

Ophthalmology Board Review Notes: Intermediate Uveitis, Posterior Uveitis

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Intermediate Uveitis

Definition: intraocular inflammation primarily affecting the vitreous

Older terms:

Vitritis

Cyclitis

Pars planitis (presence of exudates or fibrosis on the pars plana)

Uveitis characteristics:

Vitritis (> anterior chamber inflammation)

Optic disc edema*

Macular edema*

Peripheral retinal vasculitis*

* intraocular inflammation primarily involving the vitreous may have these associated findings and still be classified as 'intermediate' (as opposed to 'posterior')

Differential diagnosis:

Multiple sclerosis

Sarcoidosis

Syphilis

Lyme disease

Inflammatory bowel disease

Posterior Uveitis

Infectious causes of posterior uveitis

Bacterial	Syphilis*
	Lyme*
	Bartonella (cat-scratch disease)
	Tuberculosis*
Fungal	POHS
Viral	ARN/PORN
	CMV
Parasitic	Toxoplasmosis
	Toxocariasis
Other	Chronic postoperative uveitis*
	Endogenous endophthalmitis

Non-infectious causes of posterior uveitis

Autoimmune	VKH
	Sympathetic Ophthalmia
	Sarcoidosis*
	SLE
	Adamantiades-Behcet's Disease

White Dot Syndromes

APMPPE
MEWDS
Multifocal choroiditis and panuveitis (MCP)
PIC
Birdshot retinochoroidopathy
Serpiginous choroidopathy
AZOOR

*etiology described in 'Uveitis:overview, anterior uveitis' handout

Bartonella (cat-scratch disease)

Causative organism: *Bartonella henselae* (formerly known as *Rochalimaea henselae*)

Parinaud's oculoglandular syndrome - conjunctivitis, lymphadenopathy associated with exposure to animals

Foshay - 'cat scratch fever'

Sweeny and Drance - associated with uveitis

Leber = idiopathic stellate neuroretinitis

Bartonella (cat-scratch disease)

Margileth - estimated in CSD:

conjunctivitis 5-10%

neuroretinitis 1.5%

Clinical features of systemic disease: Myalgia, malaise, fatigue, low-grade fever, lymphadenopathy.

Ocular findings:

Optic disk edema with macular star

Other presentations include:

Inflammatory mass at nerve head

Intermediate uveitis

Anterior uveitis

Other ocular disease include:

Conjunctivitis

Orbital abscess

Diagnosis:

History/ROS: +h/o exposure to cats ~ 92%, +h/o bite or scratch ~ 76%

Diagnostic test: serologic.

In diagnostic dilemmas, may send intraocular fluid for PCR testing.

Treatment: Doxycycline, Bactrim, Rifampin, Gentamycin, Cipro

Role of steroids not clear.

Acute retinal necrosis (ARN)

1971 Urayama described six patients

No race or gender preponderance

All ages affected (youngest age reported - 13 yrs)

Patients are *immunocompetent*.

Typically unilateral (bilateral cases: BARN)

Peripheral or midperipheral yellow/white retinal lesions - enlarge and coalesce

Retinal vasculitis (arteritis) with occlusions.

Vitritis

Anterior uveitis

Optic neuropathy

Etiology: VZV isolated on EM, immunohistochemistry. HSV (1&2), CMV, syphilis also can present similarly

Diagnosis: clinical diagnosis (AUS)

- 1) one+ foci of retinal necrosis with discrete borders in the peripheral retina
- 2) rapid onset if antiviral therapy not given
- 3) circumferential spread of disease
- 4) occlusive vasculopathy with arteriolar involvement
- 5) prominent vitreous and/or anterior chamber reaction

Diagnostic dilemma or poor treatment response: vitreous and/or retinal biopsy
PCR (HSV1, HSV2, VZV, CMV, Toxoplasmosis)

Treatment: Acyclovir 500 mg/sq.m. IV q 8 hours for 10-14 days

Other treatment: Laser photocoagulation (prophylaxis), aspirin, surgery (RD)

Risk of RD is high.

Retinal detachment and optic neuropathy are causes of severe vision loss

ARN vs Progressive outer retinal necrosis (PORN)

ARN

Immunocompetent

Periphery/midperiphery

Vasculitis common

Significant vitritis

Responds to ACV

PORN

Immunocompromised

Posterior pole

Vasculitis rare

Mild vitritis

No good therapy

Ocular Toxoplasmosis

Causative organism: *Toxoplasma gondii*

Most common cause of posterior uveitis of known etiology

Ocular Toxoplasmosis - etiology

Congenital vs. acquired?

