Contents lists available at ScienceDirect

Advances in Ophthalmology Practice and Research

Full Length Article

Crossover to PDT after the unsuccessful micropulse laser treatment of central serous chorioretinopathy

Maciej Gawęcki [a,b], Krzysztof Kiciński [b], Andrzej Grzybowski [c,*]

[a] Dobry Wzrok Ophthalmological Clinic, 80-822, Gdansk, Poland
[b] Department of Ophthalmology, Pomeranian Hospitals in Wejherowo, 84-200, Wejherowo, Poland
[c] Institute for Research in Ophthalmology, Foundation for Ophthalmology Development, Poznan, Poland

ARTICLE INFO

ABSTRACT

Purpose: Subthreshold micropulse laser (SML) and photodynamic therapy (PDT) are among the most effective therapeutic modalities applied to central serous chorioretinopathy (CSCR). This study aimed to evaluate the efficacy and durability of PDT in CSCR cases unresponsive to at least two SML treatments.
Methods: The study included 26 consecutive eyes of 24 patients (21 males and three females) with chronic CSCR. In all cases, a lack of reduction in subretinal fluid (SRF) levels was noted after at least two consecutive SML sessions. The parameters of best corrected visual acuity (BCVA) and spectral domain optical coherence tomography (SD-OCT) were evaluated at baseline and 1, 3 and 12 months post-PDT.
Results: The mean duration of symptoms in the group was 53.81 ± 39.48 months, the mean age of the patients was 49.26 ± 12.91 years, and the mean subfoveal choroidal thickness (SFCT) was 572.11 ± 116.21 mm. Complete resorption of SRF was observed in 21 out of 26 eyes (80.77%) at 1 month and sustained in 18 cases (69.23%) at 12 months. At 12 months, in the sustained group, BCVA improved significantly from 0.39 ± 0.18 to 0.19 ± 0.2 logMAR ($P = 0.01$), central subfoveal thickness (CST) reduced from 316.44 ± 75.83 mm to 197.67 ± 22.99 mm ($P < 0.0001$), and SFCT reduced from 579.28 mm to 446.78 mm ($P < 0.0001$).
Conclusions: PDT provides the opportunity for the successful treatment of CSCR unresponsive to SML treatment. Improvements are possible even in cases with a long duration of symptoms and significant alterations in retinal morphology. Thus, PDT should be considered for patients with prominently increased choroidal thickness.

1. Introduction

Central serous chorioretinopathy (CSCR) is a complex medical entity with unclear pathogenesis and a lack of precise recommendations for its treatment. Despite being treated as a benign condition for many years, more recent research have proven its damaging character especially in long-lasting cases, with some reports of serious visual loss even after just a few months from disease onset.[1–4] As the main hallmark of disease is subretinal fluid (SRF) and, in chronic cases, intraretinal cysts, reducing their presence became the main goal of investigated therapies. Among treatment options tried in the treatment of CSCR was classic laser photocoagulation (LPC) of the leakage point, applicable in selected cases.[5–7] Nowadays, there is a solid trend to use non-damaging to the retina techniques, such as subthreshold micropulse laser (SML), which does not harm the retinal tissue, but improves the function of retinal pigment epithelium (RPE).[8–10] Moreover, in the face of shortage of

verteporfin (Visudyne) necessary for the photodynamic therapy (PDT), by some surgeons SML has been used as a first line treatment of CSCR.[11,12] Nevertheless, in chronic CSCR, often complicated by secondary intraretinal fluid (IRF), successful outcomes of SML, defined as complete SRF and IRF remission, are reported with variable frequency: 24%–92% depending on the study.[13–16] This leaves a significant proportion of patients unresponsive to treatment and with persistent SRF and sometimes IRF.[17]

Among other treatment modalities used in CSCR, PDT seems to provide the highest rate of remissions. Despite the use of different strategies regarding Visudyne dose and laser fluence, reported results were similar: most studies prove very high percentage of patients who present with SRF resolution after this treatment (90%–100%).[18–22] Moreover, complications associated with this treatment, such as such retinal pigment epithelium (RPE) tear or the development of macular neovascularization (MNV) occur very seldom.[23–25] As many cases of CSCR are considered the

Table 1
Descriptive statistics for numerical traits in the study cohort at baseline (n = 26).

