Case
A 42 year old gentleman presented with scotoma and defective vision of left eye for last 6 months. No subjective improvement was noted by him over the period. Best Corrected Visual acuity was Right Eye (OD) 6/6 N6 and Left Eye (OS) 6/18 N10. Serial Optical Coherence Tomography (OCT) was done and shows serous macular detachment which is not resolving over last 4 months. Fundus Autofluorescence shows hyper auto fluorescent area in the central macula. Diagnosis - Non resolving Central Serous Chorioretinopathy (CSCR). Patient was not on any steroids in any form. He was a non smoker non alcoholic, Type a personality. Fundus photo, Fundus Fluorescein Angiography (FFA) (Early, mid and late) and Indocyanine Green Angiography (ICG) (Early and late) are given below.

Questions
1. How long will you wait in a case of fresh CSCR?
2. In this case what is the preferred method of treatment?
3. What is the role of different types of Photo Dynamic Therapy (PDT) - Half dose, quarter dose, reduced fluence, full fluence in CSCR
4. In your opinion is there any role of anti Vascular endothelial Growth Factor (VEGF) drugs in CSCR with foveal leak

This 42 year old gentleman has persistent chronic central serous retinopathy necessitating treatment.

1. In a fresh CSCR, I ask the patient come back a month later after baseline OCT. If there are no quantified signs of resolution on OCT of the extent of the neurosensory detachment, I would suggest treatment. If there is evidence of improvement assessed by decrease in area of neurosensory detachment on OCT, I would watch.

2. Preferred modality of treatment in this case would be photodynamic therapy considering the multiple leaks that appear juxtafoveal. There are no other modifiable risk factors such as steroid therapy, systemic illness suggestive of hypercortisolism etc. Persistence of chronic CSC, being the indication for treatment in this gentleman.

3. Full dose PDT is best avoided, particularly in Indian population (increased Retinal Pigment Epithelium (RPE) pigmentation) to minimize risk of RPE atrophy. Half dose or half fluence can be considered and a recent head to head comparison has found half dose to resolve the SRF faster with lesser number of recurrences when compared to half fluence. Decreasing the fluence further may be ineffective or deleterious.

4. I have not had favorable results by treating CSC with anti-VEGF - this of course is my personal experience of...
less than a handful of cases and should not be given much consideration.

Dr Nitin Shetty
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1. Generally 1 -2 months. Photoreceptor damage has been reported by the 4th month - hence the need to treat much before that.

2. Would prefer a Low fluence PDT in this case

3. PDT has been found to be quite effective for CSC - thought to work by reducing the choroidal hyper permeability and by tightening the blood retinal barrier at the RPE. Low dose and low fluence PDT have both been found to be effective - has a possible advantage of causing less PDT related complications like acute vision loss and increased RPE alterations.

4. Don’t think there is a role for Anti VEGF in treatment of CSC

Dr Rajesh Puthusseri
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1. Detachment of macula for more than 3 months can result in photoreceptor atrophy. Since the fluid takes around another 1 month to disappear after laser I do the laser at 2 months . Indications for an earlier treatment are the job related requirements or poor visual outcome to observation in in the other eye . Recurrent cases also receive earlier treatment.

2. Here the leakage is just inside the edge of foveal avascular zone. Thermal laser cannot be done since it can result in a foveal scar. Low fluence or low dose PDT can be tried. PDT is currently the recommended treatment modality for CSCR since it addresses the underlying pathology of choroidal hyper permeability. Since PDT is expensive, for our patients it may be reserved for chronic CSCR with diffuse retinal pigmentary changes or non resolving acute CSCR with leakage involving the fovea

3. Full fluence PDT may cause persistent choroidal ischemia in the treated area, RPE changes, CNVM and damage to the adjacent normal choroid . Half fluence has less chance for these complications. The rationale behind half dose PDT is also the same. Half dose PDT has been reported to be more effective than 1/3 rd dose PDT.

4. VEGF levels have not been demonstrated to be elevated in the aqueous in CSCR. It is hypothesized that there is localized secretion of VEGF secondary to hypoxia in choroid and RPE, which may respond to anti-VEGF injections. Current evidence does not support the use of anti VEGF injections for CSCR.

Dr Chirag Bhatt
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Through this non resolving CSCR case you have raised very important questions:
1) In a case of fresh CSCR with good vision in other eye, we would like to wait for at least 3 to 4 months as natural history shows it resolves spontaneously and 80-90% patients return to 20/25 or better vision.

2)In this case as it has been already 4 months and still it has not resolved, it should be treated. FFA and ICG reveals leakage within Foveal Avascular Zone (FAZ) so thermal laser should not be used instead half fluence PDT should be the preferred treatment.
3) PDT is believed to hasten both fluid resorption and visual recovery. Multiple authors have used PDT as a first-line therapy for acute focal leaks from CSCR with reported success. Most papers describe resolution of subretinal fluid within 1 month of treatment.

