When to Treat and Not to Treat Patients With Central Serous Retinopathy

Reduced-fluence PDT is the current accepted treatment for CSR.

BY FRANCESCO BOSCIA, MD

Central serous retinopathy (CSR) is a pathologic condition characterized by swelling and elevation of retinal tissue near the macula due to accumulation of fluid between the photoreceptor outer segments and the retinal pigment epithelium (RPE), often leading to detachment of the neurosensory retina.[1] Also sometimes called central serous chorioretinopathy, the condition most often affects men 20 to 60 years of age, but it can also affect women.[2]

The disease is often unilateral and is self-limiting in about 60% of cases, but sometimes the retinal detachment persists, leading to damage to the RPE and the photoreceptors and resulting in vision loss.[3] As with any disease that resolves spontaneously in most cases, the clinician confronted by a patient with CSR is faced with decisions regarding whether, when and how to treat. This article summarizes my own preferences and rationale regarding how to manage patients presenting with CSR.

CHRONIC CASES ONLY

Because CSR is so often self-limiting, I reserve treatment for chronic cases: ie, cases in which the condition persists for 6 months or more, or in which long-standing fluid accumulation and retinal separation over a long period are associated with RPE changes. Chan and colleagues[4] described good visual and anatomic results treating acute CSR with half-dose verteporfin photodynamic therapy (PDT) in a randomized controlled trial. Still, however, in my opinion, there is not sufficient proof of the safety of current treatments to apply them in acute cases, most of which will self-resolve.

My only exception to this rule would be in the case of a patient with specific professional needs who must recover complete and perfect visual acuity as soon as possible. In this case I would consider treatment of acute CSR.

For patients in whom the condition persists, I consider treatable any case not associated with the use of corticosteroids. For me, the primary mode of treatment in CSR is currently reduced-fluence verteporfin PDT.

There are many studies in the literature describing treatment of this disease with thermal laser, but these studies are outdated. It was assumed in the past that the primary target in CSR was at the level of the RPE. However, ICG angiography has now shown that the disease is at the level of the inner layers of the choroid, the choriocapillaris.[5,6] In CSR there is ischemic congestion of the choriocapillaris, and therefore a treatment focused at this level is needed. PDT is the best choice to achieve this.

Inoue and colleagues[7] recently used indocyanine green angiography (ICGA) to investigate which patients with CSR respond best to PDT treatment. They found that the success rate depended on the degree of vessel hyperpermeability seen on ICGA. PDT was not effective, or the recurrence rate was high, in eyes without intense hyperfluorescence on ICGA. The patients who responded best were those in whom significant leakage was seen in the late frames of ICGA. This observation may help us to further refine indications for PDT treatment of CSR.

Thermal laser photocoagulation may be considered for focal treatment of single leaking points located well

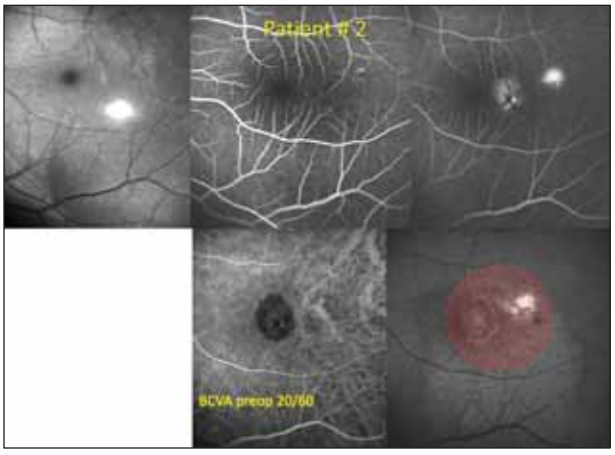

Figure 1. Patient with neurosensory retina elevation due to juxtafoveal leakage from the choriocapillaris and serous pigment epithelial detachment (PED) was treated with standard-fluence PDT.

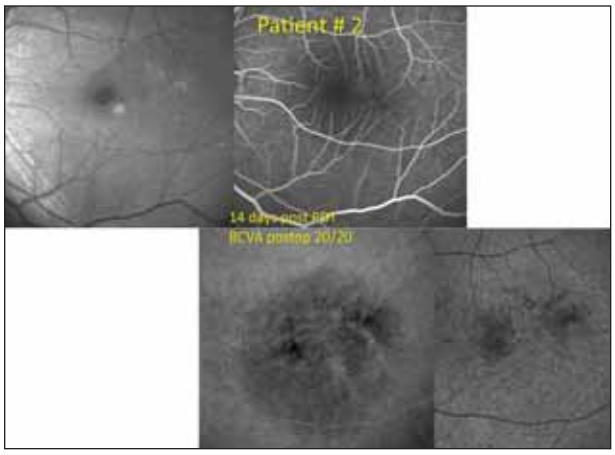

Figure 2. Same patient as Figure 1, 14 days after PDT. Visual acuity is improved, with minimal retinal pigment epithelium (RPE) changes seen on fluorescein angiography. On indocyanine green angiography (ICGA), disappearance of both the leaking choroid and PED is seen, but with moderate hypoperfusion.

outside the fovea in acute or chronic cases. For this indication, I would consider using thermal treatment with one of the newer micropulse lasers that allow regulation of the duty cycle.

