



Ophthalmology Update

Richmond Eye Associates, P.C.

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Ophthalmic Topics of Interest to the Medical Physician

Iritis / Uveitis - Medical Correlations with Ocular Inflammatory Disease

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Ophthalmology Update:

Life Threatening Ocular Disorders

- Pituitary Apoplexy
- Carotid-Cavernous Fistula
- Ocular Malignancy
- Ptosis and Lung Cancer

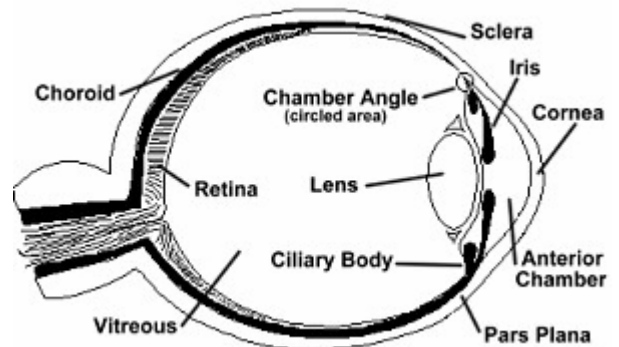
What is Uveitis?

The "Uveal Tract" of the eye includes the iris, the ciliary body, and the choroid. The ciliary body is a structure located behind the iris, and it is virtually never directly visible for examination. It is responsible for producing aqueous fluid which fills the eye (a complete turnover of fluid every 100 minutes), and for changing the shape of the lens of the eye during focusing. The choroid is a highly vascular structure located behind the retina. It satisfies the high metabolic demands of the outer layer of the retina (including the photo receptors).

Uveitis refers to inflammation anywhere in the Uveal Tract. However, this common term has come to be used to describe any inflammatory or infectious condition of the eye, including retinitis and scleritis. Terms used for uveitis include:

- Iritis - usually referring to inflammation in the anterior chamber, or front of the eye.
- Iridocyclitis - which may refer to anterior inflammation and some extension into the vitreous cavity posteriorly.

- Intermediate Uveitis - inflammation of the pars plana, which is between the ciliary body and the retina.
- Vitritis - inflammation or infection of the vitreous.
- Retinitis - inflammation or infection of the retina.
- Chorioretinitis - inflammation of the choroid and the retina.
- Scleritis - inflammation of the sclera, or the wall of the eye.
- Episcleritis - inflammation of a fibrous layer between the sclera and conjunctiva.



Systemic Diseases Associated with Anterior Uveitis

Spondyloarthropathies

Up to 50% of patients with anterior uveitis are found to be HLA-B27 positive, and 30% to 90% of HLA-B27 positive individuals with uveitis eventually experience symptoms from the underlying systemic disorder. Ankylosing Spondylitis is the most common associated systemic disorder, followed by Reiter Syndrome, inflammatory bowel disease, and psoriatic arthritis. Overall, men are affected nearly three times as often as

women. The uveitis tends to be recurrent, often bilateral, and possibly severe. In cases where symptoms such as arthritis, lower back pain / stiffness, urethritis, aphthous stomatitis, inflammatory bowel disease, or psoriasis are present, HLA-B27 testing is warranted as well as referral to an appropriate specialist such as a rheumatologist or gastroenterologist. Oral steroids or even methotrexate may be needed to control the uveitis in some cases.

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Systemic Diseases Associated with Anterior Uveitis (page 1)

Sarcoidosis

Sarcoidosis accounts for 10% to 20% of cases of anterior uveitis. It is substantially more common in African-Americans than in Caucasians at a ratio of 10:1. Between 25% to 50% of individuals with sarcoidosis will eventually develop uveitis. Sarcoidosis is a multi-system disease primarily affecting pulmonary function, as well as other lymph nodes, the liver, spleen, bone, skin, and the central nervous system. In cases of CNS involvement, a retinal vasculitis or optic neuropathy might be seen.

