Multiple Sclerosis

Ellen Yu, M.D.

Case Report

A 44 white female presented with a complaint of floaters on both eyes. There was no blurring of vision, flashes, pain nor photophobia. Past medical and family medical history were non-contributory. Visual acuity was 20/20 for both eyes. Pressures were 16 and 14 for the right and left, respectively. Slit lamp exam revealed +1 cells in the right anterior chamber. The left anterior chamber was quiet with no signs of previous inflammation. Dilated fundus exam revealed +1 vitreous cells in the inferior periphery of both eyes (Figure 1). Fundi were normal. The diagnosis was pars planitis OU with low grade iritis OD. The patient was treated with transeptal and topical steroids. Work-up was negative for any systemic illness. The patient had 3 recurrences of pars planitis over the next five years. On her last attack, the patient came in with 20/60 visual acuity on the right and 20/70 on the left, and was found to have cystoid macular edema. At this time the patient complained of numbness on both hands and shooting sensation down her back on neck flexion.

Figure 1. Dilated eye exam revealed the presence of clumps of cells in the inferior vitreous.

Work-up revealed the following:

- Lumbar puncture

Increased protein and white cells predominantly lymphocytes
Oligoclonal banding

- Cervical Myelogram: normal
- Visual Evoked Response:

Right: mod-severe conduction delay for small pattern stimulus
Left: borderline conduction delay for small pattern stimulus

MRI could not be done because the patient was claustrophobic

Differential Diagnosis

Although an underlying systemic disease is not often found on the initial evaluation in patients

with pars planitis, the following are the differentials when neurologic symptoms are present: Adamantiades-Behcets, multiple sclerosis, sarcoidosis, lyme borreliosis, toxocariasis, and intraocular lymhoma. Although they may present similarly with neurologic symptoms, systemic work-up may help with the diagnosis. The findings noted in the lumbar puncture and visual evoked response points to multiple sclerosis as the systemic disease associated with the ocular inflammation in this case.

Multiple sclerosis (MS) and Pars planitis (PP) The intriguing similarity between MS and PP is the association of both disease entities with the major histocompatibility complex gene HLADR2 and the allele HLADR15. The link between MS and HLADR2 is well established; however, the association of PP and HLADR2 is less firmly established. Incidence

Uveitis is more common in patients with MS than in the general population. Variations in patient population, criteria for diagnosis of MS & uveitis, and examination techniques account for difference in reported incidence in several studies. The incidence of uveitis in general in MS has been reported to be as high as 26.9%. The incidence of MS in patients with uveitis, on the other hand, as high as 14%. The rate of MS with PP is 7.8 to 14%. PP is the most common type of uveitis occurring among patients with MS.

Timing of onset

There is no specific temporal pattern of onset of either MS and PP. MS has been reported to be diagnosed years before, after, or at the same time as PP.

Giles (1970)	1/3 developed MS 3 years after PP
	2/3 developed MS 3-8 years before PP
Zierhut/Foster (1992)	2/7 11-17 years before PP
	3/7 3-7 years after PP
	2/7 diagnosis made with PP

Clinical presentation & findings of pars planitis

Pars planitis has a gradual onset but its course may be chronic. It may be detected accidentally, or the patient may complain of slight blurring of vision or floaters. Although vision is blurred, visual acuity is not markedly impaired, usually not less than 20/40.

Vitreous opacities composed of cells and collagen strands are found most commonly in the inferior periphery (Figure 1). Yellow-white exudates may be found over the ora serrata and/or pars plana.

Macular edema is a common cause of decreased vision (figures 2 & 3). Papilledema, venous dilation & tortuosity, vascular sheathing (Figure 4) and exudation may be found. In severe cases, preretinal or retinal hemorrhages (Figure 5), neovascularization & intravitreal bleeding may be noted.

