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Central Serous Chorioretinopathy: A Literature Review

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Abstract: **Central serous chorioretinopathy is one of the most common causes of unilateral mild to moderate vision loss seen in middle age groups. It is characterized by fluid accumulation under the retina which usually resolves spontaneously but recurrent cases may require further interventions to manage the condition. There are various management options available to help cope with the condition, out of which half dose PDT and Argon laser photocoagulation remain the mainstay. This article is a literature study which is carried out via credited databases, to include the clinical and management aspects of central serous chorioretinopathy. It discusses the various risk factors, differential diagnosis and also the medical and surgical management options that are available around the globe to manage the condition.**

***Index Terms*— Central Serous Chorioretinopathy, CSCR, chorioretinopathy, choroidal neovascularization, retinal detachment, retinal degeneration**

I. INTRODUCTION

Central serous chorioretinopathy (CSCR) is a chorio-retinal condition which is caused by accumulation of fluid under the retina. However, chronic cases may present with intra-retinal fluid as well. The fluid accumulation is due to leakage from the choroid through the retinal pigment layer (RPE) - blood retinal barrier. It mainly is seen to affect men with age of onset ranging from as early as 7 years to as late as 83 years. However, the peak age is seen to be around 40-50 years [1]. Men have 6 times higher chances of getting CSCR than women. However, there is no significant difference in the prevalence of the condition in different races.

Most patients complain of distorted vision or even central vision loss. Hyperopic shift, micropsia, central scotoma, metamorphosia, reduced colour and contrast sensitivity are the other common symptoms seen in these patients. CSCR is a self-limiting condition and hence holds a good prognosis and shows good recovery within a period of 3 months. However, the rate of recurrence is seen to be about 50% within a period of 1 year [2].

The exact etiology and the mechanism of the formation of CSCR is not exactly known however, there are some theories behind the cause. It is assumed to occur because of hyper-permeability of the choroidal vessels in addition to retinal pigment epithelium dysfunction which leads to leakage and accumulation of mostly clear fluid under the retina causing a serous detachment of the neuro-sensory retina.

II. RISK FACTORS AND ASSOCIATIONS

A. *Steroids:* The patients with a history of steroid use are seen to be on a higher risk as shown by many studies. There seems to be a strong association of the condition with steroids. Steroids are seen to potentiate vasospasm which is mediated by epinephrine and thus causes an increase in the permeability of the choroidal vessels. The level of cortisol in patients with CSCR was seen to be higher than the control group in the study carried out by Garg and colleagues in patients with CSCR [3].

B. *Helicobacter Pylori*: Many CSCR cases are seen to be associated with H.Pylori infection. In about 53% cases with CSCR, H.Pylori infection was seen to be present [4]. It has been demonstrated that treating this infection causes rapid reabsorption of the sub retinal fluid, helping resolution of the disease [5].

C. *Hypertension:* Hypertension is seen to be linked with CSCR. During physically stressful situations, CSCR patients have shown rapid and easy increase in blood pressure. This is mainly due to lack of sufficient functioning of the compensatory mechanism in the choroidal vessels [6].

D. *Psychological Factors:* Patients with obsessive compulsive disorder, Type A personality and who are very competitive, high achievers and under continuous stress have shown to be associated with CSCR [7].

E. *Other Drug Association*: MDMA, Sildenafil, Topiramate, Soradenib, Vermurafenib

F. *Other Associations:* Smoking, Peptic ulcer disease, pregnancy, sleep apnoea syndrome, premature ejaculation.

III. DIFFERENTIAL DIAGNOSIS

A. Polypoidal choroidal vasculopathy
B. Choroidal tumor
C. Neovascular age related macular degeneration
D. Myopic choroidal vasculopathy
E. Hypertensive choroidopathy
F. Retinal venous occlusion
G. Leukemic choroidal infusion
H. Posterior scleritis
I. Vogt-Koyanagi-Harada syndrome
J. Multiple myeloma Choroidopathy
K. Rhegmatogenous retinal detachment

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IV. Clinical Diagnosis

A. History

A thorough history can help narrow down and rule out many differentials and aid reaching diagnosis confidently. The risk factors like steroid use, smoking, hypertension, Helicobacter pylori infection etc. should be asked for specifically. In chronic cases, it is important to check for Cushing's disease. Knowing the causative/risk factors can help tremendously in planning suitable management for the patient. The clinical signs and symptoms should be correlated with the medical history to reach the provisional diagnosis.

