infiltrates associated with contact lens wear.

Treatment:

a- Topical antibiotics:

- Initial instillation of fortified antibiotic is at hourly intervals.
- If response is favorable, frequency is decreased to 2-hourly during waking hours.
- Then fortified drops can be replaced by weaker commercial preparations, which are then tapered and eventually discontinued.

b- Oral ciprofloxacin (750mg twice daily):

- Copious secreted in the tears.
- Lipid soluble and has excellent intraocular penetration.

***** No oral antibiotic is useful for ocular infections except ciprofloxacin as they cannot pas the barrier found there.

c- Atropine:

- To prevent the formation of posterior synechiae (adhesions between papillary margin and lens).
- Reduce pain from ciliary spasm and uveitis.

d- Steroid therapy:

It is contravesial, the potential benefits of topical steroids in reducing stromal necrosis and scaring should be weighed against decreased fibroblast activity and increased risk of perforation.

We can use it only when cultures become sterile and there is clear evidence of improvement (7-10 days after initial treatment).

2- Fungal keratitis:

Rare infection but have devastating effects, the most common pathogens are:

- Filamentous fungi (Asperigillus and Fusarium species): Infection occurs after trauma by wood usually.
- Candida albicans: Usually infects immuno-compromised patients.

Clinical features:

Symptoms:

- Gradual onset of foreign body sensation.
- Photophobia.
- Blurred vision (due to opacification of cornea, whether due to epithelial or stromal oedema) and discharge (mucopurulent).

**** Progression is much slower and less painful than in bacterial keratitis.***

Signs:

Filamentous keratitis:

- A grayish, stromal infiltration with indistinct margin.
- Surrounding, satellite, feathery, finger-like lesions (extensions).
- Hypopyon (pus in the anterior chamber).

***** There is always some sort of iritis associating keratitis.

Candida keratitis:

- A yellow-white, stromal infiltration associated with dense suppuration similar to bacterial keratitis.

Treatment:

a- Topical treatment:

Filamentous: Natamycin 5%, and may add Amphotericin 0.15%.
Candida: Imidazole 1% or Flucytosine 1%. } **for 6 weeks**

b- Systemic antimycotics: E.g. Ketoconazole (tablets) or Itraconazole in severe keratitis or endophthalmitis.

c- Therapeutic penetrating keratopathy: In unresponsive cases (if there is resistant infection).

3- Viral keratitis:

a- Herpes simplex keratitis:

Basic concepts:

- HSV is a DNA virus, which infects only human.
- Infection with HSV is common, up to 90% of the population is seropositive for HSV-1 antibodies although most infections are sub-clinical.
- HSV-1 predominantly causes infection above the waist (face, lips and eyes).
- HSV-2 typically causes venereally acquired infection below the waist (genital herpes).
- Rarely HSV-2 may be transmitted to the eye through infected genital secretions, either venereal or at birth.

i- Primary infection:

Usually in early childhood through droplet (the most common route) or direct inoculation. It may be sub-clinical or may cause mild fever, malaise and URT infection. In immuno-compromised subject, the infection may become generalized and life threatening.

ii- Recurrent disease:

- Following primary infection, the virus travels up to the ganglion (trigeminal **"Gasserian"** for HSV-1 and spinal for HSV-2), where it lies in a latent state.
- This latent state may subsequently reverse and the virus reactivates, replicates & travels down to its target tissue causing recurrent disease (genital herpes, herpes labialis & herpes keratitis).

Primary ocular infection:

- Typically occurs in children between ages of *6 months- 5 years*, and may be associated with generalized symptoms.

Signs:

- Skin vesicles typically involve the lids and periorbital area.
- Acute, unilateral, follicular conjunctivitis associated with lymphadenopathy.
- Secondary canalicular obstruction may occur (the infection by itself causes lacrimation, but if it is complicated by secondary canalicular obstruction this will cause epiphora).
- Keratitis is uncommon.

Treatment:

- Aciclovir (Zovirax®) eye ointment five times a day for three weeks to prevent keratitis.

Recurrent ocular disease (Epithelial keratitis):

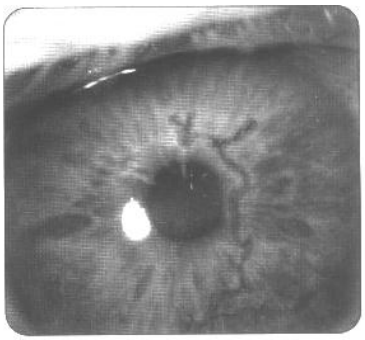
***** the virus invades the epithelium or the stroma, and we will deal with the epithelium **only** as it is the commonest one)

Presentation:

- Occurs at *any age*.
- Mild discomfort.
- Watering eye.
- Blurring of vision.

