Current diagnosis and treatment in central serous chorioretinopathy

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ABSTRACT

Central serous chorioretinopathy (CSCR) diagnosis and follow-up are performed with multimodal imaging methods. Fundus fluorescein angiography, optical coherence tomography (OCT), fundus autofluorescence, and indocyanine green angiography can be used in the diagnosis of patients with CSCR. OCT stands out as the gold standard for imaging, diagnosis, and follow-up. Although there is no gold standard method in treatment.

Keywords: Central serous chorioretinopathy, diagnosis, multimodal imaging, treatment modalities

INTRODUCTION

Central serous chorioretinopathy (CSCR) is a clinical condition characterized by idiopathic, well-demarcated serous detachment of the neurosensorial retina (NSR). Although serous detachment in CSCR occurs as a result of impaired barrier and pump functions of the retinal pigment epithelium (RPE), the main pathology is in the choriocapillaris.

CSCR is recognized as a pachychoroid spectrum disease. Pachychoroid spectrum diseases include focal or diffuse choroidal thickening. Thinning of the choriocapillaris and thickening of the outer choroidal layers are observed. Because of choroidal hyperpermeability, subretinal fluid can often accompany diseases in this spectrum. In addition to CSCR, pachychoroid pigment epitheliopathy, pachychoroid neovasculopathy, polypoidal choroidal vasculopathy/aneurysmal type 1 neovascularization, peripapillary pachychoroid syndrome, and focal choroidal excavation are among the diseases included in this spectrum.

CSCR can be multifocal, often involving both eyes asymmetrically. In some patients, CSCR extends to the peripheral retina, while in others it may even present as subtotal bulous retinal detachment. Thinning of the foveal contour, cystoid degeneration, and damage to the photoreceptor layer cause loss of visual function.

Although 90% of the subretinal fluid is resorbed spontaneously in 3-4 months in CSCR, the improvement in visual function may take up to 1 year. Mild to moderate metamorphopsia, indistinct scotomas, decreased contrast sensitivity and impaired color vision are among the frequently ongoing complaints.

CSCR is a clinical diagnosis. In the differential diagnosis of CSCR, polypoidal choroidal vasculopathy (PCV), CNV (mostly Type 1), cavitary optic disc anomalies (if with serous detachment), choroidal hemangioma (if with focal choroidal thickness increase and serous detachment), dome-shaped macula (anterior protrusion of the macula with concomitant posterior staphyloma – often punctuated pooling on fluorescein angiography and increased subfoveal choroidal thickness) and Best disease (if there are splits in the RPE and elevation in the RPE) comes first.

While there is no need to request additional examination in patients with CSCR with demographic characteristics such as type A personality, age, and gender; advanced techniques such as fundus fluorescein angiography (FFA), optical coherence tomography (OCT), fundus autofluorescence (FAF), indocyanine green angiography (ICGA) can be used to support the diagnosis in patients with more severe CSCR.

IMAGING

Today, CSCR diagnosis and follow-up are performed with multimodal imaging methods. Because it is a fast and practical imaging method, OCT has often been the first imaging method. FAF is very useful for viewing RPE alterations. FFA indicates whether there is a leak or not. All imaging methods have different advantages. Therefore, multimodal imaging is important for CSCR.

FFA

The most important and most common finding in FFA is the ‘expanding point’ under serous retinal detachment. RPE leak occurs in 95% of CSCR cases. This leak point is 90% away from the fovea and is most common in the superonasal quadrant. In chronic CSCR cases, there is more than one
RPE leakage point. Other most important characteristic FFA findings identified for CSCR are smokestack (the most classic), inkblot, and mushroom patterns.  

**OCT**

The most important advantage of OCT as an imaging method is that it is non-invasive and fast. Recently, as a result of increasing the depth of imaging with OCT with EDI (enhanced depth imaging)-OCT and SS (swept source)-OCT, imaging of choroidal vessels and choroidal thickness can be performed. As choroidal changes, thickened subfoveal choroid, dilated choroidal vessels, thinned inner choroidal layer or focal choroidal excavation can be seen in CSCR.  

Choroidal thickness increased in both the affected eye and fellow eye. This increase in choroidal thickness strengthens the hypothesis that the increased hydrostatic pressure originates from the choroid. Choroidal thickness is affected by axial length and age. Choroidal thickness values above 395 micrometers are called the thick choroid (pachychoroid). Choroidal thickening results from focal or diffuse dilatation of choroidal vessels. On OCT imaging, PED, microchips, fissions, hypertrophy, or atrophy can be detected in RPE. RPE elevation occurs in the area of dilated vessels. RPE protrusion, PED, subretinal fibrinous exudate, dipping in the outer retinal layer, and elongation in the photoreceptor outer layers may occur at the leakage site. The area where the tiny RPE defect is seen on the OCT matches the leakage point in the FFA. The elongation in the outer layers of the photoreceptor initially causes hypo-autofluorescence by suppressing the RPE, and then, with the development of atrophy (window defect), it leads to a hyper-autofluorescence image. PED appearance in OCT can be in different shapes such as dome-shaped, double-dome-shaped, flat, protruding or ruptured. Intraretinal hyperreflective deposits, distortion in the ellipsoid zone, decrease in foveal thickness and cystoid macular degeneration are other findings.  

**CURRENT TREATMENTS**

In the treatment, the presence of risk factors that may cause CSCR should be evaluated first. Risk factors should be eliminated if possible. With the discontinuation of a used steroid, CSCR regresses by 90%. In the absence of risk factors that can be intervened or eliminated, the first step in the treatment of acute CSCR is follow-up because it resolves within 3–4 months. There is no consensus on when to start treating a CSCR attack. Treatment is initiated in cases of persistent macular NSR detachment, which usually lasts longer than 4 months, severely reduced visual acuity, recurrence, CSCR attack causing low final BCVA in the fellow eye, and in cases where the patient is from the occupational group that needs rapid improvement of vision.

**Focal Laser Photocoagulation**

Laser applications at green (514 nm) and yellow (580 nm) wavelengths close the leakage point. This closure effect is provided by the induction of RPE cells and fluid efflux, as well as thermal damage. The effect of photocoagulation is at the RPE level and has no effect on the choroid. After the damage created on the RPE, the surrounding RPE cells also undertake the task in that region. Laser photocoagulation therapy does not contribute to the final BCVA and may rarely cause paracentral scotoma and iatrogenic CNV. Therefore, it should be preferred in extrafoveal leaks. While there are studies indicating that laser photocoagulation has no effect on recurrences, there are studies showing that it reduces recurrences. According to the previous study, the recovery period is shortened by 2 months with photocoagulation.

If the leakage point is detected, laser photocoagulation still appears to be a good treatment alternative in cases 500 microns away from the fovea and lasting longer than 4 months.

**Photodynamic Therapy**

Verteporfin (Visudyne, Novartis, Switzerland) is an agent that causes vessel occlusion by causing endothelial vascular damage. With the stimulation of light with a wavelength of 693 nm and oxygen, free radicals are formed in the vascular network and cause vascular damage. With this mechanism, hyperpermeable vessels in the choiociapillaris are taken under control. In the follow-ups, it was observed that there was a decrease in vascular permeability and even a decrease in choroidal thickness. In the Photodynamic Therapy (PDT) protocol applied for CSCR, application with 25 J/cm² (lower fluence, ½ fluence) setting is preferred. Low fluence application causes fewer side effects with a good effect in CSCR treatment. Half-dose PDT (3 mg/m²) can also be preferred to reduce side effects with a good effect.  

This image is due to an atrophic RPE or PED. Atrophic areas are observed as a faintly hyperfluorescent focus due to increased permeability in choroidal vessels. In the late phase, previously hyperfluorescent areas may become permanent hyperfluorescent spots or these areas may be surrounded and covered by a central displacement of another hyperfluorescent focus. There is thinning and atrophy of the choiociapillaris due to the compression effect of the dilated choroidal vessels. Hyperfluorescent areas on ICGA have non-perfused choiociapillaris. Laser Doppler flowmetry has also shown that the blood flow in the choiociapillaris is slow.
PDT application is not as effective as half-dose PDT. There is no definitive data on whether half-dose PDT or half-fluence PDT is superior. No long-term studies are showing the results and safety of PDT.

PDT results in a reduction in serous NSR detachment and symptoms, and an increase in BCVA. Success is achieved when PDT is performed after the determination of the hyperfluorescent point after ICGA. PDT performed without showing the presence of hyperfluorescent spots with ICG does not have much benefit. Complications such as a change in RPE, choriocapillaris hypoperfusion, and development of CNV may occur as a result of PDT.

Although there is a rapid regression in serous NSR detachment with low-fluence PDT at 3-month follow-up comparing PDT to focal laser photoacoagulation, there is no difference in anatomical and functional success in the end.

**Micropulse (Subliminal) Laser Photoacoagulation**

Subthreshold micropulse laser is also used in the treatment of CSCR. Induction of RPE cells is provided by giving short-term multiple pulses to the RPE cells. Higher wavelengths have a better effect on the choroid and do not damage the inner retinal layers. In some studies, subthreshold diode micropulse laser has been shown to give better results than green argon laser (faster recovery and better contrast sensitivity).