The diagnosis of sarcoidosis is supported by an abnormal Chest X-ray an elevated ACE or lysozyme level. Sarcoidosis produces a type of uveitis referred to a “granulomatous”, due to the appearance of large precipitates on the inside surface of the cornea. In cases where the diagnosis of sarcoidosis is unsure and the ocular inflammation is granulomatous, it is reasonable to perform skin testing to rule out tuberculosis, which also produces granulomatous uveitis.

Behcet’s Disease

Behcet’s disease is a systemic vasculitis associated with uveitis.

Oral, genital, or intestinal ulcers, arthritis, thrombophlebitis, erythema nodosum, and cerebritis are systemic findings. The disorder is more common in Asians or those of Middle Eastern descent. Retinal vasculitis and focal retinal infarction are also possible. Other conditions such as tuberculosis, syphilis, sarcoidosis, and collagen vascular diseases should be ruled out.

Juvenile Rheumatoid Arthritis

Children with a pauciarticular (less than five joints involved) onset and monoarticular JRA account for 90% of cases of uveitis in cases of JRA (systemic JRA associated with fever and rash rarely develops uveitis). Up to 80% of cases of JRA with uveitis are ANA positive, and rheumatoid factor is negative. Uveitis can develop prior to the arthritis, or as late as 20 years after onset of the arthritis. Most cases of uveitis occur within 5 years of JRA onset. Girls are affected 4 to 1 over boys. Often, the affected eye appears uninfamed. Delay in diagnosis often leads to a poor prognosis, with chronic inflammation leading to silent damage, including cataract formation, glaucoma, membrane formation within the eye, and corneal clouding. Regular screening eye exams should be done.

Clinical Pearl: Distinguishing Between Etiologies of Ocular Inflammation

There are many causes of ocular redness, and in many cases symptoms and findings overlap. The chart below shows the typical symptoms for each disorder. Note that the symptoms of acute anterior iritis / uveitis are very similar to

acute angle closure glaucoma. Thus, it may be difficult to distinguish these two disorders, and a same-day referral should be made unless the intraocular pressure can be checked to rule out acute glaucoma.

	Redness	Pain	Light Sensitivity	Vision	Other Symptoms
Anterior Iritis / Uveitis	Peri-limbal flush is common, or diffuse injection	Significant aching pain	Hallmark symptom - often severe	Often blurred, sometimes with halos	Floaters possible; usually no discharge or tearing
Acute Angle Closure Glaucoma	Peri-limbal flush or diffuse injection	Significant aching pain	May be sensitive to light	Usually blurred, with halos and rainbows	Nausea and vomiting are possible
Corneal Abrasion	Diffuse injection	Foreign body sensation and pain	Often light sensitive	May be blurred, but can be clear	Profuse tearing is very common
Scleritis	Diffuse injection, often a violet hue	Severe, deep “boring” pain	May be light sensitive	Can be very blurred	May be systemically very ill
Conjunctivitis	Diffuse injection	May be mildly painful	No	Vision usually not blurred	Itching, tearing, and discharge
Subconjunctival Hemorrhage	Spotches of solid, bright redness	Not painful	No	Vision Normal	Sudden appearance of redness

Infectious Causes of Uveitis

Syphilis

Syphilis accounts for 2% - 8% of cases of uveitis seen at large referral centers. Most cases of syphilitic uveitis are non-distinctive, and the diagnosis is made through having a high index of suspicion for the disease. Occasionally, arthritis and dermatitis affecting the palms, soles, or scalp may be present. Confirmatory lab tests include the FTS-ABS, MHATP, and the RPR and VDRL.

It is recommended to check the cerebrospinal fluid for evidence of syphilis in cases of syphilitic uveitis. However, it is also recommended that patients receive intravenous penicillin 6 million units every 6 hours for 10-14 days regardless of the CSF results.

Tuberculosis

While tuberculosis is an uncommon cause of uveitis, the overall rate of tuberculosis is increasing in certain populations, raising the index of suspicion in these groups. The uveitis is sometimes accompanied by iris nodules and granulomatous deposits on the internal surface of the cornea, but other times the inflammation is indistinct. Tuberculosis should be considered in cases of uveitis associated with respiratory symptoms, weight loss, fever, night sweats, and possible exposure to the disease itself.

