USCAP 2015
Specialty Conference
Ophthalmic Pathology

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Dr. Nora V. Laver declares she has no conflict of interest to disclose.
Case Presentation
Clinical History

• An 18-year-old African-American female suffered a penetrating wound to the right eye in the superior limbal area.
• The wound was repaired with excision of a prolapsed iris and vitreous loss.
Clinical History

• Two weeks post injury she developed endophthalmitis and was treated with a one week course of antibiotics and steroids.
• A month after the injury the patient complained of persistent pain and decreased vision with only hand motion in her right eye and decreased vision on her left eye of 20/200.
• Systemic and topical steroids were resumed.
• The eye became painful and blind.
• An enucleation was performed six weeks after the penetrating injury.
Histopathology
Histopathological findings

- Diffuse granulomatous inflammatory reaction within the uveal tract.
- Composed of lymphocytes and epithelioid histiocytes containing phagocytosed melanin pigment.
Pan-uveitis
What is the differential diagnosis of granulomatous inflammation present in uveal and retinal tissues?
Differential Diagnosis of Uveal Inflammation

- **Trauma** (recent or delayed)
  - Sympathetic ophthalmia

- **Infectious / Inflammatory causes**
  - Tuberculosis
  - Syphilis
  - Retinitis / CMV
  - Uveitis

- **Lymphoma**

- **Inflammatory**
  - Sarcoidosis
  - Vogt-Koyanagi-Harada syndrome
  - Behcet’s syndrome
Vogt-Koyanagi-Harada Syndrome (VKH)

- Rare cause of posterior or diffuse uveitis that may have ocular and systemic manifestations
- Asian or Native American ancestry
- 30-50 years of age
- Bilateral decreased visual acuity, pain, redness, and photophobia.
- Strong association with HLA-DR4
- Serous retinal detachment and optic nerve involvement
- Proposed mechanism is an immune reaction to uveal melanin-associated protein, melanocytes or pigment epithelium
Systemic manifestations include alopecia, poliosis (loss of pigmentation of eyelashes and eyebrows), vitiligo, dysacusis (difficulty processing details of sound due to distortion in frequency or intensity), headaches, and seizures.

Chronic, diffuse granulomatous uveitis without spearing of the choriocapillaris.
Behçet Disease

• Systemic disorder characterized by recurrent aphthous ulcers and intraocular inflammation.
• The clinical triad of uveitis with recurrent oral and genital ulcers bears the name of Hulusi Behçet, a Turkish dermatologist who described 3 patients who had this triad.
• During acute inflammation, the iris, the ciliary body, and the choroid show diffuse infiltration with neutrophils.
• In late stages, a proliferation of collagen fibers, thickening of the choroid, formation of cyclitic membrane, and sometimes hypotonia and phthisis bulbi are noted. Lymphocytic and plasma cell infiltration occurs during remission.
• Of all ocular tissues, the retina suffers the most damage.
Clinical Course

• The patient was diagnosed with sympathetic ophthalmia.
• She was treated with high dosage oral prednisone (1.0 to 2.0 mg/kg/day).
Sympathetic Ophthalmia

- Uncommon bilateral granulomatous panuveitis that occurs after accidental or surgical injury to an eye (inciting eye) followed by a latent period and development of uveitis in the uninjured eye (sympathizing eye).
- The inflammation may occur as early as 9 days or as late of 50 years following the suspected triggering incident.
- The typical latency period is 4-8 weeks.
- The disease is vision-threatening may lead to significant vision loss especially if treatment is not instituted quickly.
Sympathetic Ophthalmia

• The incidence ranges from 0.2 to 0.5% after ocular injuries and 0.01% after intraocular surgery.
• Vitreoretinal surgery and cyclodestructive procedures considered risk factors.
• There is no racial, age or sex predisposition.
• The diagnosis is based on clinical findings rather than serological testing or pathological studies.
• Fluorescein angiography shows areas of pinpoint hyperfluorescence which leak on later phases (corresponding to areas of retinal detachment).
• OCT for retinal detachments
Clinical Presentation

- Insidious onset of blurry vision, pain, epiphora, and photophobia in the sympathizing, non-injured eye.
- Classically this is accompanied by conjunctival injection and a granulomatous anterior chamber reaction with mutton-fat keratic precipitates on the corneal endothelium.
- Serous retinal detachment is a common finding
Acute anterior uveitis with keratic precipitates

Pathogenesis
Cell-mediated immune response directed against ocular self-antigens found on photoreceptors, the retinal pigment epithelium (RPE) and/or choroidal melanocytes.
Sympathetic Ophthalmia

• What are the risk factors for the development of SO?
• Recent or delayed trauma (surgical or non-surgical)
• Associated with particular major histocompatibility antigen (MHC) DR4 (HLA-DR4, and closely related HLADQw3 and HLA-DRw53) phenotype.
  • These phenotypes are also found more frequently in patients with Vogt-Koyanagi-Harada disease
Histopathology Findings

- **Diffuse granulomatous inflammatory reaction** appears within the uveal tract. The **choriocapillaris** is typically non-involved.
- Varying degrees of inflammation in the anterior chamber as evidenced by **collections of histiocytes** deposited in the corneal epithelium (or mutton-fat keratic precipitates).
- **Dalen-Fuchs nodules** are collections of epithelioid histiocytes and lymphocytes between the retinal pigment epithelium and Bruch’s membrane. Are found in one-third of enucleated eyes with SO. Dalen-Fuchs nodules may be present in Vogt-Koyanagi-Harada syndrome.
- **Retinal infiltrates** have been reported in 18% of SO cases with perivasculitis, retinal detachment, and gliosis.
- Occasionally, eosinophils, neutrophils, and plasma cells may be present.
Sympathetic Ophthalmia

Dalen Fuchs nodules

Epithelioid histiocytes and lymphocytes between the RPE and Bruch’s membrane.
Sympathetic Ophthalmalmia

Unexpected SO in a blind painful eye s/p retinal detachment surgery

Retinal involvement with granulomatous inflammation
Chronic uveitis
Immunohistochemistry

CD68 stain
Sympathetic Ophthalmia Treatment

• Systemic corticosteroids are the first line therapy.
• Treatment is initiated with high dosage oral prednisone (1.0 to 2.0 mg/kg/day) and tapered slowly over 3 to 4 months.
• In severe cases, intravenous pulse steroid therapy can be employed (methylprednisolone 1.0 g/day for 3 days).
• Adjunctive topical corticosteroids and cycloplegics are used to prevent synechia formation from the anterior chamber reaction.
• If patients are non-responsive to steroid therapy or have clinically significant side effects, cyclosporine, azathioprine or other immunosuppressive agents can be used for long-term immunomodulatory therapy.
Conclusions

• Rare and potentially visually devastating bilateral panuveitis, typically following surgery or non-surgical penetrating injury to one eye.
• High index of suspicion is vital to ensure early diagnosis and initiation of treatment, thereby allowing good final visual acuity in most patients.
• Diverse clinical presentations are possible and any bilateral uveitis following vitreoretinal surgery should alert the surgeon to the possibility of SO.
Selected References


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The End

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