REDUCED FLUENCE PDT

My first line of treatment for CSR is PDT with reduced fluence rate. There is currently no indication for use of standard-fluence PDT in CSR. The consensus of most experts is that reduced-fluence PDT is as effective as standard-fluence PDT, but safer.

We recently participated in a prospective, multicenter, investigator-masked trial comparing the efficacy of reduced-fluence and standard-fluence PDT in patients with central serous chorioretinopathy.[8] In this trial, both treatments resulted in visual acuity improvement and complete reabsorption of subretinal fluid, but the reduced fluence rate appeared to be safer. Moderate to significant choriocapillaris nonperfusion was seen in 44% of eyes treated with standard fluence compared with 0% of eyes treated with reduced fluence. Reduced fluence had the same efficacy as standard fluence, but there was less associated damage to the surrounding healthy choriocapillaris (Figures 1-4).

In the photodynamic process there are three main actors: verteporfin, oxygen, and photons of laser energy. In CSR, because there is sluggish blood flow in the choriocapillaris, PDT is performed in an environment rich with verteporfin but relatively hypoxic. The supply of oxygen to the treated area is restricted by the diseased capillaries, and therefore oxygen is the limiting factor in the PDT process. As a result, there is an excess of laser energy photons. Meanwhile, in the surrounding normal choriocapillaris, where there is an excess of oxygen as compared with the diseased area, PDT can create additional damage without additional benefit.

When the fluence rate is reduced, the laser energy is better balanced with the oxygen content in the treated environment, resulting in a more focused treatment delivered to the diseased area and a reduction in potential damage to the surrounding choriocapillaris. Damage to the RPE is reduced, and so is the possibility of ischemia and its sequelae, the overexpression of vascular endothelial growth factor (VEGF) and other growth factors and the induction of a neovascular response or further damage to the RPE. For these reasons, we consider reduced fluence the current standard for PDT treatment.

The selection of the reduced fluence light dose (25 J/cm^2) is based on the phase 1/2 studies that introduced PDT into practice[9] and other work in the ensuing decade.[10,11] The normal fluence rate (50 J/cm^2) was chosen not for treatment of CSR, of course, but for a completely different disease, choroidal neovascularization secondary to age-related macular degeneration (AMD). The standard fluence rate was selected because it resulted in the highest percentage of AMD patients showing absence of leakage and the longest period without recurrence of leakage. But the dose-ranging studies found that hypoperfusion was minimal in eyes treated with 25 J/cm^2, definitely reduced in comparison with the standard fluence rate. This makes the reduced fluence rate a more appropriate treatment modality for CSR.

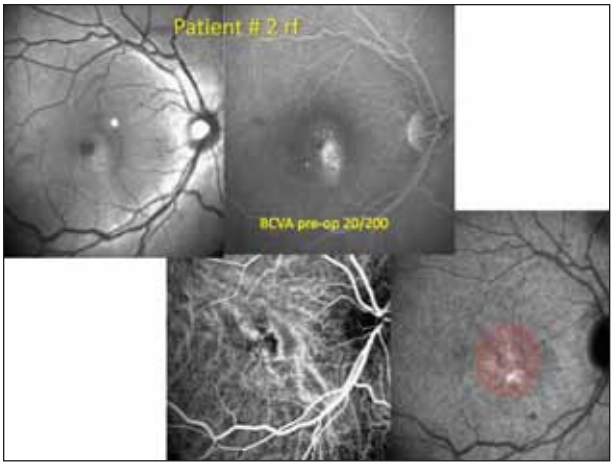

Figure 3. Patient with neurosensory retina elevation due to subfoveal leakage from the choriocapillaris was treated with reduced-fluence PDT.

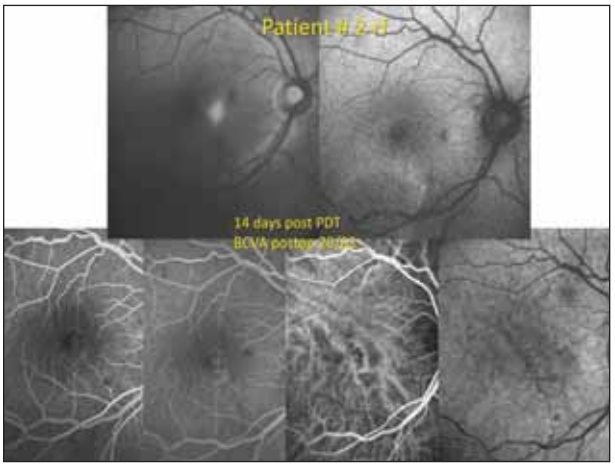

Figure 4. Same patient as Figure 3, 14 days after PDT. Visual acuity is improved, with minimal RPE changes on fluorescein angiography and minimal hypoperfusion on ICGA.

