**Abstract**

This case report discusses the many ocular manifestations of Multiple Sclerosis (MS), while describing a case of recurrent vitritis in a patient with presumed MS.

**Case History**

Patient demographics:
- 45 year old white female

Chief complaint:
- A defined area of blurred vision/soft focus in the left eye

Ocular/medical history:
- An episode of optic neuritis OS 6 months previously. Medical history is positive for migraine, asthma, shoulder pain, Gastroesophageal reflux disease, allergic rhinitis, dysthemia, hypothyroidism, abnormal papamicolou smear of the cervix and a probable diagnosis of MS.

Medications:
- Propoxyphene 650mg, Zolmitriptan 5mg, Flunisolide Inhaler 250mcg, Naproxen 500mg, Valproic Acid 250mg, Ipratropium Bromide Inhaler 17mcg, Formoterol fumarate Inhaler 12mcg, and Levothyroxine 0.5 mU/L.
- The patient is also taking the following supplements: Garlic oil, Dandelion powder, Nettle capsules, Zinc sulfate, Ascorbic acid, Parsley oil, Calcium, Magnesium, Selenium, Flaxseed, Lecithin, Vitamin B, Ergocalciferol capsules and fish oil capsules.

**Pertinent Findings**

**Clinical:**

Symptoms: no pain or discomfort OU, no dimming of vision OU. Area of 'soft focus' in nasal field of view OS.

VA: 20/20 OD and OS

Pupils: Equal, round, reactive to light with a 1+ afferent pupil defect OS

EOM's: no pain or diplopia

Confrontation fields: Full to finger counting OD and OS

Cover Test: No phoria or tropia

Red Desaturation Test: 100% saturation OD, 85% saturation OS

Slit Lamp Examination:

Lids/Lashes: Clear OU

Sclera/Conjunctiva: White and quiet OU, no circumcular flush OS

Cornea: Clear and intact OU

Iris: Flat and brown OU

Anterior Chamber: Clear and quiet OD, 1+ cells with no flare OS

Angles 4/4 by Van Herrick

Dilated fundus exam using 78D Volk lens and 20D lens with Binocular Indirect Ophthalmoscope

Dilated using 1gtt Tropicamide 1% and 1gtt Phenylephrine 2.5% OU:

Lens: Clear OU

Vitreous: OD: Clear

OS: Area of coalesced snowballs along inferior temporal arcade

Optic Nerve: OD: Healthy rim tissue with no pallor, C/D 0.50

OS: Mild temporal pallor with an intact neuroretinal rim, C/D 0.35, no papillitis

Macula: Flat with clear foveal reflex and no macular edema OU

Vessels: Healthy OD with arterial-venous ratio of 2/3 OU, small area of venous sheathing under area of snowballing OS

Periphery: Flat with no holes or tears OU, no snowbanking OU

Small area of venous sheathing superior periphery OS

IOP:

OD: 17mmHg

OS: 16mmHg @ 9:40am using contact tonometry
Humphrey Visual Field 30-2:
OD: Full field
OS: Small scotoma in the nasal field above the horizontal midline

D-15 Color Vision Test: No color vision defect OD or OS and no difficulty completing test OS

Physical:
- Lumbar Puncture: 7/21/09 showed five oligoclonal bands. OGB's have high sensitivity (>90%) but modest specificity (~60%) for MS.
- Slight weakness of the left hand per neurologist's findings June 2010.
- Chest x-ray 08/04/2009 was clear.

Laboratory studies:
ESR: Aug 10 – 12mm/hr (normal range: 0-20)
CBC with diff: Aug 10 – normal
ACE: Aug 10 – 32 U/L (normal range: 9-67)
ANA: Aug 10 – negative
CRP: Aug 10 – 9.91mg/L (normal range: 0.00-7.43)
RPR Screen: Aug 10 – Non reactive
HLA B27: Aug 10 – Negative
Lyme AB Serum: Aug 10 – Negative
CRP: Jan 20 – 9.03mg/L (normal range: 0.00-7.43)
ESR: Jan 20 – 14mm/hr (normal range: 0-20)
CBC with diff: Jan 20 – normal
ESR: Dec 07 – 13mm/hr (normal range: 0-20)

Radiology studies:
MRI: 6/16/09 showed at least seven white matter FLAIR hyperintensities in the periventricular and peri-callosal distribution with one juxtacortical. No enhancing lesions.