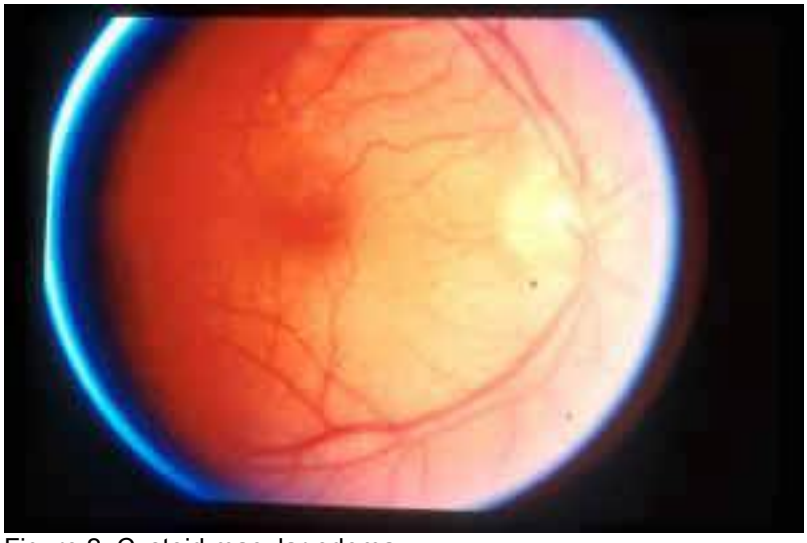

Figure 2. Cystoid macular edema

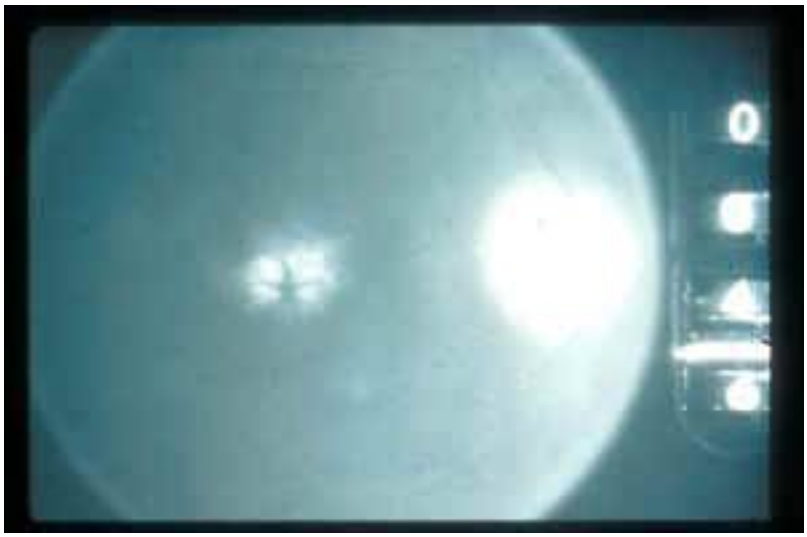

Figure 3. Late phase of fluorescein angiogram of Figure 2 showing dye leakage in a petalloid pattern typical of cystoid macular edema

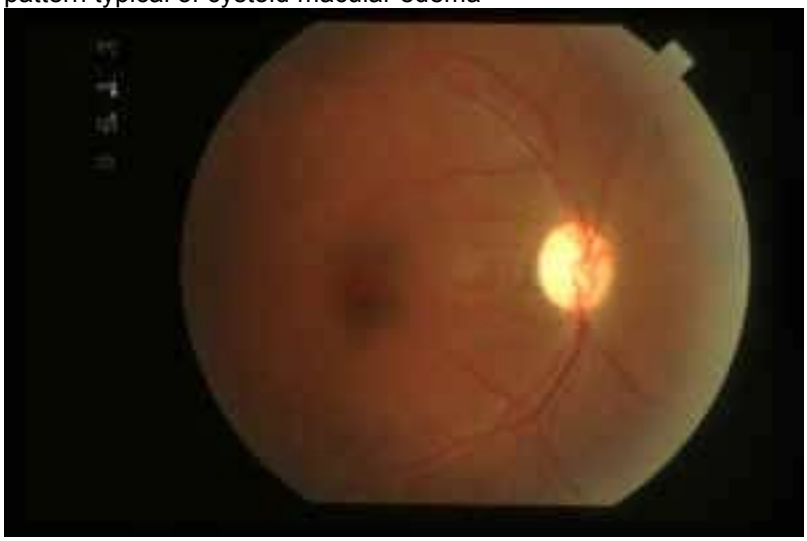

Figure 4. Vascular sheathing of the superior and inferior temporal arcades.

