Central serous chorioretinopathy (CSC) affects roughly 10 men and two women per 100,000 people, and they are often younger, working-aged individuals with high visual demands. Randomized clinical trials in CSC are scarce and typically evaluate dozens of patients rather than the hundreds or even thousands of patients evaluated in trials for age-related macular degeneration (AMD), retinal vein occlusion, and diabetic retinopathy. Unfortunately, to date there are no FDA-approved medications for CSC, leaving ophthalmologists without a large treatment armamentarium.

Confirming the diagnosis
The first step in approaching CSC is confirming the diagnosis. There are a number of pitfalls to exclude on the differential diagnosis list. In any patient older than 50 years, differentiation must be made from exudative AMD, which can typically be achieved with fluorescein angiography (FA). Polypoidal choroidal vasculopathy is well known to masquerade as CSC and can be differentiated with indocyanine green (ICG) angiography. Pachychoroid pigment epitheliopathy is a recently described entity seen on enhanced depth imaging optical coherence tomography (EDI-OCT) in eyes with a thickened choroid but without subretinal fluid and may lie on a spectrum with CSC. Additionally, posterior uveitis may coexist with CSC due to concomitant steroid use. Uveitis can also mimic CSC, such as in the case of exudative serous detachment in Vogt-Koyanagi-Harada syndrome.
Multimodal imaging

Multimodal imaging is indispensable for both diagnosis and management of CSC. Nearly pathognomonic signs for CSC include the smokestack sign, gravitating tracts, and the acute focal retinal pigment epithelium (RPE) leak or “blow-out” (Figure). While FA and ICG angiography have been the mainstay for diagnostic testing and the guide for treatment, noninvasive imaging with EDI-OCT and fundus autofluorescence (FAF) imaging has gained increasing importance to evaluate the extent of subretinal fluid and pigment epithelial detachment as well as the health of the RPE.

Work-up in CSC

A work-up is usually not necessary for patients in the typical demographic: young men, those with a “Type A” personality, and pregnant women. Patients should be asked about sleep apnea, phosphodiesterase inhibitors for erectile dysfunction, and use of illicit drugs, such as the sympathomimetic “ecstasy.” In atypical or severe cases, however, a work-up for Cushing’s syndrome is warranted. A 24-hour urinary free cortisol can be an initial screening test, and other methods include low-dose dexamethasone suppression test, dexamethasone-corticotropin-releasing hormone test, or evening serum and salivary cortisol level. Ophthalmologists might opt to consult an endocrinologist, especially if there is a concern for pituitary adenoma or adrenal tumor.

Treatment modalities

Risk factor reduction

The first treatment that should be applied is risk factor reduction. Patients on steroids of any form (oral, inhaled, topical, intra-articular, epidural, or intravenous) should be counseled to reduce or ideally eliminate exogenous steroids if possible. The majority of CSC cases secondary to exogenous steroids will resolve if the steroids are withdrawn. Lifestyle modification

Figure. Selected findings in CSC. (A) Classic “smokestack sign” seen in a left eye on fluorescein angiography (FA) and (B) indocyanine green (ICG) angiography. Choroidal hyperpermeability in another left eye less prominent with FA than mid-phase ICG (D) angiogram. “Blow-out” of the retinal pigment epithelium in a right eye seen as a focal leak on FA (E) and hypo-autofluorescent spot (F) on fundus autofluorescence imaging, with disruption in the retinal pigment epithelium visible on oblique OCT scan (G) through the defect.
with stress reduction is crucial in those with a type A personality but often difficult to achieve. Limiting work hours, increasing vacation time, encouraging exercise and adequate sleep, changing attitudes about work-life balance, and even professional counseling are all elements that can reduce endogenous cortisol levels.

**Observation**

Observation is advisable following the initial diagnosis of acute CSC in the majority of patients because the disease is often self-limited. After 2 to 6 months of risk factor reduction, if the disease fails to improve and is encroaching on or involving the fovea, consideration of treatment is reasonable. Factors that might prompt early treatment include recurrent CSC, vocational demands, and a history of poor response in the fellow eye to initial observation.

**Clinical trials**

The Table summarizes 12 randomized trials in CSC performed since 1990. A 2013 search of the PubMed terms “central serous AND randomized trial” resulted in 59 citations, 12 of which were randomized trials of CSC published since 1990.

**Photodynamic therapy**

Photodynamic therapy (PDT) is considered by most as the first-line therapy for treatment of CSC, despite its off-label status. Yannuzzi et al first described ICG-guided PDT treatment in 20 eyes, with complete resolution of fluid in 60% by 6 months.\(^{22}\) PDT was administered to hypercyanescent plaques (observed on the mid-phase ICG) at full fluence as in the TAP study: After a 10-minute infusion of verteporfin at a dose of 6 mg/m\(^2\) and a wait time of 5 minutes, laser treatment was performed for 83 seconds at 689 nm. Other trials supported these findings. However, PDT is not entirely benign and can be associated with pigmentary change, RPE atrophy, choroidal ischemia, and secondary choroidal neovascularization (CNV). In an effort to reduce collateral damage, less intensive strategies have been employed with reduced-fluence PDT (half the exposure or half the duration of laser treatment) or reduced-dose PDT (half the dose of verteporfin). Chan et al performed a randomized, controlled trial of half-dose PDT versus placebo and demonstrated that 95% of treated patients versus 58% of controls had complete absence of fluid at 1 year; visual acuity was also significantly improved.\(^{12}\) Re-treatment is reasonable to consider when there remains persistent fluid at least 3 months since the previous PDT, especially if there has been a positive response.

