Expert Panel

Management of central serous chorioretinopathy: Expert panel discussion

Jay Chhablani, Giridhar Anantharaman[1], Francine Behar-Cohen[2], Camiel Boon[3], George Manayath[4], Rishi Singh[5]

Central serous chorioretinopathy (CSCR), one of the most common diseases in retina clinics, needs a special attention by retina specialists. Considering the challenges in diagnosis, classification, and management of this enigmatic disease and lack of level 1 evidence, there is a need for consensus with regard to establishing management protocols.

Key words: Central serous chorioretinopathy, management, choroid, retina, expert panel

Access this article online

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_1411_18

Quick Response Code:

This panel discussion includes opinions from the experts about clinically relevant questions in CSCR management. Panel includes experts across the world to provide their perspective to these practical questions, considering the differences in demographics, disease presentations, economic burden, and healthcare systems.

Question 1: What is the utility of OCT angiography (OCTA) and its role in the management of CSCR in 2018?

Dr. Anantharaman: In my practice today, I use OCTA in patients presenting with CSCR above the age of 50 years and patients with bilateral peripapillary disease. These are patients who clinically have NSD but would be having an underlying pachychoroid neovasculopathy to visualize the network. In fact, even in fellow eyes where you have an irregularly elongated retinal pigment epithelium (RPE) which is an early double layer sign, the OCTA demonstrates a silent neovascular network.

Dr. Behar-Cohen: There are two conditions in which OCTA is particularly useful:

- Diagnosis of choroidal neovascularization (CNV) in cases with flat irregular pigment epithelial detachment (PED). In this case, OCTA is the instrument of choice to visualize CNV perfusion. It is superior to indocyanine green angiography (ICGA) and fluorescein angiography (FA). But it does not help in treatment decision.
- Research tool to evaluate choriocapillaris perfusion and extension of flow voids.

Dr. Boon: In the field of CSCR, OCTA has mainly improved our capacity to recognize small CNVs complicating CSC, which have proven to be difficult to see on FA and ICGA. Patients with small CNV should receive anti-vascular endothelial growth factor (VEGF) treatment in combination with half-dose photodynamic therapy (PDT). OCTA had also given us insights on choriocapillaris nonperfusion in CSCR.

Dr. Manayath: OCTA is primarily used to detect hypo- and hyper-perfusion areas along with abnormal choroidal vessels. Such abnormal choroidal vessels should be interpreted with caution, as in many cases this could be distinct from CNV. Additionally, OCTA allows noninvasive detection of CNV

Smt. Kanuri Santhamma Centre for Vitreo-Retinal Diseases, L V Prasad Eye Institute, Hyderabad, Telangana, India, [1]Department of Vitreoretinal Services, Giridhar Eye Institute, Cochin, Kerala, India, [2]Department of Ophthalmology, University of Lausanne, Jules-Gonin Eye Hospital, Fondation Asile des Aveugles, Lausanne, Switzerland; Sorbonne Universités, UPMC Université Paris 06, Centre de Recherche des Cordeliers, Team 1 and 17, Paris, France; INSERM, Centre de Recherche des Cordeliers, Paris, France; Université Paris Descartes, Sorbonne Paris Cité, Centre de Recherche des Cordeliers, Paris, France, [3]Leiden University Medical Center, Department of Ophthalmology, Leiden, The Netherlands & Amsterdam University Medical Centers, Department of Ophthalmology, Amsterdam, The Netherlands, [4]Department of Retina and Ocular Oncology, Aravind Eye Hospital, Coimbatore, Tamil Nadu, India, [5]Cole Eye Institute, Cleveland, Ohio, USA

Correspondence to: Dr. Jay Chhablani, Smt. Kanuri Santhamma Centre for Vitreo-Retinal Diseases, L V Prasad Eye Institute, Banjara Hills, Hyderabad - 500 034, Telangana, India. E-mail: jay.chhablani@gmail.com

Manuscript received: 22.08.18; Revision accepted: 03.09.18

Cite this article as: Chhablani J, Anantharaman G, Behar-Cohen F, Boon C, Manayath G, Singh R. Management of central serous chorioretinopathy: Expert panel discussion. Indian J Ophthalmol 2018;66:1700-3.

in chronic CSC or pachychoroid neovasculoapthy (abnormal tangled filamentous vessel pattern), even when other imaging techniques do not show evidence of any CNV.

Dr. Singh: The role that I found for OCT angiography is simply for the surveillance of chronic CSR for the conversion to CNV. This is more common than is thought and would then require different regimens for treatment. Unfortunately, OCTA is still cumbersome and time-consuming to perform and analyze.