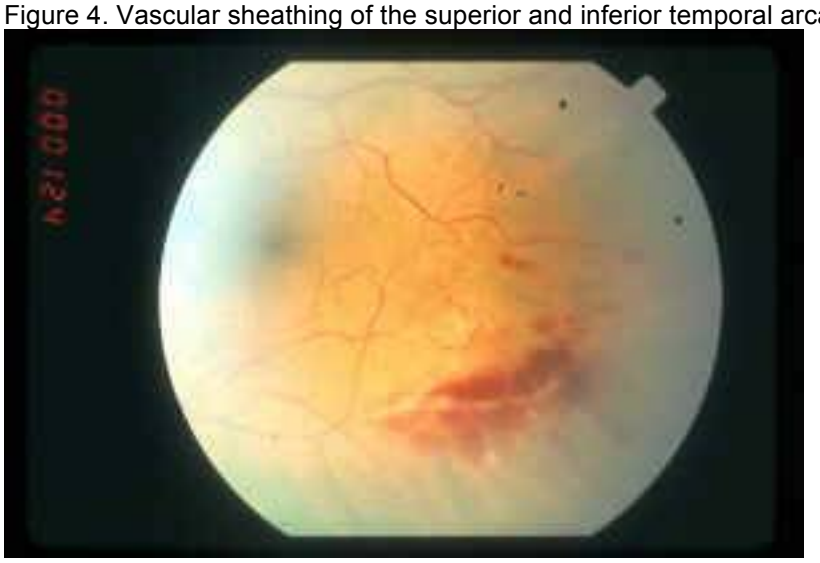

Figure 5. Vascular sheathing and branch vein occlusion in a patient with multiple

The exudates found in the peripheral fundus may be invaded by connective tissue components. Subretinal exudation may occur leading to non-rhegmatogenous retinal detachment. Rhegmatogenous retinal detachment may also occur from breaks occurring at the edge of the membrane.
In a study of patients seen from 1985 to 1990 from the MEEI with pars planitis, the rate of development of complications such as CME, optic disc edema and periphlebitis were the same in patients with and without MS. This may be due to adequate therapy, mostly with immunosuppressives in these patients.

Fluorescein angiogram
Although in most cases the diagnosis of pars planitis can be made from the characteristic clinical findings, fluorescein angiography can help demonstrate the presence of changes in the macular area, disc and retinal vessels which may not be obvious.
Larger retinal veins may show local staining and/or dye leakage but changes in the retinal vessels are not confined to the periphery.

Pathophysiology
Many authors believe that pars planitis is not a primary inflammation of the pars plana but rather a retinal vasculitis involving the veins, i.e. primary peripheral perivasculitis followed by process of vascular occlusion and inflammation leading to vitritis and snow bank formation. Others have hypothesized, however, that it is a primary vitreal inflammation.
Treatment Treatment of pars planitis in multiple sclerosis is similar to treatment of idiopathic pars planitis. Transeptal corticosteroid injections is first in the stepladder approach for patients with active inflammation. Immunosuppressive agents such as methotrexate, azathioprine or cyclosporine may be necessary for persistent or aggressive inflammation. The neurological problem should also be addressed.

Other ocular findings in Multiple Sclerosis
(1) Vascular sheathing
Rucker in 1944 was the first to describe isolated clinical sheathing of the retinal veins in patients with MS. Sheathing is considered to be a result of a chronic form of vasculitis. Since that time, sheathing has been found in as high as 22% of cases.
Vascultits & CNS activity:
Engell et al showed that patients with MS with active periphlebitis in the retina showed significantly more abnormal technetium brain scans than patients with no active retinal vasculature changes. This is thought to be an indication that disruption of the blood-brain barrier and active periphlebitis retinae may occur simultaneously. In a later study, it was shown that periphlebitis in MS is of a recurring nature possibly reflecting the activity of the neurological process. Periphlebitis was found significantly more often in patients with progressive disease than in patients with a benign course.
(2) Retrobulbar neuritis.
The most frequent ocular manifestation of MS is retrobulbar neuritis. According to Lightman et al, an isolated optic neuritis with vascular abnormalities is a risk factor for the development of MS. According to Rizzo & Lessel, more than 50% of patients with optic neuritis will develop MS in 15 years.
On the other hand, optic nerve atrophy appears to protect[2] against inflammation especially vasculitis. This is explained by reduced retinal vascularization, which occurs with atrophy, lessening the chance for immunologic reactions at the vascular endothelium.
(3) Granulomatous uveitis.
The association of multiple sclerosis and granulomatous uveitis (Figure 6) was first observed by Wuseke in 1953. Since then several case series has reported the presence of chronic granulomatous uveitis in patients with MS.