Lai et al described the use of half dose verteporfin in the treatment of CSCR. They proposed 3 mg/m² of verteporfin infused over 8 minutes, followed 2 minutes later with ICG guided PDT. Of the eyes treated, 85% showed complete resolution of the neurosensory retinal detachment and/or pigment epithelial detachment by 1 month after treatment. Reibaldi et al evaluated the treatment efficacy of standard-fluence PDT versus low-fluence PDT using microperimetry. The study found improvement of macular sensitivity following treatment along with greater efficacy in treatment overall using low-fluence PDT.

Another option is ICG mediated photothrombosis is a technique using a low-intensity laser combined with ICG dye infusion to treat focal areas of hyperpermeability in the choroid. Like PDT, it addresses treatment to the level of the choroidal vasculature. An 810-nm laser is applied after infusion of ICG dye. Without prior ICG dye, investigators have also used the 810-nm laser as transpupillary thermotherapy (TTT) with moderate anecdotal success.

4) Intravitreal bevacizumab (Avastin) has been used to successfully treat the rare complication of choroidal neovascularization following CSCR. There are reports of Anti-VEGF agents such as bevacizumab and ranibizumab being used to treat the neurosensory detachment of CSCR in the absence of choroidal neovascularization. Bae et al conducted a prospective randomized study comparing intravitreal ranibizumab to low-fluence photodynamic therapy in chronic CSCR. At 6 months, they concluded that the anatomic outcomes with ranibizumab injections were “not promising” compared with low-fluence photodynamic therapy. Semeraro et al compared intravitreal bevacizumab to low-fluence photodynamic therapy for treatment of chronic CSCR. The series was limited to 22 patients total and no statistical significant difference could be identified. At present we believe there is not concrete evidence to treat neurosensory detachment in CSCR without Choroidal Neovascular Membrane (CNVM) with intra vitreal AntiVEGF.

In this patient, the best treatment option would be PDT, either half fluence PDT (25 J/cm²; 300mW) or half dose PDT (3mg/m²) with standard fluence. Both the safety enhanced Half and half fluence PDT have shown similar safety and efficacy with respect to SRF resolution and visual improvement. In our experience, half fluence PDT has around 90% success in chronic CSCR cases. We base it on FFA and try to keep the treatment spot size to the minimum (Always < 4500 microns), to prevent collateral photoreceptor damage.

Standard fluence PDT works well, but has the risk of vision loss due to RPE atrophy, foveal thinning, and choroidal ischaemia. There are anecdotal reports of Avastin use in CSCR. However, the current evidence does not recommend its use in Chronic CSCR. In a recent comparative study of PDT versus Avastin in CSCR, though the visual outcome was maintained in both groups, only 25% in avastin group had SRF resolution compared to 75% in PDT group, at final follow up.

If this patient cannot afford PDT, then graded sub threshold TTT (Transpupillary thermotherapy) with 50% reduction of the threshold power, is a good and safe option with around history of the disease, that 75% cases of fresh CSCR takes 4-6 months for resolution. I would wait for a minimum of 4 months in a case of acute CSCR before intervention, with serial OCT follow-ups in 2 months. If SRF shows signs of reduction on OCT, then conservative approach is sufficient. If patient is one eyed or his profession requires early visual rehabilitation, then plan an early FFA and LASER. Focal laser to the RPE leak points only hastens the recovery and does not prevent recurrence or changes the final visual outcome.

Dr George Manayath
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As mentioned, this is a clear-cut case of chronic CSCR of 6 months duration and subfoveal ink-blot leak. This patient requires intervention. As we know from the natural
80% success, comparable to the PDT results, but requiring marginally higher treatment sittings (1-3 sittings). This is a cost-effective option in Indian scenario.

Conclusion
For non-resolving central serous chorioretinopathy with foveal leak photodynamic therapy using verteporfin appears to be a promising treatment. It addresses the actual pathology of CSCR i.e. choroidal hyperpermeability. Enhanced depth imaging of choroid of CSCR patients have demonstrated that there is an increase in choroidal thickness in affected as well as other eye of patients with CSCR. Thermal laser just closes the leak but will not prevent the recurrence of CSCR. But PDT reduces choroidal hyperpermeability and choroidal thickness. This helps to prevent further recurrences also. The exact dosage of PDT, whether half dose or quarter dose or full fluence or reduced fluence is beneficial is still under investigation. Generalized feeling is that half or reduced dose with reduced fluence will help in the preservation of retinal pigment epithelium function and reducing the adverse events.

References: