Serpiginous Choroiditis: An Update

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G eographic Helicoid Peripapillary Choroidopathy (GHPC) is a rare, usually bilateral, chronic, progressive and recurrent disease of unknown aetiology affecting the retinal pigment epithelium, choriocapillaris and choroid. It characteristically starts at the juxtapapillary or peripapillary region and progresses centrifugally from the disc to involve the macula area¹,²,³ It is also known as serpiginous choroiditis because of its peculiar extension in a serpiginous fashion. The disease has a relentless destructive course. As the lesions resolve, retinal pigment epithelial and choroidal degeneration begin, leading to fibrous scarring and pigment hyper or hypoplasia.¹⁻⁶ Subretinal neovascular membrane (SRNVM) formation may occur after a chronic course.⁷⁻¹⁰ On rare occasions, serpiginous choroiditis may present initially as lesions involving the macula exclusively.¹¹,¹²

The word “serpiginous” is an adjective which means “with a wavy or indented margin”. The serpiginous choroiditis shows the similar wavy or amoeboid like lesions in choroid as a result of inflammation of unknown aetiology. Jonathan Hutchinson first described this entity in 1900 in Archives of Surgery. This clinical entity was first reported by Junius in 1932 who termed it as “peripapillary retinochoroiditis”. Thereafter, this clinical entity has passed through various nomenclatures by various authors (Table 1). The term “serpiginous choroidopathy” was coined by Gass in 1987.

Serpiginous choroiditis is a rare cause of posterior uveitis, usually less than 5% in most of the studies from the world¹¹. However, it has been reported in various studies that the incidence of serpiginous choroiditis is higher in India (Table 2).¹⁴,¹⁵,¹⁶,¹⁷ The disease affects healthy, young to middle aged adult with higher male predominance. Though there is no familial predisposition, in one study the clinical entity was found to be associated with HLA B7.¹⁸

Table 1: Different nomenclatures of Serpiginous choroiditis by various authors

- Peripapillary choroidal sclerosis by Sorsby, 1939
- Helicoid peripapillary chorioretinal degeneration by Franceschetti, 1962
- Geographic helicoids peripapillary choroidopathy by Schatz, 1974
- Geographic choroiditis by Baarsma, 1976
- Serpiginous choroidopathy by Gass, 1987
Aetiopathogenesis

The etiology of serpiginous choroiditis is unknown. Association of various infective agents has been implicated in aetiopathogenesis of this clinical entity. A role of possible viral aetiology has been suggested by Gass et al. who reported a case of serpiginous choroiditis following Herpes zoster. Priya et al. reported that two-thirds of aqueous humor samples from patients with serpiginous choroiditis in their study were positive for varicella zoster virus (VZV) or herpes simplex virus (HSV) using the polymerase chain reaction. Gupta et al. reported seven cases of ocular tuberculosis who presented with serpiginous choroiditis and showed considerable improvement in terms of visual acuity and clinically, when treated with antitubercular drugs. Laatikainen and Erkkila reported nine patients with serpiginous choroiditis and all of them had positive tuberculin skin tests. With advent of newer diagnostic tests like interferon (IFN-γ) release assays-QuantiFERON TB gold tests, the diagnosis of tubercular infection has become easier and more accurate. With the help of this test, Friederike et al. reported that 11 of 21 serpiginous choroiditis patients (52%) were tested positive in their study, indicating a tuberculous etiology in this uveitis entity. There are also reports of an immune-mediated mechanism attributable to HLA-B7 and retinal S antigen associations. An elevation of factor VIII-von Willebrand antigen has been found in a small series of patients.

Histopathogical Features

The characteristic finding of the lesions in serpiginous choroiditis are atrophy of the choriocapillaries, retinal pigment epithelium and photoreceptors. Among them most affected structures are choriocapillaries, which appear acellular. The larger choroidal vessels are generally spared. Lymphocytic infiltrates are seen near the margins of the lesions.