Epidemiologic studies in Brazil suggest acquired may account for more ocular disease than previously thought (traditional teaching is its recurrence of congenitally acquired)

Pathophysiology: Release of actively proliferating tachyzoites, with subsequent Immune response to retinal elements

Ocular findings:

Large atrophic scar

Focal chorioretinitis at edge of scar

Satellite lesions

Vasculitis, focal (area of inflammation)

Vitritis

Anterior uveitis

Glaucoma

Diagnosis: clinical appearance

Non-classic clinical appearance:

Serologic testing

PCR (vitreous biopsy)

In immunocompetent patient, disease is self limited

Treatment criteria:

Lesion within temporal arcade

Lesion near or involving the optic nerve

Lesion induced a large hemorrhage

Significant inflammation or vision reduction

'Classic': Sulfadiazine 1 gm PO QID, Pyrimethamine 25 PO BID, Folic acid 5 gm PO 3x/week

Other medications: Clindamycin 300 mg PO QID, Trimethoprim-sulfamethoxazole DS PO BID, or Atovaquone

Add prednisone 0.5 to 1 mg/kg after starting antibiotic therapy. Discontinue prednisone before discontinuing antibiotic therapy. Periocular steroids is contraindicated

No randomized controlled trial has demonstrated that antibiotic treatment is superior to placebo.

Adamantiades-Behcet's Disease

1937 Behcet: recurrent eye inflammation, oral and mucosal ulcerations

Diagnostic Criteria: several different conventions:

Behcet's Disease Research Committee of Japan

Major: Oral and genital ulcers, skin lesions, uveitis

Minor: Arthritis, epididymitis, vasculitis, neurologic involvement

Complete, incomplete, and suspect

International Study Group for Behcet's Disease

Recurrent oral ulcers +

2 of: genital ulcers, uveitis, skin lesions, pathergy

Systemic manifestations:

Recurrent aphthous ulcers

Skin lesions

Genital ulcers
Arthritis
Epididymitis
Intestinal ulcers
Vascular disease
Neuropsychiatric symptoms (neuro-Behcet's)

Ocular disease:

Usually 2-3 years after initial symptoms

Bilateral, recurrent, explosive

Can present in one of two forms:

Non-granulomatous anterior uveitis

Can be associated with hypopyon in 1/3 cases

Retinal vasculitis (with vaso-occlusion)

Can be associated with optic neuropathy

High risk for blindness

Other ocular disease:

Episcleritis

Filamentary keratitis

Conjunctivitis

Subconjunctival hemorrhages

Diagnostic tests: no definitive tests for ABD (clinical criteria)

HLA-Typing: HLA-B51

Pathergy test

Treatment: systemic immunosuppressives.

Vogt-Koyanagi-Harada Disease

Vogt - single case report

Harada - posterior uveitis with SRD and + white cells in CSF

Y. Koyanagi - six cases of chronic uveitis associated with poliosis, vitiligo, dysacusia

Vogt-Koyanagi-Harada Disease

Epidemiology:

Japanese, Latin America

Second to fourth decade

HLA-DR4 (Risk=15)

Ocular findings:

Bilateral

Granulomatous

Multifocal choroiditis

Exudative retinal detachment

Systemic findings

Headache, neck stiffness

Vertigo, hearing loss
Pleocytosis on lumbar puncture
Vitiligo
Poliosis
Alopecia

Pathophysiology: Immune reaction targeting melanin-containing cells? (would explain involvement of choroids, meninges, skin, and hair).

Treatment:

Systemic steroids. If inflammation becomes chronic, steroid-sparing immunosuppressives.

Sympathetic Ophthalmia

Bilateral granulomatous uveitis following penetrating trauma to one eye

Very rare:

Incidence 0.2%-0.5% trauma, 0.01% surgical

Ocular findings:

Granulomatous anterior uveitis
Vitritis
Multifocal choroiditis

Sympathetic Ophthalmia and VKH

Histology comparisons

VKH: inflammation in choroid and choriocapillaris; Dalen-Fuchs nodules

Sympathetic: sparing of choriocapillaris

Some cases of SO associated with vitiligo and/or poliosis

Treatment: systemic corticosteroids. If chronic, steroid-sparing immunosuppressives.