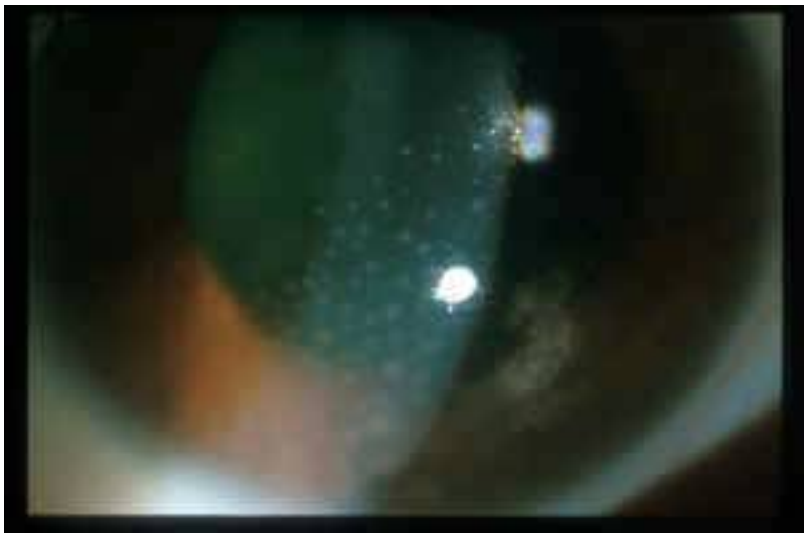
Figure 6. Anterior granulomatous uveitis in a patient with multiple sclerosis.
(1) Posterior uveitis
(2) Panuveitis

Multiple sclerosis: Brief review

Multiple sclerosis is characterized by chronic inflammation with demyelination and scarring. MS is the most frequent cause of neurologic disability in early to middle adulthood aside from trauma. It is more common in females. An autoimmune etiology is suspected and susceptibility increases with the presence of the HLA-DR2 allele.

MS derived its term from the multiple scarred areas in the brain termed plaques. The acute lesion in MS is characterized by perivenular cuffing and tissue infiltration by mononuclear cells predominantly T lymphocytes and macrophages. As the lesion evolves, demyelination occurs, with macrophages and microglial cells scavenging the myelin debris. Proliferation of astrocytes lead to scar formation.

The most common initial symptoms include weakness in one or more limbs, blurring of vision secondary to optic neuritis, sensory disturbances, diplopia and ataxia. CSF abnormalities consist of mononuclear cell pleocytosis, an elevation in the level of total Ig, and the presence of oligoclonal Ig. Evoked response testing may detect slowed or abnormal conduction in visual, auditory, somatosensory, or motor pathways. On MRI, periventricular lesions may be found on T2 weighted MRI brain scans. However, no clinical sign or diagnostic test finding is unique for MS.

Treatment may be for symptomatic management, or focused to arrest the disease with chemotherapeutic drugs, depending on the pattern of MS.

Conclusion

It is important to examine patients with multiple sclerosis thoroughly for any signs of inflammation which may lead to ocular damage. Patients presenting with pars planitis initially should also be followed-up and worked-up thoroughly. Due to the possible delay between the onset of pars planitis and multiple sclerosis, sequential diagnostics should be made.

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Multiple Sclerosis

Erik Letko, M.D.

1. The occurrence of uveitis in patients with multiple sclerosis is:

a) 27%

b) 47%

c) 57%

d) 77%

2. The occurrence of multiple sclerosis in patients with uveitis is:

a) 14%

b) 24%

c) 44%

d) 54%

3. All of the following are likely to cause a decrease in visual acuity in patients with pars planitis EXCEPT:

a) cystoid macular edema

b) retinal vasculitis

c) optic nerve edema

d) cataract

e) vitritis

4. Which gene has been associated with pars planitis and multiple sclerosis?

a) HLA-B15

b) HLA-DR3

c) HLA-DR4

d) HLA-DR2

e) HLA-B27

5. Multiple sclerosis can be diagnosed:

a) before the onset of pars planitis or at the time of onset of pars planitis

b) after the onset of pars planitis

c) at the time of onset of pars planitis or after the onset of pars planitis

d) before the onset of pars planitis, at the time of onset of pars planitis or after the onset of pars planitis

6. Vasculitis associated with pars planitis is most commonly localized to:

a) periphery of the retina

b) periphery of the macula

c) peripapillary retina

d) juxtapapillary retina

7. All of the following are likely to be found in a patient with pars planitis and multiple sclerosis EXCEPT:

a) retinal vasculitis

b) retrobulbar neuritis

c) granulomatous uveitis

d) posterior uveitis

e) peripheral retinitis

f) panuveitis

8. The most frequent ocular manifestation in patients with multiple sclerosis is:

a) pars planitis

b) retinal vasculitis

c) retrobulbar neuritis

d) granulomatous uveitis

e) peripheral retinitis

9. The likelihood that a patient diagnosed with retrobulbar neuritis will develop multiple sclerosis later in life is:

a) 10%

b) 20%

c) 30%

d) 40%

e) 50%

10. The likelihood of developing retrobulbar neuritis in a patient with optic nerve atrophy is:

a) unchanged

b) decreased

c) increased

Correct answers:

1-c, 2-a, 3-b, 4-d, 5-d, 6-a, 7-e, 8-c, 7-e, 8-b