INTERMEDIATE UVEITIS AND PARS PLANITIS

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All about the Eye

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Intermediate Uveitis and pars planitis

1. Describe signs and symptoms, management of pars planitis. D2010
2. Discuss pathogenesis, clinical features, diagnosis, differential diagnosis and management of intermediate uveitis. D2012
3. Clinical features and management of intermediate uveitis. 4+6 D2016
4. Pars planitis. (2005) (2000) (1999)

Introduction

- SUN Working Group defines intermediate uveitis as the subset in which the predominant site of inflammation is in the vitreous.
- This subset accounts for up to 15% of all cases of uveitis.
- Intermediate uveitis is characterized by ocular inflammation concentrated in the vitreous and the vitreous base overlying the ciliary body and peripheral retina– pars plana complex.
- Inflammatory cells may aggregate in the vitreous ("snowballs"), where some coalesce.
- In some patients, inflammatory exudative accumulation on the inferior pars plana ("snowbanking") seems to correlate with a more severe disease process.
- There may be associated peripheral retinal phlebitis.
- Anterior chamber reaction of varying severity may also occur.
- Intermediate uveitis can be associated with various conditions, including

sarcoidosis, peripheral toxocariasis	multiple sclerosis syphilis	Lyme disease tuberculosis	primary Sjögren syndrome Infection with human T-cell lymphotropic virus type 1 (HTLV-1).

Pars Planitis

1. The term pars planitis refers to the subset of intermediate uveitis in which snowbank or snowball formation occurs in the absence of an associated infection or systemic disease.
2. It is the **most common form of intermediate uveitis**, constituting approximately 85%–90% of cases.
3. Previously also known as chronic cyclitis and peripheral uveitis.
4. The condition most commonly affects persons aged 5–40 years.
5. It has a bimodal distribution, concentrating in younger (5–15 years) and older (20–40 years) groups.
6. No overall sex predilection is apparent.
7. The pathogenesis of pars planitis is not well understood but is thought to involve autoimmune reactions against the vitreous peripheral retina, and ciliary body.

Clinical characteristics

1. Approximately 80% of cases of pars planitis are **bilateral**, which can often be **asymmetric** in severity.
2. **In children**, the initial presentation may consist of significant anterior chamber inflammation accompanied by redness, photophobia, and discomfort.
3. The onset **in teenagers and young adults** may be more insidious, with the presenting complaint generally being floaters.
4. Ocular manifestations include a variable number of **anterior chamber inflammatory cells, vitreous cells, snowballs and pars plana exudates.**
5. Inferior peripheral **retinal phlebitis** with retinal **venous sheathing** is common.
6. With long-standing inflammation, **CME** often develops; this condition becomes chronic and refractory in approximately 10% of patients and is the major cause of vision loss.
7. Ischemia from retinal phlebitis, combined with angiogenic stimuli from intraocular inflammation, can lead to **neovascularization** along the inferior snowbank in up to 10% of cases.
8. These neovascular complexes can result in **vitreous hemorrhages**, more common in children than adults; they also may contract, leading to **peripheral tractional and rhegmatogenous retinal detachments**.
9. Retinal detachments occur in 10% of patients with pars planitis.
10. In rare cases, the complexes evolve into **secondary peripheral retinal vasoproliferative tumors**- vascular masses with exudative retinopathy and minimally dilated vessels-years after the initial diagnosis.
11. With chronicity, **posterior synechiae and band keratopathy** may also develop.
12. Other possible causes of loss of vision include **cataracts, epiretinal membrane, and vitreous opacification**.

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Differential diagnosis

- The differential diagnosis of pars planitis includes syphilis, tuberculosis, Lyme uveitis, sarcoidosis, intermediate uveitis associated with MS, and toxocariasis.
- Lyme and syphilitic uveitis may simulate any anatomical subtype of uveitis.

1. Lyme uveitis	Measurement of Lyme antibody titers may be particularly useful in regions where the disease is endemic, especially in the presence of cutaneous and articular disease
2. MS	Anterior and intermediate uveitis may occur in up to 20% of patients with MS
3. Sarcoidosis	associated uveitis presents as an intermediate disease in 7% of cases
4. Toxocariasis	A peripheral granuloma such as that seen in toxocariasis can mimic the unilateral pars plana snowbank in a child and should be ruled out. Serologic testing can be helpful in these cases
5. 1℃NS lymphoma	Vitritis without other ocular findings can be suggestive of primary central nervous system (CNS) lymphoma These patients are generally much older at presentation than patients with pars planitis, usually in their sixth decade of life or older
6. FUS	Fuchs heterochromic uveitis can produce mild to dense vitritis but has characteristic KPs and iris heterochromia.

