8.7.4. Immune-mediated diseases (IV): Conjunctiva (III): Mucous Membrane Pemphigoid (MMP)

differential diagnosis of cicatrizing conjunctivitis

- infectious
  - trachoma
  - adenovirus
  - corynebacterium diphtheriae
  - streptococcal conjunctivitis
- allergic
  - atopic keratoconjunctivitis
  - Stevens-Johnson syndrome
- autoimmune
  - mucous membrane pemphigoid
  - sarcoidosis
  - lupus
  - scleroderma
  - lichen planus
  - graft-vs-host disease
- miscellaneous
  - rosacea
  - trauma
  - chemical burn
  - radiation
  - neoplasia
  - medicamentosa
- linear IgA dermatosis
  - can result in an ocular syndrome that is clinically identical to MMP
- diagnosis of unilateral MMP should be made with caution

laboratory evaluation

- conjunctival biopsy
  - direct immunofluorescent staining
  - immunoperoxidase staining
  - immunohistochemical staining
    - complement 3
    - IgG
    - IgM
    - IgA
    - in the BMZ of the conjunctiva
  - false-negative results are not uncommon
    - from an actively affected area
    - if involvement is diffuse, from the inferior fornix
- oral mucosal biopsies
- circulating anti–basement membrane antibody
  - may be negative in end-stage disease

management

- multidisciplinary approach
- high-risk
  - criteria
    - ocular, genital, nasopharyngeal, esophageal, and laryngeal mucosae
    - rapidly progressing disease
  - dapsone
    - initial drug of choice in mild cases
    - may cause hemolytic anemia
    - avoid in patients with
      - glucose-6-phosphate dehydrogenase (g6pd) deficiency
        - test for g6pd deficiency
      - sulfa allergy
  - mild disease
  - severe disease
    - cyclophosphamide
      - mainstay of therapy in severe disease
      - 1.5–2.0 mg/kg per day in divided doses
      - target white blood cell count of 2000–3000 cells/µl
    - azathioprine
  - patients not responding to conventional therapies
    - biologic agents
      - rituximab
      - infliximab
      - etanercept
      - intravenous immunoglobulin
- low-risk
  - criteria
    - disease occurring only in the oral mucosa or oral mucosa and skin
  - much lower incidence of scarring
  - progression is often slow
  - topical vitamin A
- surgical correction of eyelid deformities
- eyelash ablation for trichiasis
- hard palate and buccal mucosal grafting
  - fornix reconstruction in severe cases
  - intraocular surgery is best delayed until disease activity has been under control for an extended period
- dry eye
  - punctal occlusion
    - higher rate of spontaneous extrusion of silicone punctal plugs
    - permanent punctal occlusion with cautery
- standard PK
  - very guarded prognosis
- boston keratoprosthesis

pathogenesis

- atopic keratoconjunctivitis is primarily type IV
- SJS is primarily type III
- cytotoxic (type II) hypersensitivity
  - autoantibodies directed against a cell surface antigen in the basement membrane zone (bmz)
    - bullous pemphigoid antigen II
    - antibody activates complement
      - membrane breakdown
- proinflammatory cytokines
  - IL-1
  - tumor necrosis factor α
    - induces expression of
    - migration inhibition factor
  - macrophage colony-stimulating factor
- cellular immunity
  - HLA-DR4
  - HLA typing is not useful!

pseudopemphigoid

- long-term use of certain topical ophthalmic medications
  - pilocarpine
  - echothiophate iodide
  - demecarium bromide
  - epinephrine
  - timolol
  - idoxuridine
- progression ceases once the offending agent is recognized and removed

epidemiology

- F>M
- usually >60 years
  - rarely younger than 30

clinical presentation

- mucous membranes
  - conjunctiva
  - mouth and oropharynx
    - difficulty swallowing
    - oral mucosal lesions may be a clue that can lead to early diagnosis
  - genitalia
  - anus
- skin
  - 15%
- recurrent attacks of mild and nonspecific conjunctival inflammation
  - bilateral
  - conjunctival hyperemia
    - chronic red eye
  - edema
  - ulceration
  - tear dysfunction
  - occasional mucopurulent discharge
  - transient bullae of the conjunctiva
- 1 stage I
  - subepithelial fibrosis
    - fine gray-white linear opacities
    - best seen with an intense but thin slit beam
    - deep conjunctiva

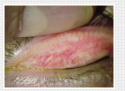

Figure 7-11 (© 2020 American Academy of Ophthalmology)

- 2 stage II
  - shortening of the fornices
    - inferior forniceal depth < 8 mm
    - should prompt further evaluation
- 3 stage III
  - symblepharon formation
    - subtle inferior symblephara
      - lower eyelid is pulled down while the patient looks up

Figure 7-12 (© 2020 American Academy of Ophthalmology)

- 4 stage IV
  - restricted ocular motility with extensive adhesions between the eyelid and the globe
- chronic cicatrizing conjunctivitis
  - loss of goblet cells
  - obstruction of the lacrimal gland ductules
  - keratinization/epidermalization of the conjunctiva
  - entropion
  - trichiasis
  - corneal changes
    - abrasion
    - vascularization
    - ulceration
    - scarring
  - aqueous and mucous tear deficiency
- remissions and exacerbations are common
  - surgical intervention can incite further scarring

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