B. Clinical Examination

The visual acuity in CSCR cases can range from 20/20 to 20/200. They may present with relative afferent pupillary defect (RAPD), decrease in colour and colour saturation. Direct ophthalmoscopy will show a round serous macular detachment without hemorrhages or small yellow deposits called drusens. The sub-retinal fluid is usually clear but may be greyish white due to accumulation of serofibrinous exudates. Mottling of the retinal pigment layer can be seen in chronic or recurrent CSCR cases [8].

C. Diagnostic Tests

Optical Coherence Tomography (OCT) in CSCR patients usually shows a thick choroid. RPE detachment is seen in 63% of the eyes on an OCT. OCT scan is valuable in not only diagnosing patients with CSCR but also allows us to monitor them effectively [9]. Fundus Fluorescein Angiography (FFA) is required to rule out other possible causes. An early phase of FFA shows hyper-fluorescent demarcation in the sub-retinal space. Hyper-fluorescent ink blots are seen at the site where the dye leaks. The leak then expands vertically, giving a smoke stack appearance. In the late phase, the dye starts expanding laterally towards the sides at the top of the sub-retinal cavity in an umbrella or mushroom like manner. The mechanism of this is unclear but gravitational effect of the fluid has been hypothesized to be the likely cause resulting in a comet tail appearance [10]. OCT and FFA are usually sufficient to confirm the diagnosis. However, Fundus Auto-fluorescence (FAF) and Indocyanine Green (ICG) can also be performed additionally. FAF provides functional images as damaged photoreceptors are hyper-fluorescent due to the buildup and accumulation of lipofuscin allowing to see effects of chronic CSCR. An ICG shows hyper-permeability of choroidal vessels in the late phase.

V. Managment

A. Risk Factor Modifications

Once the risk factors are identified, the first step of management would be risk factor modifications in order to prevent recurrent episodes of the condition. It is important to keep the blood pressure under check and monitor patient compliance with the medications. Weight reduction in patients with high BMI can also help hence, regular exercises should be encouraged. If patient is a smoker, offering services like smoking cessation clinics can help patients to quit smoking. Steroids should ideally be discontinued if possible, however if discontinuation is not possible, the dose of the steroids should be reduced to help resolve the CSCR.

B. Observation

As CSCR is a self-limiting condition and usually resolves within 2-3 months by itself, observation is the standard care for the patient presenting with 1st episode of CSCR. Studies have shown that majority of the patients resolve spontaneously and only observation is needed to keep it under check. Surgical and medical intervention is generally required for recurrent, chronic or severe acute cases.

C. Surgical Intervention

a) Laser Photocoagulation:

Persistent visual defects and lack of resolution of sub-retinal fluid indicates a need for alternative therapies like laser photocoagulation. This procedure requires angiography to identify the hyper-fluorescent demarcation of the detachment in order to photocoagulate it using focal argon laser. The laser induces scarring at sites and helps reattach the retina by fibrosis. The normal heathy pigment epithelial cells pump the sub-retinal fluid back to the choroidal vessels and escalate resolution. However, this option can only be considered if the RPE detachment does not involve the fovea in order to preserve the central vision. It is seen that the duration of the condition is reduced up to 2 months with the laser allowing increased speed of visual acuity improvement. Although the long term benefits of this procedure are still unclear, the rate of recurrence was seen to be significantly reduced after 9-18 months of follow up. A written patient consent prior to the procedure is of utmost importance. The patient needs to be made aware of all the possible risks and complications of the laser. The possibility of developing scotomas at the site of treatment or unfortunate further visual loss in cases where laser ruptures the Bruchs's membrane should be explained in simple language [11][12].

b) Photodynamic Therapy (PDT):

