DIFFERENTIALS OF NONINFECTIOUS POSTERIOR UVEITIS
Jennifer Snyder, OD
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I. Definition of posterior uveitis
   A. Ocular inflammation of the choroid or retina
      1. Focal retinitis, focal chorioiditis, multifocal retinitis, multifocal choroiditis, retinochoroiditis, chorioretinitis
      2. Optic nerve, peripapillary, or vascular involvement

II. Classification of uveitis
   A. Anatomic location
      1. Anterior
      2. Intermediate
      3. POSTERIOR
      4. Panuveitis
   B. Demographics
      1. Age, race, sex, geographic location
   C. History
      1. Medical
      2. Social
      3. Family
      4. Travel
      5. Occupation
   D. Onset
      1. Sudden
      2. Insidious
   E. Duration
      1. Acute
      2. Chronic
   F. Unilateral or Bilateral
   G. Granulomatous or nongranulomatous

III. Etiology (not all inclusive)
   A. Infectious
      1. Viral
         a. Cytomegalovirus
         b. Herpes simplex
         c. Herpes zoster
         d. Human immunodeficiency virus
      2. Bacterial
         a. Syphilis
         b. Tuberculosis
         c. Lyme disease
      3. Fungal
         a. Histoplasmosis
      4. Parasitic
         a. Toxoplasmosis
b. Toxocariasis

B. Noninfectious
   1. Sarcoidosis
   2. Lupus
   3. Vogt-Koyanagi-Harada
   4. Behcet’s disease
   5. Sympathetic Ophthalmia
   6. White dot syndromes
      a. Acute Posterior Multifocal Placoid Pigment Epitheliopathy (AMPEE)
      b. Multiple Evanescent White Dot Syndrome
      c. Birdshot Retinochoroidopathy
      d. Serpiginous Choroidopathy
      e. Multifocal Choroiditis
      f. Punctate Inner Choroidopathy

C. Masquerade Syndromes
   1. Intraocular lymphoma
   2. Leukemia
   3. Choroidal melanoma
   4. Cancer-associated retinopathy (CAR)
   5. Retinoblastoma
   6. Retinal detachment
   7. Intraocular foreign body

IV. Laboratory testing
   A. Angiotensin-converting enzyme
      1. Sarcoidosis
   B. Antinuclear Antibody
      1. Lupus
   C. Chest X-Ray
      1. Sarcoidosis
      2. Tuberculosis
   D. Complete blood cell count with differential
      1. Leukemia
      2. Lymphoma
      3. Bacterial or viral etiology based on white cell differential
   E. Enzyme linked immunosorbent assay
      1. Toxoplasmosis
      2. Toxocariasis
      3. Human immunodeficiency virus
      4. Lyme disease
   F. Erythrocyte sedimentation rate
      1. Non-specific, measures presence and intensity of inflammatory activity
   G. HLA-A29
      1. Birdshot Retinochoroidopathy
   H. HLA-B51
      1. Behcet’s
   I. Purified protein derivative and anergy panel
      1. Tuberculosis
J. Rapid plasma reagin, FTA-ABS
   1. Syphilis
K. Tissue biopsy
   1. Intraocular lymphoma

V. Characteristics of noninfectious causes
A. Sarcoidosis
   1. Description
      a. Idiopathic, multisystem granulomatous disorder
         i. Primarily affects the lungs; also skin, lymph nodes, eyes, CNS, heart, bones, reticuloendothelial system
      b. Northern European or African descent; 20-40s
      c. Bilateral and chronic
   2. Ocular signs
      a. Patches of cream-colored peripheral choroidal depigmentation (Dalen Fuchs’ nodules)
         i. Overlying hypo- or hyperpigmentation of RPE upon resolution
      b. Vitritis, vitreous snowballs, granulomatous anterior uveitis
      c. Retinal vasculitis with perivenous sheathing (candle wax drippings)
      d. Optic disc and macular edema
      e. Optic disc or choroidal granulomas
      f. Lacrimal gland enlargement
      g. Complications- Occlusive vasculopathy, neovascularization
   3. Diagnostic Testing
      a. Chest X-ray
      b. Angiotensin-converting enzyme
   4. Management
      a. Systemic steroids
      b. Immunosuppressants

B. Lupus
   1. Description
      a. Autoimmune, multisystem connective tissue disorder
         i. Inflammation, vasculitis, immune complex deposition, end organ damage
         ii. Rash, ulcer, arthritis, renal disorder, hematologic disorder
      b. African American and Asian females; 20-50s
      c. Bilateral > Unilateral, chronic
   2. Ocular signs
      a. Choroidopathy- rare
      b. Dry eye
      c. Vitritis, anterior uveitis
      d. Retinal vasculitis
      e. Retinopathy (CWSs, hemorrhages)- common
      f. Optic Neuritis
      g. Complications- Occlusive vasculopathy, neovascularization
   3. Diagnostic Testing
      a. Antinuclear antibody test
      b. CBC with differential
      c. Erythrocyte sedimentation rate
4. Management
   a. Systemic steroids
   b. Immunosuppressants