The micropulse diode laser provides an effect like PDT, but it acts more slowly. Iatrogenic side effects are very rare. However, there is no data on how long the treatment should continue.

**Sub-Threshold Non-Damaging Retinal Laser Photoacoagulation**

The non-damaging retinal laser therapy (NRT) was recently defined. The non-damaging hyperthermia was demonstrated in mice by observing the expression of heat shock protein. Based on those reported results; the titration protocol has been developed by adjusting laser power and duration. This protocol is called Endpoint Management (EpM) and is related to the minimal tissue effects in visible titration. The EpM laser therapy uses an Arrhenius integral algorithm to control laser power and pulse duration, optimizing the therapeutic effect of the laser at sub-visible levels. The laser power is titrated to create a barely visible lesion at a pulse duration of 15 or 20 milliseconds, and EpM using 15 milliseconds is called NRT.

Ilhan et al. treated 23 eyes of 23 treatment-naïve chronic CSCR patients with NRT. The irradiation of 577 nm yellow light was conducted on the serous detachment area after switching over to the NRT algorithm. At the 2nd-month follow-up visit after NRT, complete resorption of subretinal fluid was observed in 78.3% of eyes and incomplete resorption in 21.7% of eyes. Worse values of BCVA and CMT before NRT were found to have an increased risk for incomplete resorption. They concluded that significant functional and anatomical improvements can be observed in the early period after NRT in patients with chronic CSCR. They emphasized that patients having worse baseline BCVA and CMT have an increased risk for incomplete resorption.

**Selective Retinal Therapy**

It acts only on intracellular melanosomes in RPE cells. Since NSR is not affected, it does not cause scotoma. It has been observed to be successful in the treatment of juxtafoveal lesions.

**Anti-VEGF**

Anti-VEGF therapy has a reducing effect on choroidal permeability. However, there is no increased VEGF level in CSCR. Therefore, anti-VEGF should be used only in cases where CSCR is associated with CNV. With the use of bevacizumab as an anti-VEGF agent, visual acuity increases, leakage decreases, and the amount of subretinal fluid decreases. However, the superiority of bevacizumab treatment over other treatment methods has not been demonstrated. The benefit of anti-VEGF therapy is evident in cases where CSCR is associated with CNV. While similar benefits are seen in the treatment of chronic CSCR, cases unresponsive to treatment have also been observed. Some studies stated that anti-VEGF injection did not change the outcome of BCVA in acute CSCR. Subretinal deposits are thought to be the reason for this unresponsiveness, preventing the reabsorption of fluid.

**Mineralocorticoid Receptor Antagonist**

Aldosterone and cortisol bind to mineralocorticoid receptors (MR). MR blockade is beneficial in the treatment of endothelial dysfunction, atherosclerosis, hypertension, heart failure, and chronic renal failure. In the treatment of retinopathy of prematurity, MR antagonists have an anti-angiogenic effect.

Spironolactone is a competitive MR antagonist drug. Spironolactone is a prodrug molecule and is converted to active metabolites in the liver. It was first used in the treatment of hypertension. Due to its binding to progesterone receptors, it causes gynecomastia, decreased libido, erectile dysfunction, and menstrual irregularities.

Eplerenone has fewer MR antagonist effects than spironolactone and has fewer hormonal side effects. Both molecules cause electrolyte imbalances and hyperkalemia. However, this side effect usually occurs in the presence of renal dysfunction.

It was observed that the foveal subretinal fluid decreased in patients treated with spironolactone and eplerenone.

**Glucocorticoids**

Glucocorticoids play a role in the pathogenesis of CSCR. Therefore, anti-glucocorticoid therapy is among the treatment options for CSCR. Mifepristone (RU-486) is a glucocorticoid and progesterone receptor antagonist. In a study conducted with a small number of patients, the efficacy of mifepristone in patients with chronic CSCR has been demonstrated. However, due to side effects such as hypotension, syncope, vaginal bleeding, and gastrointestinal disorders, it has not been a standard treatment method.

**Acetazolamide**

Although case reports are showing that acetazolamide treatment reduces subretinal fluid, there is no increase in final BCVA and does not reduce recurrences. Its use can be tried in patients who need rapid recovery.

**Beta-Blocker**

Case studies have reported that metoprolol, metipranolol, trimepranol, and propranolol provide improvement. No significant difference was observed between the non-selective beta-blocker metoprolol and the beta-1-selective blocker metipranolol.
**CONCLUSION**

OCT stands out as the gold standard for imaging, diagnosis, and follow-up. Although there is no gold standard method in treatment, reduced dose and low-fluence PDT seems to be the best treatment option.

**ETHICAL DECLARATIONS**

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