9.6.20. Panuveitis (IV): Behcet Disease

General considerations

- epidemiology
  - onset 25-35 years
    - as early as age 10–15 years!
  - most are sporadic
  - most common in the Northern Hemisphere
    - eastern Mediterranean
    - eastern rim of Asia
    - along the Old Silk Route
  - prevalence
    - 80–300 cases per 100,000 in Turkey
    - 8–10 per 100,000 in Japan
    - 0.4 per 100,000 in the United States
- diagnostic criteria
  - See Table 6-4
  - See Table 6-5
- classification
  - "complete" type
    - 4 major criteria
    - M>F
  - "incomplete" type
    - 3 major criteria or ocular involvement with 1 other major criterion
    - M=F
- chronic
- relapsing
- occlusive systemic/multisystem vasculitis
  - can have its predominant effect on a single system
    - neuro-BD
    - ocular BD
    - intestinal BD
    - vascular BD
- can affect both the anterior and the posterior segments
  - often simultaneously

Complications

- macular edema
- complex cataract
- glaucoma
- secondary and neovascular glaucoma
- retinal and optic disc neovascularization
- retinal detachment
- vitreous hemorrhage

Pathogenesis

- no known environmental factors
- specific HLA associations
  - HLA-B12 with mucocutaneous lesions
  - HLA-B51 with ocular lesions
- of little diagnostic value
- delayed-type hypersensitivity reactions
  - early
- immune-complex–type reactions
  - late

Pathology

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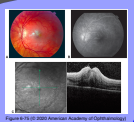
- nongranulomatous, necrotizing, obliterative vasculitis

Diagnostic tests

- of little value
  - HLA typing, cutaneous pathergy testing, ESR & CRP
- FA
  - marked dilatation and occlusion of retinal capillaries with perivascular staining
  - retinal ischemia
  - leakage of fluorescein into the macula (CME)
  - retinal neovascularization
- adjusting therapy may prevent the development of inflammatory damage
  - subtle vascular leakage before clinical evidence of disease activity
- OCT
  - macular edema
  - disruption of the retinal architecture
- chest x-ray, chest CT, and brain MRI with contrast enhancement



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Differential diagnosis

- HLA-B27–associated anterior uveitis
- reactive arthritis syndrome
- sarcoidosis
- systemic vasculitides including systemic lupus erythematosus, PAN, and GPA
- necrotizing herpetic retinitis

Treatment

corticosteroids

- for explosive-onset (acute) anterior segment and posterior segment inflammation
- most patients eventually become resistant to corticosteroid therapy
- 1.5 mg/kg/day of oral prednisone with a gradual taper
- periocular and intravitreal steroids

immunomodulatory medications

- start systemic steroid + IMT
  - sight-threatening posterior segment inflammation
- colchicine
  - for mucocutaneous disease
  - ineffective for ocular BD
- azathioprine
  - effective in controlling oral/genital ulcers and arthritis
- infliximab
  - ← treatment of choice for Behçet retinal vasculitis
  - rapid remission of disease activity, long-term disease control
  - at ≥10 mg/kg carries a greater risk of
    - disseminated TB
    - malignancy
- American expert panel recommended
  - anti-TNF therapy with infliximab or adalimumab as first- or second-line corticosteroid-sparing therapy
  - infliximab as first- or second-line treatment for acute exacerbations of preexisting Behçet disease
- European League Against Rheumatism recommends
  - azathioprine (with corticosteroids) as first-line treatment
  - cyclosporine or infliximab as second-line treatment
- cyclosporine
  - risk of nephrotoxicity
  - increased risk of neuro-BD in patients treated with cyclosporine
  - not as effective as other cytotoxic drugs
- tacrolimus
  - less toxic
  - substitute for cyclosporine
  - used successfully in Japan
- mycophenolate mofetil
  - successful in treating ocular BD in small-case series
- interferon alfa-2a
  - efficacious and well tolerated
  - highly effective in Behçet uveitis
  - somewhat less effective in non–Behçet uveitis
- chlorambucil
  - effective even at relatively low doses
  - may be the most effective immunomodulatory drug in achieving durable remission
  - more effective than cyclosporine for posterior segment ocular BD
  - reserve the use of alkylating agents for patients with refractory disease
- cyclophosphamide
  - alternative to chlorambucil
  - oral or pulsed intravenous therapy
  - greater risk of systemic complications

