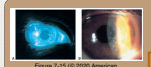
# 8.7.6. Immune-mediated diseases (VI): Cornea (I)

## Thygeson Superficial Punctate Keratitis

- pathogenesis
  - unknown
  - +- immune-mediated
  - no inflammatory cells
- clinical presentation
  - children to older adults
  - bilateral
    - may develop initially in 1 eye
    - may be markedly asymmetric
  - recurrent episodes
  - symptoms
    - tearing
    - foreign-body sensation
    - photophobia
    - reduced vision
    - symptoms may far exceed the apparent signs
  - each opacity is a cluster of multiple smaller gray, granular pinpoint opacities
  - multiple (2-40)
  - slightly elevated corneal epithelial lesions
    - greatest density in the central cornea
    - stain faintly with fluorescein and rose bengal
    - "negative staining"
    - In contrast to adenoviral keratoconjunctivitis
      - minimal conjunctival reaction
    - change in location and number
      - waxing and waning appearance of individual epithelial opacities
    - in patients who have received topical antiviral therapy
      - +- mild subepithelial opacity



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- management
  - mild cases
    - artificial tears
  - persistently symptomatic cases
    - low-dose topical corticosteroids
      - fluorometholone 0.1%
      - very responsive to corticosteroids
      - recur in the same or different locations after the topical corticosteroids are stopped
      - the use of corticosteroids should be minimized
    - topical cyclosporine 0.05%
      - preferred over corticosteroids
      - tacrolimus ophthalmic suspension 0.1%
      - bandage soft contact lenses

## Interstitial Keratitis Associated With Infectious Diseases

- pathogenesis
  - type IV hypersensitivity
    - to infectious microorganisms
      - herpes simplex virus
      - varicella-zoster virus keratitis
      - mycobacterium tuberculosis
      - mycobacterium leprae
      - borrelia burgdorferi (lyme disease)
      - measles virus
      - epstein-barr virus (infectious mononucleosis)
      - chlamydia trachomatis (lymphogranuloma venereum)
      - leishmania spp
      - onchocerca volvulus (onchocerciasis)
    - to other antigens
  - nonsuppurative inflammation of the corneal stroma
    - cellular infiltration
    - vascularization
    - no primary involvement of the corneal epithelium or endothelium
- congenital syphilis>>acquired syphilis
  - develops late in the first decade of life (or even later)
  - bilateral (80%)
    - both eyes may not be affected simultaneously or to the same degree
  - noncular signs of congenital syphilis
    - dental deformities: notched (hutchinson) incisors and mulberry molars
    - bone and cartilage abnormalities: saddle nose, palatal perforation, saber shins, and frontal bossing
    - cranial nerve VIII (vestibulocochlear) deafness
    - rhagades (circumoral radiating scars)
    - cognitive impairment
- congenital syphilis
  - only rarely in acquired (as opposed to congenital) syphilis
    - uveitis and retinitis are much more common manifestations of acquired syphilis than keratitis
  - manifestations of congenital syphilis that occur early in life (within the first 2 years) are infectious
  - IK is an immune-mediated manifestation of congenital syphilis
    - develops late in the first decade of life (or even later)
  - unilateral in 60%

- Syphilitic interstitial keratitis
  - clinical presentation
    - symptoms
      - pain
      - tearing
      - photophobia
      - perilimbal injection
    - sectoral superior stromal inflammation and keratic precipitates (early)
      - spreads centrally
        - corneal opacification and edema
      - deep stromal neovascularization
        - cornea appears pink
        - salmon patch
    - inflammation may last for several weeks if left untreated
      - sequelae
        - corneal scarring & opacification
        - corneal thinning
        - ghost vessels
  - laboratory evaluation
    - serology
      - rapid plasma reagin (RPR) test
      - FTA-ABS
      - microhemagglutination assay for Treponema pallidum (MHA-TP)
  - management
    - cycloplegic agents
    - topical corticosteroids
    - systemic syphilis (or neuroretinal manifestations)
      - penicillin or an appropriate alternative antibiotic
    - necessity of lumbar puncture in syphilitic IK is uncertain

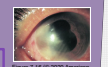

Figure 7-16 (© 2020 American Academy of Ophthalmology)

