Central Serous Chorioretinopathy (CSC)

Subjects: Pathology

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Central serous chioretinoapthy (CSC) is a common chorioretinal disorder characterized by an idiopathic retinal serous detachment of the retina, associated with one or multiple areas of leakage originating from the choroid through a defect in the retinal pigment epithelium (RPE), the outer blood–retina barrier. Several pharmacological treatment options have been investigated for its treatment; however, there is still no significant evidence about the role of pharmacological agents for the management of CSC. To date, photodynamic therapy (PDT) remains the gold standard.

Central serous chorioretinopathy choroid retina

1. Introduction

CSC accounts for the fourth most frequent cause of retinopathy, after age-related macular degeneration, diabetic retinopathy and retinal vein occlusions[1]. The reported incidence of the disease is approximately 9.9 cases per 100,000 men and 1.7 per 100,000 women, showing an increased prevalence in men (almost six times higher) as compared with women[2]. Several risk factors have been associated with the pathogenesis of CSC; in particular, psychosocial stressors, a type A personality, glucocorticosteroid use, trait anxiety, endogenous hypercortisolism and pregnancy have been shown to display important roles in this regard[1][3][4].

Clinically, CSC presents with a central scotoma, which may be often associated with distorted vision (metamorphopsia) and alterations in color perception (dyschromatopsia); at the first visit, the best-corrected visual acuity (BCVA) generally ranges from 20/20 to 20/200[5].

Many authors subdivide CSC into two clinical subtypes: the acute form (aCSC), which typically resolves within 3–4 months without need for being treated, and the chronic form (cCSC), which is characterized by the presence of persistent serous detachment visible by optical coherence tomography (OCT) for longer than 4–6 months; in some cases, cCSC may lead to permanent structural damage of the RPE and the photoreceptor cell layer, causing irreversible long-term visual impairment[6][7][8].

2. Photodynamic Therapy (PDT)

Photodynamic therapy was introduced as an off-label treatment modality for CSC in 2003. This technique works by stimulating with a nonthermal infrared laser light (wavelength of 689 nm) verteporfin, a photosensitive dye injected intravenously, which accumulates in the altered choroidal vessels; then, verteporfin photo-stimulation leads to

oxidative damage and remodeling of the choroidal microvasculature, causing ultimately SRF reabsorption[9]. Importantly, due to PDT high selectivity, the retinal photoreceptors layer is usually spared[10].

In the pivotal study, Yannuzzi et al. analyzed the effect of ICG-guided full-dose (6 mg/m^2) PDT in 20 eyes of patients with cCSC. The authors found the complete resolution of macular detachments in 12 patients and incomplete resolution in another eight eyes. After a 6-week follow-up period, the mean BCVA increased significantly by 0.55 lines; no procedure-related adverse events were reported[11]. Similarly, Cardillo Piccolino et al. found that macular exudation resolved completely in 81% of the patients with cCSC after PDT treatment[12].

In a subsequent non-randomized, multicenter study, 82 eyes of 72 patients with cCSC were treated with full-dose PDT. They reported a complete resorption of SRF in 100% of the patients and an increase in BCVA (1.9 ± 2.4 Snellen lines) after an average follow-up period of 12 months. In the same study, reactivation of the disease was found only in two eyes (2%)[13].

In another multicenter, prospective, non-randomized study, 42 patients with cCSC were enrolled and treated with either ICGA-guided full-fluence PTD or low-fluence PDT. They found a complete reabsorption of SRF in 15 eyes in the full-fluence and 21 eyes in the low-fluence PDT groups (79% vs. 91%; $p = 0.5$). In addition, BCVA improved significantly in both the groups in all times ($p < 0.01$)[14].

Full-dose PDT has been reported not to be free from possible adverse events, including focal RPE losses, treatment-related CNVs, chronic hypoperfusion of the choroid and pigmentary changes[15].

In this regard, different PTD algorithms have been investigated, in order to decrease the probability of procedure-related adverse events. Verteporfin can be administered intravenously either at full-dose (6 mg/m^2) or at half-dose (3 mg/m^2); moreover, the applied light at the wavelength of 689 nm can be modulated either at a fluence of 50 J/cm^2 or at half-fluence (25 J/cm^2); lastly, treatment duration can be 83 s (full-time PTD) or 42 s (half-time PDT)[6].

In a retrospective study on 64 eyes from 60 patients with cCSC, 36 eyes were treated with low-fluence PDT (25 J/m^2) and 28 eyes with half-dose verteporfin PDT (3 mg/m^2). It was described that 91.6% of the eyes in the low-fluence group and 92.8% of them in the half-dose one had full reabsorption of SRF ($p = 0.703$). Moreover, BCVA improved, respectively, by 7.4 letters and 4.8 letters in the low-fluence and half-dose groups ($p = 0.336$)[16].

Differently, in a retrospective, multicenter study on 56 patients with cCSC, Nicolò et al. compared the clinical efficacy between 28 patients treated with half-dose PDT and 28 treated with half-fluence PDT. They reported a significant increase ($p < 0.001$) in average logMAR. BCVA improved significantly in the half-fluence group (from 0.187 (±0.187) to 0.083 (±0.164)) and in the half-dose group (from 0.126 (±0.091) to 0.068 (±0.091)) at 12 months, without a significant difference between the two treatment regimens. Moreover, after 1 month, complete reabsorption of SRF was found in 61.3% and 86.2% of the eyes in half-fluence and half-dose PDT groups, respectively ($p = 0.04$). After 12 months, full resolution of SRF was obtained in 83.9% and 100% of the eyes in half-

fluence and half-dose PDT groups, respectively (p = 0.0529). Results from this study suggested that half-dose PTD may achieve more rapid and lasting resolution of the fluid as compared with half-fluence PDT[17].

Other studies reported that half-fluence PDT had a similar clinical efficacy to full-fluence PDT, and likewise, the half-dose PDT achieved comparable outcomes to the full-dose PDT[18][19].

Shiode et al. revealed that also halving the PDT irradiation time for treating patients with cCSC has led to similar clinical outcomes to adopting the half-dose PDT regimen[20]; these results were subsequently confirmed by Liu et al. in another study[21].

Furthermore, the multicenter PLACE trial revealed that a half-dose of PDT was superior to high-density subthreshold micropulse laser treatment, another laser technique commonly adopted for treating cCSC[22].

With regard to the optimal PDT dosage, it was found that half-dose PDT was more effective than a 30% dosage, with 95% of patients obtaining a complete SRF resolution, as opposed to 75% in the 30% dosage group[23].

Overall, PDT may be considered a safe procedure; in fact, Silva et al. reported in a 4-year follow-up safety study that full-dose PDT was not associated with the onset of side effects[24]; however, a meta-analysis revealed that patients treated with full-dose PTD had a greater percentage of side effects compared to the placebo group (22–42% vs. 16–23%), including abnormal vision, decreased vision and visual field defects[25]. Given this background, a reduced-setting PDT (half-dose, half-fluence and half-time PDT) has been largely employed in the clinical practice for the treatment of CSC, showing overall a good tolerability profile and the lack of any serious procedure-related adverse events[22].

However, it should be repeated that PDT might be ineffective or partially effective in inducing the resolution of the fluid in advanced forms of cCSC, associated with posterior cystoid retinal degeneration[26].

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