Dr. Chhablani: OCTA has very important role in unrevealing the vascular networks which could be the cause of persistent fluid in chronic cases, especially associated cystoid degeneration. Careful OCTA evaluation in eyes with double-layer sign is essential, as other imaging modalities may fail to diagnose CNVMs.

Question 2: What are the treatment modalities you use for chronic CSCR management?

Dr. Anatharaman: This can be explained with different scenarios.

i. Young patients presenting with first episode of CSCR, who still have active disease even after 4–6 months, I would go ahead with fluorescein angiography and advice focal laser photocoagulation for an extrafoveal leak and low fluence PDT for a subfoveal leak. In case of no leak, I advice low fluence PDT to the area of dilated choroidal vessels.
ii. For chronic CSCR, the clinician has to first rule out any underlying or precipitating factors. In these cases, I would advice focal laser to the leak outside the foveal center and PDT in other locations.

Dr. Behar-Cohen: When a chronic case is diagnosed (based on the previously described signs and also on history and risk factors), I also consider if both eyes are affected, the age and the sex and the occupation of the patient to decide the treatment options.

1. I choose a treatment option for the current serous detachment based on the duration of subretinal fluid (SRF), length of segments, presence of fibrin, and on location of the leakage site.

Mineralocorticoid antagonists (MRA) can be used as first choice alone in some cases knowing that resolution could take several months. It can be associated with argon laser. I usually do not opt for PDT at first. PDT is combined with MRA if no signs of resolution after 4 months. In inflammatory cases, I may associate oral MRA with drops of dexamethasone (four times per day). In extremely severe case, I have associated with efficacy, MRA, and intraocular steroids.

2. I treat associated CNV with intravitreal anti-VEGF and usually associate it with MRA.
3. I manage the risk factors (corticosteroids, hypertension, coronary risks, sleep disorders, shift work) and rule out tuberculosis if not typical.
4. I usually keep the patient under low-dose oral MRA (25 mg/day) for years.

Dr. Manayath: Initial management of CSC is careful observation with modification of various risk factors. Treatment should be considered in cases with persisting macular SRF or reduced visual acuity, and an angiography and further active intervention should be planned. In general, focal laser is directed to extrafoveal focal leaks, micropulse laser for juxtafoveal or subfoveal focal or diffuse leaks, and PDT or subthreshold diode (810 nm) laser to subfoveal leaks. Currently, drugs like eplerenone are also being used as alternative to laser therapy, when the latter is not practical or unresponsive in a particular patient.

Dr. Boon: We recently published the results of the PLACE trial in *Ophthalmology*, the first large investigator-initiated multicenter randomized controlled treatment trial in chronic CSCR, in which we compared ICGA-guided half-dose PDT with ICGA-guided high-density subthreshold micropulse laser treatment. In this trial, we found clear superiority of PDT over micropulse laser treatment, both in terms of complete resolution of subretinal fluid and in terms of functional outcome. Based on these results, I routinely use half-dose PDT for typical chronic CSCR cases, and I estimate that this results in complete resolution of subretinal fluid within 3 months after treatment in at least 80% of cases.

Dr. Singh: For chronic CSCR, there are multiple management options available. If the FA shows multiple hotspots which are not subfoveal, then I would consider PDT. If the lesions are subfoveal, then I treat with oral agents. I do a thorough investigation of topical medications or over-the-counter supplements that patients are taking. You would be surprised to find that many supplements contain testosterone and simply discontinuing some of these can improve the clinical picture.

Dr. Chhablani: Other than conventional laser indications as described previously, for subfoveal leaks, subthreshold laser is my preferred choice, considering its cost, and that it can be repeated without fear of RPE atrophy, as with PDT. I use eplerenone often for chronic and persistent CSCR, and if not responding then PDT is the choice. The goal is not to have any fluid especially in chronic cases.

Question 3: Please explain the role of PDT and its protocol in your practice?

Dr. Anatharaman: Our indications for the use of PDT in CSCR are:

i. Nonresolving CSCR of more than 4–6 months duration with a subfoveal leak.
ii. Chronic CSCR with serous macular detachment and active disease for more than 6 months duration.
iii. Recurrent CSCR.

We use half-fluence and half-dose PDT in our practice. We do not use anti-VEGF injection after PDT in case of chronic CSCR. Based on the FA and ICG features, we treat the areas of leak along with the areas of dilated choroidal vessels.

Repeat PDT can be considered for nonresolving SRF which is symptomatic. However, fundus autofluorescence and OCT images need to be seen very carefully, and in case there is already significant RPE damage with reasonably good vision I may not proceed with a repeat PDT.

