Vogt-Koyanagi-Harada Syndrome

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Overview

- *Definition*
  - Also known as uveomeningitic or uveomeningoencephalic syndrome.
  - Systemic autoimmune disease affecting pigmented (melanin-containing) tissues in multiple organ systems including ocular, auditory, nervous, and integumentary.
  - Eye disease may occur alone or with extraocular manifestations.

    Complete VKH – revised criteria 1–5

    Incomplete VKH – revised criteria 1–3, 4 or 5

    Harada's disease/Probable VKH – revised criteria 1–3
    - Ocular disease only

    Revised criteria
    - No history of penetrating ocular trauma or surgery prior to onset of uveitis
    - No clinical or lab evidence of other ocular disease
    - Bilateral
    - Neurologic/auditory findings
    - Integumentary findings (found after all other findings)
- Symptoms:
  - Blurring
  - Pain
  - Redness
  - Photophobia
  - Floaters
- Laterality
  - Bilateral.
  - Second eye may be delayed by 1–3 days.

C. S. Foster et al. (eds.), *Uveitis*, https://doi.org/10.1007/978-3-030-52974-1_17

- Course
  - Multiple phases
    - Early (prodromal, acute uveitic)
    - Late (convalescent, chronic recurrent)
- Age of onset
  - Typically 20–50 years, may occur in children
- Gender/race
  - Females slightly more than males
  - Found worldwide, more frequent in darkly pigmented races
    - Common in Asian, Hispanic, Middle Eastern, Native American
- Systemic association:
  - Neurologic
  - Auditory
  - Dermatologic

Exam: Ocular

- Early phase (prodromal, acute uveitic) (days to weeks)
  - Early systemic findings days prior to uveitis onset (prodromal phase)
  - Acute choroidal infiltrate or thickening (acute uveitic phase)
    - Early onset exudative retinal detachment
    - Annular ciliary edema or detachment (leading to narrow angle glaucoma)
    - Optic disc edema or hyperemia
  - Vitritis
  - Dalen-Fuchs nodules
    - Collection of mononuclear inflammatory cells
    - Present in *all phases* of disease
  - No anterior uveitis
- Late phase (convalescent, chronic recurrent) (months to years)
  - Granulomatous anterior uveitis
    - Mutton-fat KP and iris nodules
    - Iris atrophy
  - Sugiura's sign – perilimbal vitiligo (most often in Japanese, 85%)
  - Sunset glow fundus – depigmentation of choroid (common in Asians)
    - 2–3 months after acute uveitic phase
  - Foci of RPE hyperpigmentation and atrophy (most often in Hispanics)
  - Posterior uveitis recurrence uncommon
  - Secondary complications occur mostly later in this stage
    - Cataract
    - Glaucoma
    - Hypotony
    - Retinal neovascularization
    - Subretinal fibrosis or neovascular membrane

Exam: Systemic

- Prodromal phase (2–3 days)
  - Sensitivity to touch of hair, skin (72%)
  - Flu-like symptoms including fever, headache
  - Tinnitus (75%, often with ocular involvement)
  - More common
    Dysacusia, confusion, nausea, meningismus, orbital pain
  - Less common
    Vertigo, ataxia, cranial neuropathies, hemiparesis, aphasia, transverse myelitis, ganglionitis
- Acute uveitic phase (weeks)
  - May include signs from prodromal phase
  - Uveitis as above
- Convalescent phase (months)
  - May include signs from prodromal phase
  - Alopecia
  - Poliosis
  - Vitiligo – head, periocular, trunk
- Chronic recurrent (years)
  - May include signs from prodromal phase
  - Uveitis as above

Imaging

- OCT: exudative retinal detachment, intraretinal cysts
- FA:
  - Early (acute) phase:
    "Starry sky" appearance – Multiple punctate hyperfluorescent dots in areas of exudative retinal detachment
    Disc leakage (70–90% in acute phase)
    Choroidal hypofluorescence (delayed filling)
  - Late phase:
    "Moth-eaten" or "salt and pepper" appearance
    - Alternating hyper- and hypofluorescence from RPE window defects and RPE hyperplasia

    Retinal vasculitis
- ICG: early dark background; later choroidal stromal vessel hyperlucence and leakage, hypolucent dots, disc hyperlucence
- B-scan: diffuse thickening of posterior choroid with low to medium reflectivity, posterior pole or inferior serous retinal detachment, vitreous opacities without posterior vitreous detachment, posterior thickening of sclera or episclera
- ERG: decreased amplitudes and prolonged implicit times of all full-field scotopic and photopic responses, usually improves with therapy

Laboratory and Radiographic Testing

- No confirmatory laboratory testing:
  - Rule out other infectious or noninfectious entities, systemic disease
  - HLA-DRB1*0405 association, not definitive
  - Antiretinal antibodies found in 50% against recoverin, carbonic anhydrase II, α-enolase (not felt to influence outcome)
- MRI – differentiates posterior scleritis from choroidal thickening in VKH, detects subclinical ocular or CNS inflammation.
- Lumbar puncture – CSF pleocytosis within 1 week, resolved by 8 weeks
  - Mostly lymphocytes, also melanin-laden macrophages

Differential Diagnosis

- Sarcoidosis
- Sympathetic ophthalmia (will have history of ocular trauma or surgery)
- Primary intraocular lymphoma
- White dot syndromes: APMPPE, MEWDS
- Bilateral diffuse melanocytic hyperplasia
- Lupus choroidopathy
- Uveal effusion syndrome
- Chronic myeloid leukemia
- Posterior scleritis
- Other causes of exudative detachment
  - Toxemia of pregnancy
  - Renal disease
  - Hypoprotenemia

Treatment

- Early phase
  - Early high-dose oral or IV corticosteroids with slow taper
  - Early initiation of immunomodulatory therapy (IMT) associated with better Va outcomes
- Late phase
  - Topical corticosteroid for anterior uveitis flares *without* active posterior inflammation
  - High-dose oral or IV corticosteroids with taper for posterior disease
  - Initiation of immunomodulatory therapy
- Immunomodulatory therapy
  - Antimetabolites
    Methotrexate, azathioprine, mycophenolate
  - Calcineurin inhibitors (alone or supplemental)

    - Cyclosporine, tacrolimus
  - Biologics
    - TNFα inhibitors – adalimumab, infliximab
    - Anti-IL6 – tocilizumab
  - Alkylating agents
    - Chlorambucil or cyclophosphamide
  - Other agents
    - IV-Ig
    - Subcutaneous corticotropin gel
- Intravitreal therapy
  - Anti-VEGF
  - Corticosteroid injections, implants (isolated ocular disease)

Referral/Comanagement

- Neurology
- ENT
- Dermatology