9.6.19. Panuveitis (III): Vogt-Koyanagi-Harada Syndrome

epidemiology

affects certain ethnic groups
- Asian
- Asian Indian
- Hispanic
- Native American
- Middle Eastern

incidence varies geographically
- uncommon among whites
- rare among sub-Saharan Africans
- up to 4% of all uveitis referrals in United States
- up to 8% of all uveitis referrals in Japan
- the most common cause of noninfectious uveitis in Brazil and Saudi Arabia

pathogenesis

T lymphocytes directed against self-antigens associated with melanocytes of all organ systems
- cell-mediated autoimmune process

genetic predisposition
- in Japanese patients
  - HLA-DRB*0405
  - HLA-DR4 among Japanese patients
- HLA-DR1 or HLA-DR4 among Hispanic patients from southern California

pathology

lymphocytes and macrophages admixed with epithelioid and multinucleate giant cells

acute uveitic stage
- ciliary body
- iris
- peripapillary choroid is the predominant site of the granulomatous inflammatory infiltration
- diffuse, nonnecrotizing, granulomatous inflammation
- identical to that seen in SO
- preservation of the choriocapillaris
- proteinaceous fluid exudates in the subretinal space

unlike acute uveitic and chronic recurrent stages

convalescent stage
- uveal infiltration of lymphocytes, few plasma cells, and the absence of epithelioid histiocytes
- nongranulomatous inflammation
- sunset-glow fundus
- number of choroidal melanocytes decreases with loss of melanin pigment
- nummular chorioretinal scars in the peripheral retina
- focal loss of RPE cells with chorioretinal adhesions

chronic recurrent stage
- granulomatous choroiditis with damage to the choriocapillaris

essential diagnostic features of VKH syndrome

- bilateral involvement
- no history of penetrating ocular trauma
- no evidence of other ocular or systemic disease
- highly specific
  - exudative retinal detachment during the acute phase
  - sunset-glow fundus during the chronic phase
- See Table 6-3

differential diagnosis

SO, uveal effusion syndrome, posterior scleritis, primary intraocular lymphoma, uveal lymphoid infiltration, APMPPE, and sarcoidosis

diagnostic tests

FA

acute uveitic stage
- numerous punctate hyperfluorescent foci at the level of the RPE
- pooling of dye in the subretinal space in areas of neurosensory detachment
- disc leakage
- CME and retinal vascular leakage are uncommon

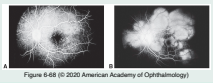


Figure 6-68 (© 2020 American Academy of Ophthalmology)

convalescent and chronic recurrent stages
- focal RPE loss and atrophy produce multiple hyperfluorescent window defects

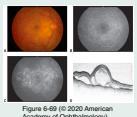
ICG angiography

- delay in choriocapillaris and choroidal vessel perfusion
- early choroidal stromal vessel hyperfluorescence and leakage
- disc hyperfluorescence

ultrasonography

- may be present even when the funduscopic and FA findings are unremarkable
- sensitive markers for the detection and monitoring of subclinical choroidal inflammation
- multiple hypofluorescent spots throughout the fundus
- hyperfluorescent pinpoint changes within areas of exudative retinal detachment
- most prominent in the peripapillary area, with extension to the equatorial region
- diffuse, low to medium reflective thickening of the posterior choroid
- exudative retinal detachment
- vitreous opacification
- posterior thickening of the sclera

OCT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- fibrin bands extending from the retina to the RPE (acute phase)
- serous macular detachments

SD-OCT

- decreases with treatment
- choroidal thickening in the acute phase

CME

choroidal neovascular membrane

FAF imaging

- granular hyperautofluorescence in areas of inflammation

lumbar puncture

- prominent neurologic signs and a paucity of ocular findings
- in highly atypical cases
- lymphocytic pleocytosis

treatment

acute stage

early and aggressive treatment with corticosteroids
- 1–1.5 mg/kg/day of oral prednisone
- ≥1 g of intravenous methylprednisolone daily x3 days followed by high-dose oral corticosteroids
- patients intolerant of systemic therapy
  - intravitreal corticosteroids
- systemic corticosteroids are tapered slowly according to the clinical response, on average over a 6–12 month period
- tapering corticosteroids too soon can result in early recurrence
- oral corticosteroids reduce
  - risk of CNV and subretinal fibrosis by 82%
  - risk of visual acuity decline to 20/200 or worse in better-seeing eyes by 67%
- oral versus intravenous routes of administration show no differences in outcome