C. Vogt-Koyanagi-Harada
   1. Description
      a. Autoimmune, multisystem disorder
         i. Primarily affects pigmented tissues in ocular, auditory, integumentary
            and central nervous systems
         ii. Vitiligo, alopecia
      b. Japan and Latin America, African Americans, Native Americans; 20-40s
      c. Bilateral and chronic
   2. Ocular signs
      a. Diffuse choroiditis with focal areas of subretinal fluid or bullous serous RDs
      b. Vitritis, granulomatous panuveitis
      c. Poliosis, Sugira sign
      d. Choroidal depigmentation with a sunset glow fundus in late stages
         i. Nummular chorioretinal depigmented scars, RPE clumping
      e. Complications- CNV, subretinal fibrosis
   3. Diagnostic Testing
      a. IVFA
         i. Early hypofluorescence with late pooling of dye
      b. ICG
         i. Early hypofluorescent spots and late hyperfluorescent spots with
            confluent areas of hypofluorescence
   4. Management
      a. Oral steroids
      b. Immunosuppressants

D. Behcet’s disease
   1. Description
      a. Idiopathic, multisystem inflammatory disorder
         i. Strong association to HLA-B51
         ii. Predominantly venous inflammation
         iii. Ocular inflammation- 85% of patients
         iv. Recurrent oral aphthous ulcers, recurrent genital ulcers, skin lesions, arthritis, thrombosis, neurological disease
      b. Japan, Middle East, eastern Mediterranean, North Africa; <50 years
      c. Bilateral and chronic
   2. Ocular signs
      a. Yellow-white retinal infiltrates
         i. Necrotizing retinitis
      b. Vitritis, recurrent uveitis with hypopyon, panuveitis
      c. Retinal vasculitis
      d. Optic disc and macular edema
      e. Complications- Occlusive vasculopathy, neovascularization
   3. Diagnostic Testing
      a. IVFA
i. Diffuse microvascular leakage and late staining of retinal vasculature, areas of capillary nonperfusion
b. HLA-B51

4. Management
   a. Steroids
   b. Immunosuppressants

E. Sympathetic Ophthalmia
   1. Description
      a. Occurs after surgery or penetrating trauma to one eye
      b. Men > Women
      c. Bilateral with insidious onset
   2. Ocular signs
      a. Focal elevated yellow-white lesions (Dalen Fuchs’ nodules) in the midperiphery
         i. At the level of outer RPE and choroid
         ii. Choroidal atrophy after resolution of lesions
      b. Vitritis and anterior granulomatous uveitis
      c. Papillitis
      d. Retinal vasculitis
      e. Complications- CNV, subretinal fibrosis, optic atrophy, occlusive vasculopathy, neovascularization, serous RD
   3. Diagnostic Testing
      a. IVFA
         i. Early hyperfluorescence with late pooling of dye in subretinal space
      b. ICG
         i. Early multifocal hypofluorescent spots that become prominent in late stages
   4. Management
      a. Systemic steroids
      b. Immunosuppressants

F. Acute Posterior Multifocal Placoid Pigment Epitheliopathy (AMPEE)
   1. Description
      a. White dot syndrome
         i. Idiopathic
      b. Young adults; 20-40s
      c. Bilateral and acute with rare recurrence
   2. Ocular signs
      a. Multiple yellow-white creamy flat lesions scattered throughout posterior pole
         i. At the level of outer retina and RPE
         ii. Mottled RPE and/or depigmentation after resolution of lesions
      b. Vitritis and anterior uveitis
      c. Retinal vasculitis
      d. Optic disc edema
      e. Complications- RD, occlusive vasculopathy
   3. Diagnostic Testing
      a. IVFA
         i. Early hypofluorescence with late hyperfluorescence
      b. ICG
         i. Hypofluorescent lesions in all stages
4. Management
   a. Steroid use controversial
   b. Self-limiting
      i. Fundus lesions resolve over 9-14 days
   c. Good prognosis with visual recovery to 20/40 or better
   d. Recovery of vision in 3 weeks - 3 months

G. Multiple Evanescent White Dot Syndrome
   1. Description
      a. White dot syndrome
         i. Rare, idiopathic, multifocal inflammatory retinochoroidopathy
      b. Females 17-40s
      c. Unilateral and acute with rare recurrence

2. Ocular signs
   a. Multiple small creamy gray-white dots perifoveal and peripapillary
      i. At the level of outer retina and RPE
      ii. Extends to midperiphery
      iii. If fovea involved, yellow-orange dots
      iv. RPE window defects after resolution of lesions
   b. Vitritis, uveitis
   c. Optic disc edema and macular edema
   d. Complications- CNV

3. Diagnostic Testing
   a. IVFA
      i. Early hyperfluorescence of lesions with late focal staining
   b. ICG
      i. Hypofluorescent spots in intermediate and late phase; more extensive
      than seen on IVFA