Prognosis

- visual acuity <20/200
  - 25%
  - caused by
    - occlusive retinal vasculitis
    - macular edema
    - optic atrophy
    - glaucoma
- current patients appear to have a better visual prognosis
- adult men tend to have poorer vision outcomes
- predictive factors for vision loss
  - posterior synechiae
  - persistent inflammation
  - elevated IOP
  - hypotony

Noocular systemic manifestations

- oral aphthous ulcers
  - most frequent finding
  - significant discomfort and pain
  - lips, gums, palate, tongue, uvula, and posterior pharynx

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  - discrete, round or oval
    - 2–15 mm
  - white with red rims
  - recur every 5–10 days or every month
    - last 7–10 days
  - heal with little scarring
- skin lesions
  - erythema nodosum
    - over extensor surfaces
    - painful
    - recurrent
    - face, neck, and buttocks
    - disappear with minimal, if any, scarring
  - acne vulgaris & folliculitis-like skin lesions
    - upper thorax and face
  - cutaneous pathergy
    - 40%
    - sterile pustule at the site of a venipuncture
    - not pathognomonic of BD
- genital ulcers
  - male patients
    - on the scrotum or penis
  - female patients
    - vulva and the vaginal mucosa
  - variable amounts of pain
  - can be deep and leave scars
- systemic vasculitis
  - 25%
  - any size artery or vein may be affected
    - vascular complications
      - arterial occlusion
      - aneurysm
      - venous occlusion
      - varices
  - cardiac involvement
    - 17%
    - granulomatous endocarditis
    - endomyocardial fibrosis
    - myocarditis
    - pericarditis
    - coronary arteritis
  - gastrointestinal lesions
    - multiple ulcers involving the esophagus, stomach, and intestines
  - pulmonary involvement
    - pulmonary arteritis with aneurysmal dilatation
  - arthritis
    - 50%
    - knee is most affected
    - 50%
- neurologic involvement
  - 10%
  - M>F
  - 10% of patients with neuro-BD can have ocular disease
  - 30% of patients with ocular BD may have neurologic involvement
  - affects mainly areas of motor control
  - headaches
  - strokes
  - palsies
  - confusional state
    - 25%
  - mortality
    - up to 10% in patients with neuro-BD
    - lower with the use of IMT
- neuro-ophthalmic involvement
  - cranial nerve palsies
  - central scotomata caused by papillitis
  - visual field defects
  - papilledema resulting from thrombosis of venous sinuses

Ocular manifestations

- 70%
- M>F
- 80% bilateral
- explosive onset over the course of just a few hours
  - recurrent and relapsing
- more severe in men
- ocular involvement as an initial presenting problem is relatively uncommon
  - 10%
- can affect any or all portions of the uveal tract
- anterior uveitis
  - may be the only ocular manifestation of BD
  - redness, pain, photophobia, and blurred vision
  - nongranulomatous
  - transient hypopyon
    - 25%
    - can shift with the patient's head position or disperse with head shaking
    - may not be visible unless viewed by gonioscopy

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  - can spontaneously resolve even without treatment
  - other anterior segment manifestations
    - posterior synechiae, iris bombé, angle-closure glaucoma, cataract, episcleritis, scleritis, conjunctival ulcers, and corneal immune ring opacities
- posterior segment manifestations
  - most common type of uveitis found in children and adults
  - obliterative, necrotizing retinal vasculitis
    - arteries & veins
      - branch retinal vein occlusion
      - isolated branch artery occlusions
      - combined branch retinal vein and branch retinal artery occlusions
      - vascular sheathing
      - retinal vessels may become white and sclerotic

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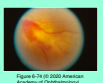
  - ← multifocal areas of chalky white retinitis
    - may be confused with acute retinal necrosis



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  - retinal ischemia
    - retinal neovascularization
    - neovascularization of the iris and neovascular glaucoma
  - variable amounts of vitritis
  - CME
  - optic nerve
    - 25%
    - optic papillitis
    - progressive optic atrophy
- severe vision loss
  - 25%

Ophthalmology Mind Maps/Arman Mashayekhi, MD