Confirmatory tests include chest X-ray and a purified protein derivative skin test (PPD).

Lyme Disease

Ocular findings can occur in all stages of Lyme Disease. Within the first month of infection, a conjunctivitis may be present in addition to typical systemic findings of the typical skin rash, headache, myalgias, arthralgias, and fever.

In Stage II of the disease, occurring one to four months after infection, ocular findings may be common. Development of a chronic uveitis or vitritis (inflammation more posteriorly in the eye) is the most characteristic ocular finding of Lyme disease. Other ophthalmic findings during this stage include keratitis (corneal breakdown), anterior iritis, and optic neuritis. Neurologic disease,

occurring in 30% - 40% of patients can include Bell's palsy, encephalitis, and meningitis. Cardiac disease and arthritis are also possible.

In Stage III of the disease, five or more months after onset, chronic meningitis, arthritis, adults respiratory distress syndrome, and keratitis can occur.

Ocular Toxoplasmosis

Toxoplasmosis accounts for 30% to 50% of all cases of posterior uveitis. The disease is primarily an exudative focal retinitis, and depending on the location of the lesion, visually important structures of the eye may be at risk. While cats are known to harbor *Toxoplasma gondii* as an intestinal parasite, humans probably acquire most cases of toxoplasmosis by the ingestion of undercooked or raw meat containing the encysted form of the parasite. During an acute flare-up of congenitally acquired ocular toxoplasmosis, the symptoms are primarily visual, consisting of floaters or blurred vision. The eye would otherwise appear to be quiet and uninfamed, at least initially.

However, a recent study¹ in the journal *Ophthalmology* reviewing 154 cases of ocular toxoplasmosis found at least 11% of cases to be postnatally acquired, with a different type of clinical presentation. This occurred primarily in elderly patients as a severe vitritis, a severe anterior granulomatous uveitis, and often an elevated intraocular pressure. The visual outcome in these patients was generally poor, often due to the administration of corticosteroids without antiparasitic drugs. Causes of legal blindness included macular scarring, retinal detachment, and optic nerve atrophy.

The diagnosis of ocular toxoplasmosis is facilitated by detection of the serum toxoplasmosis antibody, even at the most minimal level (indicating any past exposure to the disease). The differential diagnosis includes syphilis, CMV, and fungal infections. Treatment is with a combination of pyrimethamine, sulfadiazine, clindamycin, and Prednisone.

¹Bosch-Driessen, et al. *Ophthalmology* 5/2002;109:869-878.

The Dangers Associated with Scleritis

Scleritis is a severe, possibly destructive, inflammation of the wall of the eye (the sclera). This disorder is completely different from episcleritis, which is a mild inflammation of the surface of the eye that is otherwise asymptomatic and carries a good prognosis. Scleritis is often bilateral, and is usually moderately to severely painful. Women between 20 and 60 years of age are most commonly affected. The eye usually appears to be deeply inflamed, with a violaceous hue. In some cases nodules appear on the ocular surface, and in other cases the sclera may thin and even perforate.

Scleritis is often associated with systemic disease, including infectious diseases such as syphilis, tuberculosis, varicella zoster, and leprosy. It is frequently associated with autoimmune connective tissue disorders such as rheumatoid arthritis, Wegener's granulomatosis, systemic lupus erythematosus, and polyarteritis nodosa. Often over 50% of cases of scleritis are associated with a systemic

disorder, and especially in cases of necrotizing scleritis with inflammation, an increased mortality rate. Treatment includes systemic immunosuppressive medications such as methotrexate, cyclophosphamide, and azathioprine.