Clinical Pictures

Serpiginous choroiditis is a bilateral condition with asymmetric involvement of the eyes. The patient typically presents with unilateral decrease in vision, photopsias, metamorphopsia, and visual field loss. On examination, the anterior segment is usually normal. If present, the vitritis is mild and most often in the form of pigmented cells in anterior vitreous. Serpiginous choroiditis involves the peripapillary region and macula. Recurrences are common and can occur weeks to years after the initial event. Depending on the extent of lesions, serpiginous choroiditis can be divided in to the following types:

Classic or Peripapillary Geographic Serpiginous choroiditis

Classic or Peripapillary Geographic variety accounts for 80% cases of serpiginous choroiditis. The lesion begins with ill-defined patches of grayish or creamy yellow subretinal infiltrates which starts at the peripapillary area and progresses towards the periphery like a serpentine in a centrifugal manner (Figure 1,2). The overlying retina is secondarily involved and becomes oedematous. Though rare, sometimes serous exudative detachment can occur. The active lesions generally resolve within 6-8 weeks with or without treatment, ultimately leaving behind areas of choriocapillaries and retinal pigment epithelium atrophy. Many a time, the disease remains asymptomatic until the fovea is affected. It has been seen that about two third of patients with serpiginous choroiditis may present with scars or healed lesions at the time of initial presentation.

Macular Serpiginous choroiditis

Macular variety, accounts for 5.9% cases of total serpiginous choroiditis cases. The lesion begins in the macular area and is characterized by worse visual prognosis due to foveal involvement and higher risk of secondary CNVM. This variety of serpiginous choroiditis often remains under-diagnosed or misdiagnosed.

Ampiginous Choroiditis

This is a rare variety of serpiginous choroiditis where the lesions generally occur in periphery in a multifocal pattern. Ampiginous

Table 2: Reported incidence rate of serpiginous choroiditis in various Indian studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Incidence Rate</th>
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<tbody>
<tr>
<td>Biswas et al (1997)</td>
<td>19%</td>
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<tr>
<td>Gupta et al (2001)</td>
<td>25.1%</td>
</tr>
<tr>
<td>Rathinam et al (2001)</td>
<td>10.9%</td>
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<tr>
<td>Das et al (2005)</td>
<td>15.21%</td>
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choroiditis was first reported by Lyness and Bird in 1984, who described a recurrent form of acute posterior multifoc al placoid pigment epitheliopathy (APMPPPE) that resembles serpiginous choroiditis in its bilateral nature, fluorescein angiographic features, resultant pigmentary disturbances and the recurrent clinical course. The term “Ampiginous Choroiditis” was coined by Nussenblatt et al. Compared to the classic variety of serpiginous choroiditis, there is no significant difference in anterior segment inflammation, vitritis in Ampiginous Choroiditis. However the central foveal involvement is less in Ampiginous Choroiditis.

Ancilliary Tests

Fundus fluorescein angiography: FFA shows early hyperfluorescence of the active lesions. The late phase of the study demonstrates hyperfluorescence of the border of the active lesion that may extend centrally (Figure 7). Inactive lesions show early hyperfluorescence and progressive hyperfluorescence with late staining of the sclera and scar tissue.

Indocyanine Green angiography: ICG is often more sensitive than FFA in determining extent and appearance of new subclinical lesions. Some authors reported that the lesions which were not apparent on FFA can be detected with the help of ICG. Also ICG shows larger area of hypofluorescence in active lesions than seen clinically or on FFA. ICG in serpiginous choroiditis shows hypofluorescent areas beginning from early to late phase indicating non perfusion of the choriocapillaries and often areas of delayed filling, indicating late perfusion of the choriocapillaries.

Visual fields & Electrophysiological Studies: Visual field shows absolute or relative scotomas corresponding to the lesions. Electrophysiologic studies are usually normal.

Differential Diagnosis: Though serpiginous choroiditis is easy to diagnose from its characteristic lesions and pattern of involvement, few conditions which affect choriocapillaries like variety of macular lesions, that can mimic this variant form of serpiginous choroiditis. These include age-related macular degeneration, idiopathic subretinal neovascularization, idiopathic central serous retinopathy with exudation, retinal pigment epithelitis, posterior scleritis, toxoplasmic retinitis, presumed ocular histoplasmosis syndrome, tuberculosis,
sarcoidosis, acute multifocal posterior placoid pigment epitheliopathy (APMPPE) and viral diseases. It is differentiated from serpiginous choroiditis for similar clinical and angiographic pictures as their management differs significantly.