PDT (half dose) is currently the best option available for treating CSCR. It makes use of verteporfin, which is a photosensitizer, for a target therapy. Verteporfin is infused through the vein for over 8-10 mins. Around 10-15 minutes after the infusion, laser at 689nm is delivered to the site [13]. It accumulates in the blood vessels causing endothelial damage which further leads to vascular hypoperfusion, thus inhibiting the hyperpermeability of the choroidal vessels in CSCR. Following PDT, significant improvement in best corrected visual acuity (BCVA) and reduction in sub-retinal fluid, sub-foveal choroidal thickness, total and luminal choroidal area and central macular thickness is seen within 1 month [14]. Full dose PDT has unavoidable side effects like RPE atrophy and retinal thinning, choridal ischemia and formation of secondary choroidal neovascular membrane. This led to evolution and development of other safer options like half dose and half fluence PDT. Half dose treatment lead to faster resolution and reduction in recurrences than half fluence PDT. It effectively uses fluorescein angiography as a guide for the procedure [15][16]. Patients are advised to avoid the sun and physical activities for 24 hours as verteporfin can cause burns in the sun. Half dose PDT normalized the FAF after 7 years thus providing good long

term benefits. It still remains a safe and a considerable treatment option due to its good response [17].

c) Subthreshold Micropulse Laser (SML):

SML diode laser is a high density laser but possesses low intensity and selectively targets the pigment epithelium cells. It is delivered in short pulses which minimizes the chorio-retinal damage and does not cause scarring. A large area of pigment epithelial cells is thus exposed to the laser which reduces the production of cytokines and decreases inflammation. Unlike argon photocoagulation, this laser can safely and effectively be used in areas near the fovea. FFA and ICG are used as a guide for the treatment with this laser. The outcomes of the procedure are comparable with PDT with an added advantage of not having PDT side effects. However, there is a need for more long term follow up data to compare its effectiveness with PDT [18].

D. Medical Management

a) Anti-Corticosteroid Therapy :

Corticosteroid is a major risk factor in the pathogenesis of CSCR. Anti-corticosteroids like eplerenone, spironolactone, finasteride, mifepristone and rifampicin have been studied as potential treatment options for CSCR. A study in 22 hospitals in the UK studied the efficacy of eplerenone in CSCR. It concluded that the drug was not superior to the placebo group and advised ophthalmologists to discontinue the practice of prescribing it for treating the condition [19].

b) Intravitreal Anti- Vascular Endothelial Growth Factor (Anti-VEGF) Therapy :

Assumption of VEGF to be elevated in CSCR due to choroidal pathology led to devising intravitreal anti-VEGF as a potential treatment option in CSCR. However, studies have shown no difference in VEGF levels in CSCR and control patients [20][21]. A meta- analysis in 2013 that combined 4 clinically controlled studies showed no benefits of intra-vitreal bevacimumab in CSCR cases. There was no significant difference in visual acuity or in decrease of central macular thickness between both the groups [22]. Some randomized control trials compared half dose PDT with anti VEGF therapy in treating CSCR. They concluded PDT's superiority over Anti VEGF. Patients who have coexisting choroidal neovascularization are seen to benefit from this therapy [23][24][25]. A study that combined anti-VEGF and half dose PDT in treating CSCR showed that the combination was effective against choroidal neovascularization in chronic CSCR by effectively improving BCVA and significantly decreasing the sub-retinal fluid [26]. The benefits of anti-VEGF however, still remain unconvincing due to the lack of sufficient evidences.

c) Helicobacter Pylori Treatment :

A randomized control study showed that Helicobacter pylori treatment in positive patients yielded a faster resolution of sub retinal fluid than the control but demonstrated n change in BCVA [27]. Other studies that contradicted the outcomes indicated a need for larger randomized control trials. Thus due to the lack of sufficient evidences, H.pylori treatment as a treatment option for CSCR cannot be concluded.

d) Aspirin And Topical NSAIDs:

A study in 113 eyes on efficacy of low dose aspirin in CSCR showed faster improvement in visual acuity in the aspirin group than the control [28]. Topical NSAIDs in CSCR patients showed a speedy reduction in sub retinal fluid over a few weeks. However, there was no noticeable improvement seen in macular thickness and visual acuity [29].

VI. Conclusion

Central serous chorio-retinopathy is a self-limiting condition affecting most commonly men, with its peak age of onset between 40-50 years of age. The mainstay treatments are observation, half dose PDT and argon laser photocoagulation. Many studies for anti-VEGF therapy have been carried out to widen the treatment options for treating CSCR however, there are not sufficient evidences to prove their advantage over PDT. Micropulse laser is an evolving treatment option which requires larger randomized studies to prove its long term benefits. The pathogenesis of the condition is still unclear and it is trusted that it will be fully grasped in the near future enabling development of newer treatment options.

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