A recent study¹ compared the outcomes of scleritis alone with that of scleritis associated with ulceration or thinning of the peripheral cornea (peripheral ulcerative keratitis). Patients with scleritis and peripheral keratopathy had a poor ocular and systemic prognosis. 81% had decreased vision, and 61% had impending corneal perforation. 87% of cases were associated with a potentially lethal systemic disease, especially rheumatoid arthritis, Wegener's granulomatosis, and infectious disease (as listed above). Overall, scleritis associated with peripheral keratopathy indicates a poor prognosis.

¹Archives of Ophthalmology 1/2002;120:15-19.

Richmond Eye Associates, P.C.

David W. MacMillan, M.D.
James G. Ferguson, M.D., F.A.C.S.
Barry E. Roper, M.D., F.A.C.S.
D. Alan Chandler, M.D.
Malcolm Magovern, M.D.
Mary E. Price, M.D.
Herbert Wiesinger, M.D.
Donald W. Lumpkin, O.D.

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- Interactive Clinical Section concerning eye disease and physical findings
- Clinical Trials Database

Innsbrook Office

4600 Cox Rd
 Suite #120
 Markel Plaza
 Glen Allen, VA 23060
 270-0330

Stony Point Office

8700 Stony Point Pkwy.
 Suite #140
 330-3333

Mechanicsville Office

7016 Lee Park Road
 Hanover Outpatient
 Center
 Mechanicsville, VA
 23111
 730-2250

Southside Office

10800 Midlothian Trnp.
 Suite #127
 Winchester Building
 Richmond, VA 23235
 897-1510

East Henrico Office

4364 S. Laburnum Ave.
 Laburnum Park Shop-
 ping Center
 Richmond, VA 23231
 236-9900

Satellite Office

Williamsburg, VA
 270-0330

Ophthalmology Update

Editor:
D. Alan Chandler MD

Uveitis Masquerade Syndromes

A uveitis masquerade syndrome is an ocular disorder presenting as an intraocular inflammatory process, but in fact is a non-inflammatory process. In these cases, the physical findings of uveitis may be secondary to a different initial disorder, or the supposed intraocular inflammation is actually not of inflammatory origin.

Examples of cases where the uveitis is secondary to a different, more significant initial disorder include:

- **Ocular Ischemic Syndrome** - obstruction of the internal carotid artery or ophthalmic artery leads to findings simulating uveitis, including pain and blurred vision.
- **Hypertension with Vascular Obstruction** - severe hypertension with arteriosclerotic disease leads to findings simulating vasculitis or chorioretinitis.
- **Radiation Retinopathy** - ocular exposure to radiation treatment can lead to a vasculitis and uveitis years after exposure.
- **Retinal Detachment** - a chronic retinal detachment leads to findings of a low grade uveitis.
- **Other Causes include** - diabetic retinopathy, hereditary ocular disorders, retinal degenerations, and intraocular trauma or foreign body.

Cases where the supposed uveitis is of non-inflammatory origin are primarily neoplastic conditions, either ocular or systemic.

Malignant uveitis masquerade syndromes include:

- **Hematological Malignancies, such as Leukemia** - including chronic or acute lymphocytic leukemia
- **Lymphoma** - including central nervous system non-Hodgkin's lymphoma. This condition is an especially common cause of the uveitis masquerade syndrome, especially in the elderly and immunosuppressed. There is often a delay in diagnosis of this condition: in one study¹ over 14 months.
- **Metastatic Disease** - including metastatic melanoma and lung carcinoma.
- **Intraocular Malignancy** - including retinoblastoma and melanoma.

A 2001 study in the journal *Ophthalmology*¹ looked at 828 consecutive cases of uveitis in a tertiary ophthalmic center, and found that 5% had a uveitis masquerade syndrome. 2.3% had a malignancy, primarily intraocular lymphoma or leukemia, and 2.7% had non-malignant causes, including ocular vascular diseases and hereditary ocular disorders. In the group with malignancies, 9 of 19 patients died during the 4.5 year follow-up period.

Recognition and awareness of these uveitis masquerade syndromes is essential not only to preserve visual function, but also the life of the patient.

Rothova A, et al. *Ophthalmology* 2/2001; 108:386-399.