White Dot Syndromes

The 'white dot syndromes' are a group of disorders characterized by unknown etiology and retinal lesions. Only two of the disorders are recognized by uveitis specialists to likely respond to and require aggressive anti-inflammatory treatment (Birdshot retinochoroidopathy, multifocal choroiditis and panuveitis); the others have shown inconsistent to no response to anti-inflammatory treatment.

White Dot Syndromes

Acute posterior multifocal placoid pigment epitheliopathy (APMPPE)

Multiple evanescent white dot syndrome (MEWDS)

Multifocal choroiditis and panuveitis (MCP)

Punctate inner choroidopathy (PIC)

Birdshot retinochoroidopathy

Serpiginous choroidopathy

Acute zonal occult outer retinopathy (AZOOR)

The best way (in my opinion) to 'mentally organize' the white dot syndromes is to recall a one-sentence overview description of the disorder, and to familiarize oneself with representative clinical fundus and fluorescein angiogram photos.

Acute posterior multifocal placoid pigment epitheliopathy (APMPPE)

An idiopathic posterior uveitis characterized by sudden-onset bilateral vision loss, with multiple, cream-colored well-circumscribed plaque-like lesions, demonstrating early hypo/late hyperfluorescein on FA, which completely resolves without treatment.

1968 - Gass (Arch Ophthalmol 80:177-185)

Men = Women

20s - 30s

Sudden onset: blurred vision, flashes

Bilateral; simultaneous

Often associated with viral prodrome

Ocular findings:

Multiple flat, cream-colored, well circumscribed lesions in the posterior pole

Associated papillitis, uveitis uncommon; no macular edema

Usually self-limiting: lesions will fade over several weeks, with subsequent visual recovery.

Fluorescein angiography: Early hypofluorescence corresponding to lesions, late hyperfluorescence. Minimal leakage noted.

ICG shows early and late hypofluorescence.

Associated conditions:

Erythema nodosum

Episcleritis

Renal disease

Thyroiditis

Neurosensory hearing loss

Cerebral vasculitis – life threatening, requires steroid treatment

Treatment: none indicated for most cases.

Consider steroid use if macula involved or systemic involvement (cerebral vasculitis)

Multiple evanescent white-dot syndrome (MEWDS)

Idiopathic posterior uveitis characterized by sudden-onset unilateral vision loss in a young woman, with numerous small white lesions in the retina, with complete resolution without treatment.

1984 - Jampol and colleagues (Arch Ophthalmol 102:671-674) - 11 patients

Women > men

20s - 30s

Sudden onset

Unilateral

No consistent viral prodrome

No associated systemic disorders

Self-limiting

Ocular findings:

Numerous small discrete white lesions in the posterior pole

Granularity of the macula

Occasional vitritis, retinal vein sheathing

FA: early hyperfluorescence - dots seen clinically correspond to a small 'wreathes';
Late staining

ICG

Hypofluorescent lesions

Hypofluorescence around the optic nerve

Visual field testing: enlargement of blindspot (correspond to ICG findings)

Treatment: none indicated.

Multifocal choroiditis and panuveitis

Idiopathic bilateral panuveitis characterized by choroidal lesions resembling POHS lesions, but with significant vitritis and cystoid macular edema.

1973: Nozik & Dorsch (Am J Ophthalmol 76:758-762) - 2 patients

Women > men 3:1

20s - 50s

Bilateral

Myopic

Rare viral prodrome (18%)

Chronic course

Ocular findings:

Lesions look like 'histo spots'

Multiple punched-out spots throughout the fundus, often pigmented

Significant vitritis, anterior uveitis

CME in 14% - 41% of patients

Differences between MCP and POHS

MCP does not have 'streaks' or peripapillary atrophy.

MCP will present with significant vitritis, whereas POHS will NEVER present with vitritis.

Patients with MCP will not necessarily come from a Histo-endemic area,

Patients with MCP will have a negative Histoplasma skin test

Fluorescein angiography: early hyperfluorescence (typical of RPE window defects)

No underlying systemic disorder

Treatment:

Must treat CME aggressively

Systemic or periocular steroids if significant vision loss and/or inflammation

Most uveitis specialists will recommend systemic immunosuppressives because of the high likelihood of visual loss from the complications of chronic inflammation.

Punctate inner choroidopathy (PIC)

1984 - Watzke (Am J Ophthalmol 98:572-583)

Variant of MCP?