**Treatment**

Depending on the various proposed theory of aetiopathogenesis, several treatments have been tried for serpiginous choroiditis.

Systemic corticosteroids are found to be effective in controlling the active lesions and shortening the duration of active diseases, but their role in prevention of recurrence is doubtful. Serpiginous choroiditis has been reported to recur while tapering and discontinuation of systemic corticosteroids thereby emphasizing the role of long term corticosteroids therapy. However in cases of fovea-threatening lesions, aggressive rapid control of the inflammation is needed as it has been reported that the response of serpiginous choroiditis to oral steroids occurs after two weeks of treatment.

So, high-dose intravenous steroid therapy (1g intravenous methylprednisolone daily for three days) is recommended by many authors for macula-threatening cases of serpiginous choroiditis. There are also reports of intravitreal Triamcinolone Acetate (IVTA) therapy in serpiginous choroidopathy. IVTA was also used in cases where systemic corticosteroids were contraindicated and in a case of secondary choroidal neovascular membrane. It has been observed that though IVTA injection brings in the required concentration of the drug without systemic side effects to the desired tissue level and likely to be effective in the treatment of acute lesions, but it is not helpful in preventing recurrence of the disease.

The spectrum of alternative therapies to systemic corticosteroid treatment ranges from immunosuppression with cyclosporine alone or as part of a regimen with immunosuppressives and most of the study using these agents showed mixed result. Christmas et al reported 4 out of 6 patients with serpiginous choroiditis in their study, who were treated with cyclosporine alone or combined with azathioprine experienced a recurrence while on therapy.

A triple-agent immunosuppressive regimen using cyclosporine (5mg/kg/day initially) in combination with azathioprine (1.5mg/kg/day) and prednisone (1mg/kg/day) was first reported by Hooper and Kaplan in 1991. Treatment was tapered 8 weeks after initiation and discontinued after 6 months, when no recurrence was encountered. However, as the medications were weaned, recurrence of the inflammation developed in two patients. Munteau et al also reported satisfying results with this triple-agent therapy. Although prompt control of the inflammation on initiation of treatment was achieved, recurrence of inflammation after discontinuation of treatment has been reported in some studies. Also, Biswas et al reported that there was no significant change in the rate of regression of lesions in their study when this regimen was compared to the treatment with azathioprine or corticosteroids alone.

There are also reports of use of Interferon Alpha used in management of Serpiginous choroiditis. Sobaci et al reported of successfully treating 8 eyes of 5 patients with IFN alpha-2a, but they could...
not explain the mechanisms by which IFN affects the course of Serpiginous choroiditis.

Continued progression of choroiditis lesions occurred in 14% of patients after initiating antituberculosis treatment in tubercular serpiginous-like choroiditis. Increased immunosuppression with continuation of antituberculosis treatment resulted in good outcome.43 Serpiginous choroidopathy was seen in young patients and had three distinct presentations that seemed to affect the choriocapillaris primarily. Patients appeared to have a variation of serpiginous choroidopathy, typical of the Asian-Indian population, that had some important differences from that reported in Caucasians.44

Prompt diagnosis and rapid initiation of treatment of active lesions with immunosuppression and maintenance of appropriate immunosuppression for at least 6 months is essential for initial management and prevention of recurrences in Serpiginous choroiditis.

References
44. Clinical characteristics of serpiginous choroidopathy in North India. AJO, Volume 134, Issue 1, Pages 47-56, July 2002

About the Authors

Dr Alok Agrawal graduated from India in 2003. After his undergraduate degree he went and did a long-term observership in different eye hospitals in USA. He received his Postgraduate degree from India in 2008 and PhD in Ophthalmology in 2011. He did his long term fellowship training in Uveitis in 2008 at Sankara Nethralaya, India and has acquired a wealth of experience in managing patients with a variety of complex ocular inflammatory diseases after doing another International Clinical Fellowship in Ocular Immunology & Inflammation Services from Singapore National Eye Center, Singapore in 2010.

His research interests are mainly in Vogt-Koyanagi Harada Disease, Cytomegalovirus infection in the immunocompetent. Dr Alok's other passion is in uveitic cataract surgery. Dr Alok is member of various eye societies and has numerous publications in peer review journals. He is actively involved in research and has given talks in various conferences globally.

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