**Laser**

Thermal laser has been the historic treatment of choice for CSC and remains an option for focal leakage outside the perifoveal area. Typical parameters include a spot size of 100 to 200 µm for 100 ms at

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Year</th>
<th>Author</th>
<th>N</th>
<th>Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2013</td>
<td>Bae SH</td>
<td>32</td>
<td>Low-fluence PDT superior to ranibizumab for chronic CSC at 12 months.</td>
</tr>
<tr>
<td>2</td>
<td>2013</td>
<td>Roisman L</td>
<td>15</td>
<td>Subthreshold diode micropulse laser superior to sham for chronic CSC at 3 months.</td>
</tr>
<tr>
<td>3</td>
<td>2013</td>
<td>Dang Y</td>
<td>53</td>
<td>H. pylori eradication did not improve acuity or subretinal fluid.</td>
</tr>
<tr>
<td>4</td>
<td>2013</td>
<td>Behnia M</td>
<td>37</td>
<td>Macular subthreshold laser therapy improved acuity at 6 months.</td>
</tr>
<tr>
<td>5</td>
<td>2013</td>
<td>Semeraro F</td>
<td>22</td>
<td>No significant difference between bevacizumab and low-fluence PDT.</td>
</tr>
<tr>
<td>6</td>
<td>2013</td>
<td>Ratanasukon M</td>
<td>51</td>
<td>High-dose antioxidants for acute CSC showed no benefit for acuity or thickness.</td>
</tr>
<tr>
<td>7</td>
<td>2011</td>
<td>Wu ZH</td>
<td>34</td>
<td>Half-dose PDT superior to placebo for acuity at 1 year.</td>
</tr>
<tr>
<td>8</td>
<td>2011</td>
<td>Bae SH</td>
<td>16</td>
<td>Reduced-fluence PDT superior to ranibizumab at 3 months.</td>
</tr>
<tr>
<td>9</td>
<td>2011</td>
<td>Klatt C</td>
<td>30</td>
<td>Selective retina therapy with (Nd:YLF) laser superior to control at 3 months.</td>
</tr>
<tr>
<td>10</td>
<td>2010</td>
<td>Lim JW</td>
<td>24</td>
<td>Bevacizumab similar to observation at 6 months.</td>
</tr>
<tr>
<td>11</td>
<td>2008</td>
<td>Chan WM</td>
<td>63</td>
<td>Half-dose PDT superior to observation for acuity and thickness at 12 months.</td>
</tr>
<tr>
<td>12</td>
<td>2004</td>
<td>Verma L</td>
<td>30</td>
<td>Diode laser superior to argon green laser at 1 month for acuity.</td>
</tr>
</tbody>
</table>

CSC = central serous chorioretinopathy; N = sample size; PDT = photodynamic therapy; Ref. = reference number.
a low power of 100 to 200 mw. However, thermal laser can induce a scotoma, may increase the risk of late CNV, and is not effective in cases with diffuse RPE decompensation. Therefore, it is used only in select extrafoveal cases with focal leakage. Micropulse sub-threshold diode laser shows increasing promise but requires further study before widespread use for CSC.

**Anti-VEGF**

There is mounting evidence that anti-VEGF agents are not effective for CSC. A recent prospective, randomized trial demonstrated superiority of reduced-fluence PDT over ranibizumab. Care must be taken in interpreting positive study results regarding CSC because the natural history is quite favorable.

**Systemic agents**

Systemic anti-glucocorticoids seem a logical approach for refractory cases, but conclusive randomized clinical trial data are lacking to date. Small series exist to support a number of agents, including mifepristone, ketoconazole, rifampin, fenesteride, and eplerenone. Patients with chronic severe CSC that is recalcitrant to local therapy may consider these agents. Unfortunately, the data as of yet remain unconvinced to recommend detection and eradication of *H. pylori*, nor do they support high-dose anti-oxidant supplementation. Lastly, for the most severe cases with exudative detachment, surgical drainage is an option.

**REFERENCES**


Howard F. Fine, MD, MHSc, can be reached at the Department of Ophthalmology, Rutgers – University of Medicine and Dentistry of New Jersey, NJ Retina, 10 Plum St., Suite 600, New Brunswick, NJ 08901; 732-220-1600; fax: 732-220-1600; email: hffine@gmail.com email.

Michael D. Ober, MD, can be reached at Retina Consultants of Michigan, 29201 Telegraph Rd., Suite 606, Southfield, MI 48034; 248-356-8610; fax: 248-356-6473; email: obermike@gmail.com email.

Seenu M. Hariprasad, MD, can be reached at the Department of Ophthalmology and Visual Science, University of Chicago, 5841 S. Maryland Avenue, MC2314, Chicago, IL 60637; 773-795-1326; email: retina@uchicago.edu.

Disclosures: Dr. Fine is a consultant and/or speaker for Allergan, Genentech, and Regeneron and has equity or patent interests in Auris Surgical Robotics. Dr. Ober is a consultant or speaker for OD-OS, Bayer, and Allergan. Dr. Hariprasad is a consultant or on the speakers' bureau for Regeneron, Takeda, Alcon, Allergan, Bayer, Optos, Ocular Therapeutics, and OD-OS.