Dr. Behar-Cohen: I try to use PDT when there are obvious hyperpermeability and no response to MRA. I am very cautious when VA is very good (6% risk of severe side effects and potential loss of vision), and if there is fibrin and intense

protein exudation (risk of overdosing because verteprofin binds to proteins).

I prefer half-dose to half-fluence because there is more recurrence with half-fluence than with half-dose according to studies. During PDT, spot sizes varied from 400 to 2000 μm based on ICG and FA (leakage sites).

I am very cautious with repeating PDT, particularly if there are signs of reduced choroidal perfusion (OCTA and ICG) as I consider CSCR to be a vasculopathy with vascular fibrosis and I do not think PDT, which intends to induce oxidative stress to the vessels, as a rationale treatment option for these patients. Eyes with epitheliopathy are at risk of RPE atrophy after PDT.

Dr. Boon: As mentioned, half-dose PDT (using 3 mg/m^2 verteporfin instead of 6 mg/m^2) is my primary treatment choice. If there are no contraindications to ICGA, I always choose my PDT spot size based on the hyperfluorescent area on mid-phase ICG. After all, ICGA abnormalities reflect the underlying choroidal abnormalities that presumably lie at the basis of CSCR development. Treating only the "hot spot" of leakage on FA holds a risk of undertreatment, because choroidal leakage areas on ICGA abnormalities are often (much) more extensive than leaking areas on FA. I repeat PDT if there is no complete resolution of subretinal fluid or a recurrence, as long as there is still hyperfluorescence on ICG that appears to explain the persistent or recurrent leakage. Patients with limited hyperfluorescence on ICG tend to have a lower likelihood of response to PDT (as well as other treatments for CSC), as we found in a recent study from our group.

Dr. Manayath: Current indication for PDT typically includes persistent or chronic CSC with subfoveal or juxtafoveal focal leaks or diffuse RPE epitheliopathy leakage. In our published results for chronic CSC, half-fluence PDT showed complete resolution of SRF in 85% eyes during a mean period of 5.41 weeks posttreatment, which is comparable to the western data. Repeat PDT is rarely required in cases of partial response or recurrence and may be considered after a minimum of 3 months from the initial treatment.

The treatment spot size is determined by measuring the area of active angiographic leakage in the mid-arteriovenous phase of FA. Some prefer ICGA-based PDT, but multiple areas of choroidal hyperpermiability may result in larger treatment area.

Dr. Singh: I used PDT for focal hot spot lesions which are not subfoveal. If I'm able to identify one or two hotspots either juxtafoveally or extrafoveally, then I will treat with PDT full fluence to that site of leakage. The chance of macular ischemia following PDT is quite low as reported in the Retina Society retrospective series of patients, so I need not worry about full versus partial fluence treatment. If the lesion is subfoveal, I tend not to use PDT and migrate to oral agents. I use the FA for measuring the spots but inevitably most are below 1000 μm in size. I will repeat the PDT in 3 months if needed and monitor every 3 months thereafter to look for response.

Dr. Chhablani: I use half-dose or half-fluence PDT, using both FA and ICG, mainly in chronic CSCR eyes. End-stage chronic cases without much leakage on ICG and gross chorocapillaries ischemia, PDT may be more harmful. Repetition of PDT is rarely required, may be after a year or so, and if I see new patches of leakage with much RPE atrophy changes.

Question 4: What is your experience with oral medication in the management of CSCR?

Dr. Anantharaman: I do not have much experience with oral medication in the management of CSCR. My protocol for management of CSCR is initial observation, focal laser, and PDT. I have tried eplerenone 25 mg in eyes with chronic CSCR with unpredictable results. So, I am not yet convinced that many of these oral medications are effective in the management of CSCR.

Dr. Behar-Cohen: I am using MRA (mineralocorticoid receptor antagonists) as the first treatment option, but it can be associated with other treatments such as laser, anti-VEGF, and sometimes PDT as well. In chronic cases, I keep MRA for years and even for a lifetime.

Spironolactone is 40 times more potent than eplerenone, but it is less specific and can be associated with hormonal side effects usually after several months (impotence, gynecomastia, reduced libido). All side effects are reversible.

Both spironolactone and eplerenone can increase plasma potassium level. Very important to check ionogram and kidney function (urea, creatinine, MDRD) before prescribing the drug. Check for association and be careful with other potassium-sparing agents and for nonsteroidal anti-inflammatory.

Begin with 25 mg/day and check for potassium again at 1 week and then at 1 month; if no change in potassium plasma level, check for potassium again every 3 months.