Ancillary tests and histologic findings

- Diagnosis of pars planitis is made according to classic clinical findings.

Laboratory workup	To exclude other causes of intermediate uveitis, including sarcoidosis, Lyme disease, and syphilis. Measurement of serum angiotensin converting enzyme (ACE) and Lyme antibody titers, chest imaging, and syphilis serology testing can be considered.
FA	Fluorescein angiography may show diffuse peripheral venous leakage, disc leakage, and CME.
UBM	UBM may be used in the case of a small pupil or dense cataract to demonstrate peripheral exudates or membranes over the pars plana.
Histologic examination	In eyes with pars planitis shows vitreous condensation and cellular infiltration in the vitreous base. The inflammatory cells consist mostly of macrophages, lymphocytes, and a few plasma cells. Pars planitis is also characterized by peripheral lymphocytic cuffing of venules and a loose fibrovascular membrane over the pars plana.

Prognosis

- The clinical course of pars planitis may be divided into **3 types**.

Approximately 10%	self-limiting, benign course
30%	a smoldering course with remissions and exacerbations;
60%	have a prolonged course without exacerbations

- Pars planitis may remain active for many years.
- In some cases, the disease "burns out" after a few years.
- If CME is treated until resolution and kept from returning by adequate control of inflammation, the long-term visual prognosis can be good, with nearly 75% of patients maintaining visual acuity of 20/40 or better after 10 years.

Treatment

A. Medical management

I. Treat underlying cause if known

- Therapy should be directed toward treating the underlying cause of the inflammation, if possible. For example, infectious causes such as Lyme disease, tuberculosis, and syphilis should be treated with appropriate antimicrobial drugs.
- If an underlying condition is not identified, as in pars planitis, or if therapy of an associated condition consists of nonspecific control of inflammation, as in sarcoidosis, anti-inflammatory therapy should be implemented.

II. Corticosteroids

- Corticosteroids, oral or periocular, **usually constitute the first line of therapy.**

a) Periocular depot corticosteroid injections

1. Of triamcinolone or methylprednisolone may be given using the posterior sub-Tenon or orbital floor route.
2. Local treatment with corticosteroid injections is a particularly appealing approach in unilateral cases.
3. These can be repeated as frequently as every 3–4 weeks.
4. In the majority of cases, the inflammation responds and the CME improves; however, some cases prove recalcitrant and CME may recur.

5. Patients, especially those with a history of glaucoma, must be carefully monitored for corticosteroid-induced IOP elevation.
6. Other complications of periocular corticosteroids include aponeurotic ptosis, fat prolapse, enophthalmos, and, in rare instances, globe perforation.
7. Cataract formation can occur with any form of corticosteroid therapy.

b) Intravitreal triamcinolone injections

1. Intravitreal triamcinolone injections may be an alternative to periocular injections in refractory cases.
2. These injections carry risks of sustained IOP elevation and glaucoma and very small risks of retinal detachment, vitreous hemorrhage, and endophthalmitis.
3. Injections should be administered away from areas of snowbanking and areas with peripheral retinal pathology.

c) Systemic corticosteroid therapy

1. Systemic corticosteroid therapy may also be used, especially in severe or bilateral cases.
2. Patients may be treated with an initial dosage of 1–1.5 mg/kg/day, with gradual tapering every 1–2 weeks to dosages of less than 10 mg/day.

III. IMT

1. As with all autoimmune uveitis, if corticosteroid therapy fails or long-term use of high doses of corticosteroids are needed to control the inflammation, immunomodulatory treatment is indicated.
2. Systemic immunomodulatory drugs such as antimetabolites (eg, methotrexate, azathioprine, mycophenolate mofetil), T-cell inhibitors (eg, cyclosporine, tacrolimus), biologic agents (eg, TNF inhibitors, interferon), and alkylating drugs (eg, cyclophosphamide, chlorambucil) can be considered.
3. Several reports from the Systemic Immunosuppressive Therapy for Eye Diseases (SITE) cohort study indicated that cyclosporine, azathioprine, and mycophenolate mofetil were effective in achieving sustained control of inflammation in 70%–80% of patients with intermediate uveitis.
4. It should be remembered that anti-TNF therapy can exacerbate MS and therefore should be avoided in patients with MS-associated intermediate uveitis.