Signs: (in chronological)

- Opaque epithelial cells or punctuate epithelial keratitis (coarse punctuate or stellate pattern).
- Central desquamation results in a linear-branching (dendritic) ulcer. ☛



- Decreased corneal sensation (as it involves the nerves).
- Anterior stromal infiltration under the ulcer.
- Progressive centrifugal (from the center outwards) enlargement may result in a large epithelial defect with a geographical or amoeboid configuration, especially in the context of injudicious topical steroid therapy.
- Following healing, there are persistent linear-branching shapes, which represent waves of healing epithelial cells.

Differential diagnosis of dendritic ulceration: (pseudo-dendritic ulceration)

a- Herpes Zoster keratitis.
b- Healing cornel abrasion.
c- Soft contact lens wear.
d- Acanthamoeba keratitis.
e- Toxic keratopathies (kertitis medicamentosa).

Treatment of Herpes simplex epithelial keratitis:

a- Topical: without treatment, 50% resolves spontaneously, with treatment, the cure rate is 95%.

i- Aciclovir 3% ointment, five times daily for 2 weeks.

ii- Ganciclovir 0.15% (Virgan®) gel: it is a new preparation which is used five times daily and is as effective as Aciclovir.

iii- Trifluorothymidine 1% drops: it is used every 2 hours during the day for 2 weeks , like Aciclovir, it has a cure rate of 95%, but it is more toxic.

b- Debridement:

Used in dendritic but not geographic ulcers in patients who are: non-compliant, allergic to drugs, when antiviral agents are not available, resistant cases. Drugs are ideally used after debridement. Cure rate is above 50% and below 95%.

b- Herpes Zoster ophthalmicus (HZO):

It is a disease caused by Varicella Zoster virus (VZV), which is morphologically identical to HSV but different antigenically and clinically.

Chickenpox (Varicella) and Zoster are different conditions caused by the same virus, Zoster mainly affects elderly patients. Primary disease occurs during childhood is usually chickenpox, virus remains dormant in sensory root ganglia. Later, it reactivates and migrates back down sensory nerves to the skin and eye and causes the characteristic lesions. Therefore, herpes zoster in a young person make us think that that patient is either immune compromised.

- Approximately, 15% of all cases of herpes zoster affect the ophthalmic division of the trigeminal nerve (HZO).

***** If we have crust lesion at the tip of the nose "Hutchinson sign", it indicates ocular involvement (how or why? Because the distribution of the ophthalmic division of the trigeminal nerve

Clinically, HZO can be divided into:

i- Acute phase: acute symptoms, which may totally resolve after a while.

ii- Chronic phase: which may persist for years.

iii- Relapsing phase: where the acute or chronic lesions reappear years later.

Now we will discuss them separately:

i- Acute phase:

systemic features:

- Influenza-like illness: Fever, malaise, headache and depression.
- Herpetic neuralgia: Varies from a superficial itching or burning sensation to severe deep boring or lancing pain.
- Skin rash: Progress rapidly from papules →vesicles →pustules → crust and scar formation.

Ocular Features:

Keratitis, conjunctivitis, episcleritis, scleritis and anterior uveitis.

Neurological Complication:

- Cranial nerve palsies: 3rd , 4th or 6th cranial nerve palsy.
- Optic neuritis.
- Encephalitis.
- Contralateral hemiplegia.

Treatment:

- ***Systemic:*** Valaciclovir 1g t.i.d for 7 days
  Or Famciclovir 250mg t.i.d for 7 days.
- ***Topical:*** **a- Skin:** Steroid + Antibiotics skin cream, e.g. Hydrocortisone 1% with Fusidic acid 2%.
  b- Eye: Herpetic ulcer → Aciclovir ointment.
  Autoimmune → Topical steroid. Sometimes, both of them are used.

* Unlike herpes simplex keratitis, here we can use steroids from the beginning of the treatment accompanying other medications.

ii- Chronic phase:

Ocular features:

Keratitis, neurotrophic keratitis (denervation of the cornea that causes recurrent epithelial erosions or ulcers, which may not respond to treatment or heal) which may lead to severe ulceration, secondary bacterial infection and even perforation.

Other ocular complications:

- **Ptosis:** as a result of scarring which may also produce trichiasis or madarosis.
- **Mucus secreting conjunctivitis.**
- **Scleritis.**
- **Post-herpetic neuralgia:** may lead to depression and even suicidal attempts.

Treatment: Accordingly.

iii- Relapsing phase:

It may appear even 10 years after acute or chronic disease. They may be precipitated by the sudden withdrawal or reaction of topical steroids.

Ocular features:

Keratitis, episcleritis, scleritis, iritis & glaucoma .