Differential diagnosis
Primary: Multiple sclerosis with ocular manifestations

Others:
- Idiopathic
- Sarcoïdosis
- Lyme Disease
- Syphilis
- Whipple's disease
- Human T cell lymphotropic virus type 1 associated uveitis
- Intraocular lymphoma

Diagnosis and discussion
Multiple sclerosis is a demyelinating disease which is most common in young adults, affecting females more often than males, with a peak incidence in the 3rd and 4th decades.\(^{13}\) It is more common in Caucasians, particularly whites of northern European decent. The causes of MS are thought to include environmental and genetic factors with a familial recurrence rate of 20%.\(^{10}\) There has also been a question as to whether MS may be linked to viral infection (e.g. measles, mumps, rubella and Epstein-Barr virus).\(^{10}\)
Features and ocular manifestations of MS:
- Lhermitte's symptom (a tingling or electric sensation that occurs in the limbs or spine upon flexing the chin to the chest)
- Uthoff's phenomenon (transient worsening of symptoms when body temperature rises e.g. after a hot shower)
- Optic neuritis which is retrobulbar in 2/3 of cases and clinically evident as papillitis in 1/3 of patients
- Periphlebitis (venous sheathing)
- Pulfrich effect: due to the slower conduction rate of the affected optic nerve which causes a pendulum swinging in one plane to appear to swing in an ellipse
- Diplopia
- Nystagmus
- Internuclear ophthalmoplegia
- Ocular motor palsies with the 6th nerve and 3rd nerve more commonly involved
- Cerebellar eye movement disorder, most commonly saccadic undershoot or overshoot, pendular nystagmus or fixation instability

Uveitis is more common in patients with MS than in the general population, but the percentage of patients with uveitis and MS is not well documented. In a small study looking at 28 patients with MS and uveitis, the most common types of uveitis seen were panuveitis (39.3%) and pars planitis (35.7%), followed by isolated anterior uveitis (14.3%) and then posterior uveitis (10.7%). 39.3% of patients also had retinal periphlebitis. One study found that although the occurrence of uveitis in the MS population is rare, it is 10 times that of the general population. Another study of 60 patients with MS found that 15% had concurrent uveitis. The prevalence of intermediate uveitis in MS has been reported to be between 1% and 16%, and since the prevalence of intermediate uveitis in the general population has been estimated at 1.4 per 100,000, this suggests a definite link between MS and intermediate uveitis. It has been shown that the presence of peripheral retinal periphlebitis in individuals with isolated optic neuritis can predict the subsequent development of MS. However, other types of uveitis have not shown to have any predictive value in the development of MS.

Auto antibodies have been found in uveitis which may develop as a result of the disease, and similar autoantibodies have been identified in MS. Animal studies have used experimental allergic encephalomyelitis antigens to produce an autoimmune state involving both the central nervous system and the uvea simultaneously. It is possible that a similar association between two autoimmune diseases may exist in man, caused by an antigen common to both tissue types.

In this case, the cause of vitritis is most probably MS. This diagnosis is further validated by the presence of white matter lesions on MRI, oligoclonal bands on lumbar puncture, positive Uthoff's phenomenon, slight weakness of the left hand and a prior episode of optic neuritis OS.

Sarcoidosis can be ruled out on the basis of normal serum ACE levels and a clear chest x-ray. Lyme antibody serum testing was negative, and RPR screening was non-reactive making the diagnosis of Syphilis unlikely. The patient does not have any gastrointestinal symptoms making Whipple's disease unlikely. Human T cell lymphotropic virus and intraocular lymphoma are also unlikely causes as no abnormalities were found on CBC and the vitritis completely resolved on two occasions.

Treatment and Management

Treatment options:
- Interferon
- Intravenous methylprednisolone

An advisory committee of the Food and Drug Administration (FDA) has recently recommended approval of Gilenia (Fingolimod/FTY720) for treatment of patients with relapsing multiple sclerosis. This drug is an oral sphingosine1-phosphate receptor modulator which works by retaining lymphocytes in the lymph nodes to prevent them reaching the central nervous system. Normal levels of lymphocytes can again be reached upon discontinuing the treatment. In clinical trials, side effects linked to the drug include elevated liver enzymes, macular edema, hypertension, shortness of breath, bronchitis, diarrhea and bradycardia. Since fewer circulating lymphocytes means less protection against infection and cancer, clinical studies are required to look at long term side effects of the drug.
In this case, the patient has discussed treatment options with her neurologist and decided against any medical treatment for the time being. Interestingly, although there is no evidence to show that topical prednisolone acetate 1% suspension can penetrate to the retina, in this patient we have shown resolution of the snowballs OS on two occasions with the treatment of prednisolone acetate over a two week taper.

**Conclusion**

It is important to remember that although optic neuritis is the most common ocular manifestation of multiple sclerosis, there are many other ways in which the disease can affect the eyes, and all patients with MS should have a thorough ocular examination including binocular evaluation and dilated fundus exam to search for any type of ocular inflammation.
Bibliography