## Marginal Corneal Infiltrates Associated With Blepharoconjunctivitis

- Pathogenesis
  - mobilize and induce T-cells
    - express MHC class II antigens
      - antigen-presenting cells
  - circulating immune cells, immune complexes, and complement factors
    - vessels
      - limbus
  - immune-related corneal changes occur adjacent to the limbus
- Predisposing Factors
  - blepharoconjunctivitis
  - contact lens wear
  - trauma
  - endophthalmitis
- Clinical Presentation
  - gray-white infiltrates
    - well circumscribed
    - where the eyelid margins intersect with the corneal surface
      - 10-, 2-, 4-, and 8-o'clock positions
    - clear zone of cornea between infiltrate and limbus
      - 1 mm inside the limbus
    - superficial blood vessels may cross the clear interval
  - overlying epithelium
    - intact
    - punctate epithelial erosions
    - ulcerated
  - following resolution
    - stromal opacification
    - peripheral corneal thinning
    - pannus

## Cogan Syndrome

- pathogenesis
  - autoimmune disorder
  - upper respiratory tract infection 1–2 weeks before
  - young adults
- clinical findings
  - stromal keratitis
    - early
      - bilateral faint white subepithelial infiltrates
      - peripheral cornea
    - late
      - multifocal nodular infiltrates in the posterior cornea
  - vertigo
  - hearing loss
    - similar to congenital syphilis
  - systemic vasculitis
    - polyarteritis nodosa
  - ocular and vestibular changes can proceed rapidly
- laboratory evaluation
  - diagnosis of exclusion
    - exclude syphilis
      - VDRL
      - or
      - RPR test
      - may become nonreactive in congenital syphilis
      - FTA-ABS
      - or
      - MHA-TP
- management
  - topical corticosteroids
    - acute keratitis
  - oral corticosteroids
    - vestibuloauditory symptoms
      - deafness is more likely if the condition is not treated early
  - cytotoxic agents
    - for severe and unresponsive cases

## Reactive Arthritis (Reiter syndrome)

- pathogenesis
  - Salmonella, Shigella, and Yersinia
    - gram-negative bacteria
      - dysentery
  - C trachomatis
    - nongonococcal urethritis
  - predisposing conditions
    - 75%
      - HLA-B27–positive
- clinical presentation
  - should be considered in any case of chronic, nonfollicular, mucopurulent conjunctivitis with negative cultures
    - mucopurulent discharge
    - 30%–60%
      - bilateral papillary conjunctivitis
    - days to weeks
      - self-limited
  - ocular inflammation
    - episcleritis
    - 3%–12%
      - mild nongranulomatous iritis
    - keratitis
      - diffuse punctate epithelial erosions
      - superficial or deep focal infiltrates
      - superficial or deep vascularization
  - classic triad
    - urethral inflammation
    - joint inflammation
      - oligoarticular
      - highly asymmetric
  - less common manifestations
    - keratoderma blennorrhagicum
    - balanitis
    - aphthous stomatitis
    - fever
    - lymphadenopathy
    - pneumonitis
    - pericarditis
    - myocarditis
  - manifestations can appear simultaneously or separately, in any sequence
  - self-limited attacks
    - 2 to several months
    - may recur periodically over the course of several years
- management
  - palliative
    - corneal infiltrates and vascularization
      - topical corticosteroids
    - related infections
      - systemic antibiotic
    - intraocular (uveitic) component
      - systemic immune suppression

## Corneal Transplant Rejection

- tolerance of a corneal graft is an active process based on several features
  - absence of blood and lymphatic channels in the graft and its bed
  - absence of MHC class II+ APCs in the graft
  - reduced expression of MHC-encoded alloantigens on graft cells replaced with minor peptides (nonclassical MHC-Ib molecules) to avoid lysis by natural killer cells
  - expression of T-cell–deleting CD95 ligand (Fas ligand, or FasL) on endothelium, which can induce apoptosis in killer T cells
  - immunosuppressive microenvironment of the aqueous humor
    - transforming growth factor β2, α-melanocyte-stimulating hormone, vasoactive intestinal peptide, and calcitonin gene–related peptide
  - anterior chamber–associated immune deviation (ACAID) involving the development of suppressor T cells
    - ACAID is a downregulation of delayed-type cellular immunity
- allograft rejection is associated with cellular immune mechanisms
  - T-lymphocyte–mediated response
    - delayed (type IV) hypersensitivity
- for the endothelial cells to be rejected, they must express MHC class II antigens
  - endothelial cells' endogenous minor H antigens
    - recognized by the CD4+ T cells

Ophthalmology Mind Maps/Arman Mashayekhi, MD