IMT

- to achieve more prompt inflammatory control and to facilitate more rapid tapering of corticosteroids
- IMT was associated with
  - risk reductions of 67% for vision loss to 20/50 or worse
  - risk reductions of 92% for vision loss to 20/200 or worse in better-seeing eyes
- up to 70% of patients retaining visual acuity of ≥20/40

overall visual prognosis with treatment is fair

clinical presentation

4 stages

bilateral

Similar to APMPPE & MEWDS

1 prodromal

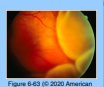
- flulike symptoms
  - headache, nausea, meningismus, dysacusia, tinnitus, fever, orbital pain, photophobia, and hypersensitivity of the skin and hair to touch
  - several days preceding the ocular symptoms
- focal neurologic signs
  - rare
  - cranial neuropathies
  - hemiparesis
  - aphasia
  - transverse myelitis
  - ganglionitis
- cerebrospinal fluid analysis
  - lymphocytic pleocytosis
    - 80%
    - may persist for up to 8 weeks
  - normal levels of glucose
- auditory problems
  - coincident with the onset of ocular disease
    - central dysacusia involving higher frequencies or tinnitus
      - 30%
      - early in the disease course
      - improve within 2–3 months
      - persistent deficits may remain
  - 75%

2 acute uveitic

- sequential blurring of vision in both eyes
- 1–2 days after the onset of CNS signs
- granulomatous anterior uveitis
  - bilateral
  - IOP may be elevated
    - forward displacement of the lens–iris diaphragm
      - ciliary body edema
      - annular choroidal detachment
  - IOP may be low
    - secondary to ciliary body shutdown
- variable degree of vitritis
- thickening of the posterior choroid with elevation of the peripapillary retinal choroidal layer
- hyperemia & edema of the optic nerve
- posterior segment findings
  - multiple focal serous retinal detachments
    - shallow

Figure 6-62 (© 2020 American Academy of Ophthalmology)

    - cloverleaf pattern around the posterior pole
    - may coalesce into large, bullous, exudative detachments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- profound vision loss may occur

3 convalescent

- several weeks later
- resolution of the exudative retinal detachment
- gradual depigmentation of the choroid
  - orange-red discoloration
    - sunset-glow fundus

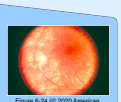
Figure 6-24 (© 2020 American Academy of Ophthalmology)

    - sunset-glow fundus may show focal areas of retinal hyperpigmentation or hypopigmentation
  - juxtapapillary depigmentation
- small, round, discrete depigmented lesions
  - inferior peripheral fundus

Figure 6-65 (© 2020 American Academy of Ophthalmology)

- perilimbal vitiligo (Sugiura sign)
  - 85% of Japanese patients

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- integumentary changes
  - 30%
  - occur weeks to months after the onset of ocular inflammation (during the convalescent stage)
  - correspond with the development of fundus depigmentation
  - vitiligo

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  - alopecia
  - poliosis

4 chronic recurrent

- repeated bouts of granulomatous anterior uveitis
  - KPs, posterior synechiae, iris nodules, iris depigmentation, and stromal atrophy
  - may occur concomitantly with subclinical choroidal inflammation, requiring systemic therapy
- posterior segment recurrences
  - vitritis, papillitis, multifocal choroiditis, and exudative retinal detachment
  - uncommon
- complications
  - cataract formation (50%)
    - posterior subcapsular cataract
  - glaucoma (33%)
  - CNV (≤15%)
  - subretinal fibrosis
- associated with
  - increased disease duration
  - more frequent recurrences
  - an older age at disease onset

clinical course

chronic
- many patients experience recurrent episodes of inflammation

Ophthalmology Mind Maps/Arman Mashayekhi, MD