B. Laser , cryotherapy, intravitreal anti VEGF

- Alternative therapies for pars planitis include peripheral ablation of the pars plana snowbank with cryotherapy and/or indirect laser photocoagulation to the peripheral retina.

1. **Cryotherapy** is rarely used at present because of concerns about further inducing inflammation.
2. **Laser photocoagulation** can be used in cases of retinal ischemia and neovascularization to prevent vitreous hemorrhage; it does not seem to increase the risk of rhegmatogenous retinal detachment.
3. **Intravitreal anti-VEGF treatment** can also be used for retinal or choroidal neovascularization in pars planitis in otherwise quiet eyes.

C. Surgical management

1. **Pars plana vitrectomy**, with or without laser photocoagulation, can also be helpful in treating complications of pars planitis or in cases recalcitrant to IMT.
2. In such cases, a perioperative increase in systemic immunosuppression and/or corticosteroids should be considered.
3. Pars plana vitrectomy may be necessary to treat severe vision loss caused by vitreous hemorrhage or traction, retinal detachment, or epiretinal membrane.
4. It can also be considered for cases with significant vitreous opacities despite adequate IMT.
5. In cases involving epiretinal membrane or vitreomacular traction, separation of the posterior hyaloid membrane during vitrectomy may have a beneficial effect in reducing CME.
6. Potential complications include retinal detachment, endophthalmitis, and cataract formation.

Complications

- Complications of pars planitis include cataract, glaucoma, CME, retinal neovascularization, vitreous hemorrhage, and tractional or rhegmatogenous retinal detachment.

1. Cataract	Cataracts occur in up to 60% of cases. Cataract surgery with IOL implantation may be complicated by smoldering low-grade inflammation; recurring opacification of the posterior capsule despite capsulotomy; recurrent retrolental membranes; and chronic CME, even in cases in which there is no active cellular inflammation. Combining pars plana vitrectomy with cataract extraction and IOL implantation may reduce the risk of these complications.
2. Glaucoma	both angle-closure and open-angle—occurs in approximately 10% of patients with pars planitis
3. CME	may occur in 50% of patients with intermediate uveitis and is a hallmark of pars planitis
4. Neovascularization	NV of the retina, disc, and peripheral snowbank has been reported.
5. Vitreous hemorrhage	Occasionally, VH is the presenting sign of pars planitis, especially in children; it can be treated effectively with pars plana vitrectomy
6. TRD, RRD	Occur in up to 15% of patients and require scleral buckling, sometimes combined with vitrectomy. Risk factors for RRD include severe inflammation, use of cryotherapy at the time of a vitrectomy, and neovascularization of the pars plana snowbank.

Multiple Sclerosis

- Uveitis is 10 times more common in MS patients than in the general population.
- The frequency of uveitis in patients with MS is reported to be as high as 30%, and the onset of uveitis may precede the diagnosis of MS in up to 25% of patients and by 5–10 years.
- MS usually affects white women 20–50 years of age, and intermediate uveitis is the most common manifestation of MS-associated uveitis.
- Up to 95% of cases are bilateral.
- Up to 15% of patients with pars planitis may eventually develop MS.
- Intermediate uveitis appears to be of milder severity in MS than in idiopathic cases.
- Macular edema is less common.
- Most patients develop mild vitritis with periphlebitis.
- Periphlebitis in MS is not clearly related to optic neuritis, systemic exacerbations, or disease severity.
- The immunopathogenesis of MS is not well understood but appears to involve humoral, cellular, and immunogenetic components directed against myelin.
- HLA-DR15 appears to be associated with the combination of MS and uveitis.
- Immunocytologic studies have shown some cross-reactivity between myelin-associated glycoprotein and Müller cells.
- It is unclear whether treatment of MS with interferon has any effect on intermediate uveitis; however, reports of macular edema associated with fingolimod therapy for MS are of interest.
- As biologic therapies for uveitis become more common, it is particularly important to consider the possibility of MS in any patient who presents with intermediate uveitis or pars planitis, as anti-TNF drugs have been associated with exacerbations of MS