PIC

Fundus lesions indistinguishable from MCP

No intraocular inflammation

Reddy and Folk: no new lesions in PIC

Birdshot retinochoroidopathy

Idiopathic chronic bilateral posterior uveitis characterized by multiple, oval, yellow, choroidal spots, associated with vitritis, retinal vasculitis, macular edema, and a high association with HLA-A29.

First described by Ryan and Maumenee in 1980

Women > Men

40s - 50s

Floaters, decreased vision

Ocular findings:

Bilateral

No prodrome

Chronic

Multiple cream-colored oval poorly-circumscribed lesions

Significant vitritis

Retinal vasculitis

CME common

Diagnosis: Clinical findings

There is a high association with HLA-A29 + (Risk: 220:1)

No systemic diseases.

Treatment: No treatment if disease mild. However, many patients have a progressive, vision threatening course, and steroids or immunosuppressives (e.g. cyclosporine) can preserve vision in these cases.

Acute zonal occult outer retinopathy (AZOOR)

Idiopathic retinopathy characterized by rapid loss of large zones of outer retinal function with no associated inflammation.

Described by Gass in 1993

Women

20s - 30s

Sudden onset loss of vision

Ocular findings:

Initially, only minimal fundoscopic changes.

Later stage demonstrate striking RPE changes.

Abnormal ERG

HVF: one or more scotomas.

No associated uveitis.

No associated systemic disorders

Steroids not consistently beneficial

Serpiginous Choroiditis

Idiopathic bilateral chronic choroiditis characterized by 'serpentine'-patterned atrophy extending from the optic disk.

Ocular findings

Painless decreased vision

Metamorphopsia, paracentral scotoma

Cream colored lesion, starting at edge of old lesions, lead to atrophy.

Mild vitritis seen in some cases.

Choroidal neovascular membrane can occur as a complication.

Fluorescein angiography: Early blockage (decreased choroidal filling), with late staining of edge of active lesion; late blockage associated with scar/RPE clumping.

No associated systemic disorders.

Treatment: systemic immunosuppressives may slow progression (controversial).

Addendum: Intermediate and Posterior Uveitis notes

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List of Masquerade Syndromes:

Malignancies

- Intraocular – CNS lymphoma
- Leukemia
- Malignant melanoma (Iris melanoma, choroidal melanoma)
- Retinoblastoma
- Metastasis
- Paraneoplastic syndromes

Endophthalmitis

- Chronic postoperative endophthalmitis
- Endogenous endophthalmitis

Nonmalignant, noninfectious

- Occult retinal detachment
- Retinitis pigmentosa
- Intraocular foreign body
- Pigment dispersion syndrome
- Ocular ischemic syndrome
- Juvenile xanthogranuloma
- Drug-induced uveitis

*Most of these conditions will be discussed in other sections

Intraocular lymphoma

- Diffuse large cell lymphoma of B-cells (usually non-Hodgkin's)
- Older adults, age 50+
- Immunosuppression is a risk factor
- May present initially/solely in the eye; CNS involvement
- Ocular presentation is posterior uveitis or vitritis
- Diagnosis: MRI/brain, brain biopsy, vitreous biopsy
- Treatment: radiation, chemotherapy
- Prognosis: poor (5% at 5 years)

- Uncommon: only 2-8% of all endophthalmitis
- Immunocompromised patients: diabetes, malignancy, SLE, HIV
- Predisposing conditions: heart valve, dental work, IVDA
- Diagnosis: biopsy
- Treatment: intraocular antimicrobials, intravenous antimicrobials, vitrectomy

Juvenile xanthogranuloma

- benign inflammatory disorder of young children affecting the skin
- no race or gender predilections
- 75% have skin lesions as only manifestation
- Iris infiltration presents as iris mass
- Spontaneous hyphema may lead to secondary glaucoma
- Can affect conjunctiva, sclera, orbit (proptosis)

- Diagnosis: skin biopsy; AC tap reveals foamy histiocytes and Touton cells
- Prognosis: excellent

Drug-induced uveitis

- Inflammation usually mild to moderate (exception: rifabutin)
- Usually anterior chamber
- Generally no systemic associations
- Treatment: removal of offending agent
- List of drugs:
 - Rifabutin
 - Biphosphonates (Pamidronate, risedronate)
 - Cidofovir
 - Metipranolol
 - Sulfonamides (TMP-SMX)