OTHER OPTIONS AND A LOOK AHEAD

A number of recently published papers have explored the use of VEGF inhibitors to treat CSR.[12-14] In my view, there is no rationale for this approach to treatment. Basic science has not shown an overexpression of VEGF in CSR. There is no angiogenesis in this disease. Therefore, the rationale for use of anti-VEGF agents is lacking.

In addition, the papers published to date on this topic have been case series with equivocal results. There is no level 1 or level 2 evidence for the use of anti-VEGF agents in CSR. By contrast, our multicenter prospective study showed convincing evidence of the effectiveness of reduced-fluence PDT for this indication.[8]

Another change that may become part the PDT protocol in the future is reduction in the dose of verteporfin, in addition to reduction in the laser fluence rate. In a prospective uncontrolled case series of patients with chronic CSR, Chan and colleagues[15] halved the standard amount of verteporfin and demonstrated convincingly good results.

In the future, then, we may have the possibility of performing PDT with a combination of reduced fluence rate and reduced verteporfin content, rendering the treatment even more focused and safer than it is currently. We look forward to investigating this new protocol. ■

Francesco Boscia, MD, is Medical Director in the Department of Ophthalmology at the University of Bari in Italy. Dr. Boscia states that he is a paid consultant for Allergan, Novartis, and Pfizer. He may be reached at +39 0805594027; or via e-mail at francescoboscia@hotmail.com.

1. Wang M, Munch IC, Hasler PW, et al. Central serous chorioretinopathy. *Acta Ophthalmol.*
1. Wang M, Munch IC, Hasler PW, et al. Central serous chorioretinopathy. *Acta Ophthalmol.* 2008;86:126-145.
2. Quillen DA, Gass JDM, Brod RD, Gardner TW, Blankenship GW, Gottlieb JL. Central serous chorioretinopathy in women. *Ophthalmology.* 1996;103(1):72-79.
3. Ober MD, Yannuzzi LA, Do DV, et al. Photodynamic therapy for focal retinal pigment epithelial leaks secondary to central serous chorioretinopathy. *Ophthalmology.* 2005;112:2088-2094.
4. Chan WM, Lai TY, Lai RY, Liu DT, Lam DS. Half-dose verteporfin photodynamic therapy for acute central serous chorioretinopathy: one-year results of a randomized controlled trial. *Ophthalmology.* 2008;115(10):1756-1765.
5. Guyer DR, Yannuzzi LA, Slakter JS, et al. Digital indocyanine green videoangiography of central serous chorioretinopathy. *Arch Ophthalmol.* 1994;112:1057-1062.
6. Spaide RF, Hall L, Haas A, et al. Indocyanine green videoangiography of older patients with central serous chorioretinopathy. *Retina.* 1996;16:203-213.
7. Inoue R, Sawa M, Tsujikawa M, Gomi F. Association between the efficacy of photodynamic therapy and indocyanine green angiography findings for central serous chorioretinopathy. *Am J Ophthalmol.* 2010;149(3):441-446.
8. Reibaldi M, Cardascia N, Longo A, et al. Standard-fluence versus low-fluence photodynamic therapy in chronic central serous chorioretinopathy: a nonrandomized clinical trial. *Am J Ophthalmol.* 2010;149(2):307-315.
9. Miller JW, Schmidt-Erfurth U, Sickenberg M, et al. Photodynamic therapy with verteporfin for choroidal neovascularization caused by age-related macular degeneration: results of a single treatment in a phase 1 and 2 study. *Arch Ophthalmol.* 1999;117:1161-1173.
10. Visudyne in Minimally Classic Choroidal Neovascularization Study Group. Verteporfin therapy of subfoveal minimally classic choroidal neovascularization in age-related macular degeneration. 2-year results of a randomized clinical trial. *Arch Ophthalmol.* 2005;123:448-457.
11. Michels S, Hansmann F, Geitzenauer W, Schmidt-Erfurth U. Influence of treatment parameters on selectivity of verteporfin therapy. *Invest Ophthalmol Vis Sci.* 2006;47:371-376.
12. Lim SJ, Roh MI, Kwon OW. Intravitreal bevacizumab injection for central serous chorioretinopathy. *Retina.* 2010;30(1):100-106.
13. Schaal KB, Hoeh AE, Scheuerle A, Schuett F, Dithmar S. Intravitreal bevacizumab for treatment of chronic central serous chorioretinopathy. *Eur J Ophthalmol.* 2009;19(4):613-617.
14. Seong HK, Bae JH, Kim ES, Han JR, Nam WH, Kim HK. Intravitreal bevacizumab to treat acute central serous chorioretinopathy: short-term effect. *Ophthalmologica.* 2009;223(5):343-347.
15. Chan WM, Lai TY, Lai RY, et al. Safety enhanced photodynamic therapy for chronic central serous chorioretinopathy: one-year results of a prospective study. *Retina.* 2008;28:85-93.