4. Management
   a. Self-limiting
      i. Typically no intervention
   b. Excellent prognosis with visual recovery to 20/20-20/30

H. Birdshot Retinochoroidopathy- AKA Vitiliginous Chorioretinitis
   1. Description
      a. White dot syndrome
         i. Rare, idiopathic retinochoroiditis
         ii. Possible autoimmune with strong association to HLA-A29
      b. Caucasians 40-60s; Women > Men
      c. Bilateral and chronic with insidious onset

2. Ocular signs
   a. Small, scattered hypopigmented or creamy lesions with indistinct borders
      i. At the level of the RPE and choriocapillaris
      ii. Begins in midperiphery and spreads to the posterior pole especially
      nasal and inferior to the optic disc
      iii. Depigmented spots can precede creamy lesions by a few years
      iv. May have elongation of peripheral lesions
   b. Vitritis, minimal to no anterior uveitis
   c. Retinal vasculitis
d. Optic disc and macular edema
e. Complications- Occlusive vasculopathy, neovascularization, CNV

3. Diagnostic Testing
   a. IVFA
      i. Early hypofluorescence with late staining of lesions
   b. ICG
      i. Early hypofluorescence spots more extensive than seen on IVFA with late hyperfluorescence
   c. HLA-A29

4. Management
   a. Systemic steroids
   b. Immunosuppressants
   c. Variable visual recovery

I. Serpiginous Choroidopathy- AKA Geographic Helicoid Peripapillary Choroidopathy
   1. Description
      a. White dot syndrome
         i. Rare, idiopathic choroiditis
   b. Caucasians 30-70s; Men > Women
   c. Bilateral and chronic

2. Ocular signs
   a. Gray or yellow-white lesions that begin peripapillary
      i. Destruction of the choroid, choriocapillaris, and RPE
   b. Progresses in serpentine pattern and evolves into geographic areas of chorioretinal atrophy toward macula and midperipheral retina
   c. Macular involvement and peripapillary sparing in some cases
   d. New lesions occur at the edge of old ones
   e. Thinning of overlying sensory retina and RPE clumping after resolution
   b. Mild vitritis, anterior uveitis
   c. Retinal vasculitis
   d. Complication- Occlusive vasculopathy, neovascularization, CNV

3. Diagnostic Testing
   a. IVFA
      i. Active lesions
         Early hypofluorescence with late diffuse staining
      ii. Inactive lesions
         Early central hypofluorescence with staining around the lesion edge and late staining
   b. ICG
      i. Hypofluorescent lesions in all stages more extensive than seen on IVFA

4. Management
   a. Active lesions spontaneously resolve after 6-8 weeks
   b. Systemic steroids
   c. Immunosuppressants
   d. Final visual acuity unpredictable; occurs between 2-22 months

J. Multifocal Choroiditis
   1. Description
      a. White dot syndrome
i. Rare, idiopathic, inflammatory choroidal disease
b. Caucasian myopic females; 10-60s
c. Bilateral > Unilateral, chronic with insidious onset

2. Ocular signs
   a. Small, multifocal, round gray to yellow-white lesions in the posterior pole
      i. At the level of inner choroid and RPE
      ii. Lesions may coalesce, become fibrotic and encroach on macula
      iii. New lesions occur at the edge of old ones
      iv. Atrophic chorioretinal scars after resolution
   b. Vitritis, anterior uveitis
   c. Optic disc and macular edema
d. Complications- CNV, progressive subretinal scarring

3. Diagnostic Testing
   a. IVFA
      i. Early hyperfluorescence of lesions with late staining or leakage
   b. ICG
      i. Hypofluorescent spots more extensive than seen clinically

4. Management
   a. Systemic steroids
   b. Immunosuppressants
c. Guarded prognosis

K. Punctate Inner Choroidopathy

1. Description
   a. White dot syndrome
      i. Rare, idiopathic, inflammatory choroidal disease
   b. Caucasians myopic females; 20-40s
   c. Bilateral > Unilateral, chronic with sudden onset

2. Ocular signs
   a. Small, multiple discrete gray to yellow-white lesions in the posterior pole
      i. At the level of inner choroid and RPE
      ii. Linear or cluster pattern
      iii. Minimal subretinal fluid overlying lesion
      iv. New lesions occur at the edge of old ones
      v. Atrophic chorioretinal scars after resolution
   b. No anterior uveitis or vitritis
   c. No optic disc or macular edema
d. Complications- CNV, progressive subretinal scarring

3. Diagnostic Testing
   a. IVFA
      i. Early hyperfluorescence of lesions with late staining or leakage
   b. ICG
      i. Hypofluorescent spots more extensive than seen on IVFA

4. Management
   a. Systemic steroids
   b. Immunosuppressants
c. Good prognosis with 2/3 of patients’ visual recovery to 20/40 or better
REFERENCES