After 1 week, if the potassium is normal, increase to 50 mg/day (both drugs). Usually if enough, very rarely can increase to 75 mg/day. If potassium is >5 mmol/L, I reduce the dose. For stopping MRA, reduce progressively the dose to 25 mg for 3 months, then every other day for 3 months. Recurrence can occur if treatment is stopped abruptly. In chronic cases, the treatment could be kept for years. In case of pregnancy, it must be stopped. It can also be used in children.

Dr. Boon: I have tried eplerenone treatment in quite some chronic CSC patients now, with disappointing results. I use 50 mg of eplerenone for 3 months (25 mg in the first week, and dosing dependent on potassium levels), after which I checked the result. Prospective randomized controlled trials (VICI trial and SPECTRA trial) may bring evidence.

Dr. Manayath: This group includes ketoconazole, mifepristone, rifampicin, finasteride, spironolactone, and eplerenone. Owing to excellent selectivity and fewer side effects compared to spironolactone, eplerenone is being evaluated as a promising therapeutic agent in management of chronic CSC. Along with the variable treatment results noted in various studies and in our experience, dose and duration of oral eplerenone therapy are also not well-defined.

Dr. Singh: We have published extensively on our experience with oral medications in the management of CSCR. We initially published on our use of rifampin in a select number of patients.

Unfortunately due to the side effect profile of the drug, patients were unable to tolerate this drug for long term. We published the first series of patients treated with eplerenone for chronic CSCR. A couple on insights developed. First you needed atleast 90 days of therapy before response was seen. Also doubling the dosing from 25 to 50 mg po per day increased some patients that were initially nonresponse. We check a serum potassium first at baseline. If normal, we begin therapy and have the patient return in 2 months for follow-up testing. We see them in 2–3 months intervals, thereafter to gauge treatment response.

Dr. Chhablani: We published our case series on eplerenone with satisfactory outcomes. Some of my patients are on long-term eplerenone and doing really well for almost 2 years. I have used rifampicin in few nonresponders; however, concerns about the multi-drug-resistant tuberculosis in a country like India prevent me to use it often. Yes, there are cases who do not respond to oral medications as well; we need to try alternative therapies.

Question 5: Please discuss the role of subthreshold laser in the management of CSCR and your experience?

Dr. Anatharaman: I do not have much experience with the role of subthreshold laser in the management of CSCR. The reason being, the results are unpredictable. All my colleagues have been using subthreshold laser for CSCR and they have been using it mainly for chronic CSCR. They have been using 577 nm, spot size of 200–300 μm, 5% duty cycle and gone up to the power of 1000 MW, and their experience has not been very encouraging. Of course they have used it only in case of chronic CSCR.

Dr. Behar-Cohen: I have not yet used this laser.

Dr. Boon: In the PLACE trial, we used ICG-guided high-density 810 nm subthreshold micropulse laser treatment, with a high power of 1800 mW (sometimes tapered down in case of possible suprathreshold effect), and a duty cycle of 5%. Despite this relatively intense treatment scheme, half-dose PDT was clearly superior over micropulse laser. That is why I now use micropulse laser treatment only rarely in CSCR.

Dr. Manayath: I use subthreshold diode laser which is a cost-effective treatment option for chronic CSC compared to PDT that causes temperature-based closure of the choriocapillaris which leads to stasis of blood flow and stops leakage using a 810-nm long-pulse low-energy diode laser (Oculight Slx; Iridex, Irvine, CA, USA), a modification of the transpupillary thermotherapy (TTT) technique. Concern of producing a foveal burn and collateral damage promoted evolution of the safety enhanced graded subthreshold laser. In subthreshold diode laser, a starting power at 40% of the threshold extramacular test burn using 2–3mm spot size and 60-s exposure for a foveal laser treatment is planned. If an inadequate response is observed at 6 weeks after treatment, retreatment is done with a 20% increase in power, thus grading the desired response by producing invisible burns and limiting adverse events. The results are comparable to half-fluence PDT with complete resolution in 77.3% eyes by 7.14 weeks and without the risk associated with intravenous drug administration.

Dr. Chhablani: I have been using yellow 577 nm (Navilas® and Iridex®) for few years with very satisfactory results in both acute as well as chronic cases, at much lower cost to the patient. We use 5% DC, with 200 μm spot size, 30% of the threshold power with confluent burns including subfoveal area. I usually repeat same settings if I do not see any response at 3 months. This laser had had a big impact in our clinical practice.

Dr Singh: I don't use sub threshold laser in this condition.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.