Analyzed trait	Complete fluid resorption	Statistical parameter				
		M	SD	Me	Q_1-Q_3	P-value
Age (years)	Yes	44.86	9.41	43.00	40.00–51.00	**0.0016**
	No	67.60	8.76	69.00	59.00–75.50	
	Overall	49.26	12.91	44.50	41.75–56.25	
Best corrected visual acuity (logMAR)	Yes	0.41	0.19	0.40	0.30–0.49	0.5073
	No	0.43	0.27	0.40	0.18–0.70	
	Overall	0.42	0.20	0.40	0.27–0.53	
Disease duration (months)	Yes	56.05	42.60	48.00	22.00–90.00	0.8701
	No	44.40	23.08	48.00	21.00–66.00	
	Overall	53.81	39.48	48.00	23.00–75.00	
Number of micropulse laser sessions	Yes	3.19	1.47	3.00	2.00–4.00	**0.0284**
	No	4.80	1.92	4.00	3.50–6.50	
	Overall	3.50	1.65	3.00	2.00–4.00	
Photodynamic therapy, diameter (μm)	Yes	5933.33	2009.56	6000.00	4500.00–6500.00	0.4579
	No	5200.00	1643.17	6000.00	3500.00–6500.00	
	Overall	5792.31	1936.37	6000.00	4500.00–6500.00	
Central subfoveal thickness (μm)	Yes	289.20	73.35	307.00	255.00–368.00	0.2685
	No	315.24	115.27	270.00	208.50–379.50	
	Overall	310.23	80.87	288.00	240.25–364.00	
Subfoveal choroidal thickness (μm)	Yes	587.43	116.29	584.00	503.50–673.50	0.1733
	No	507.80	101.95	535.00	432.00–570.00	
	Overall	572.11	116.21	567.50	505.25–650.00	
Macular volume (mm³)	Yes	8.44	0.73	8.46	7.98–8.77	0.6020
	No	8.24	0.92	7.77	7.67–9.05	
	Overall	8.40	0.75	8.35	7.82–8.76	

M – mean; Me – median; SD – standard deviation; Q – quartile.

spectrum of pachychoroid diseases and PDT directly targets the choroidal vasculature, some surgeons regard PDT as the only effective option for chronic CSCR.[26]

The goal of our study was to evaluate the efficacy of crossover to PDT after the unsuccessful SML treatment of chronic CSCR, assess the durability of the treatment effect, as well as provide baseline characteristics of eyes with CSCR unresponsive to SML.

2. Materials and methods

The study was approved by the local bioethics committee of Okręgowa Izba Lekarska w Gdańsku (approval no. KB -35/23) on August 16, 2023 and conducted according to the guidelines of the Declaration of Helsinki. The material comprised 26 eyes of 24 patients (21 males and three females, with two bilateral cases) with chronic CSCR who were subjected to SML treatment but showed no significant morphological effect, defined as the complete resorption or reduction (measured as the reduced fluid height) of subretinal and intraretinal fluid (IRF was present in long-lasting cases with significantly altered retinal morphology, similarly to reports of other authors.[17] Unresponsiveness to SML was defined as a lack of improvement after a minimum of two SML sessions. Both 577 nm and 810 nm micropulse lasers were considered in the study. SML 577 was applied in different centers before the patient came under the care of Dobry Wzrok Ophthalmological Clinic. At least one session of SML 810 nm was tried in our center, however without success.[27] Our laser protocol followed the LIGHT society guidelines with 1.7 W laser power, 500 μm spot size, 0.3s Spot duration and 5% Duty Cycle.

All patients were consecutive and treated with PDT in the Dobry Wzrok Ophthalmological Clinic between July and September 2022, when a series of verteporfin vials could be obtained at the time of a drug shortage. Due to that shortage, only one PDT session was possible to be applied for each patient. Recurrencies were treated with other treatment modalities, such as Eplerenone or another SML. Now of PDT treatment and during the follow-up, none of the patients, excluding recurrencies, were receiving any concurrent medications.

The diagnosis of CSCR was made or confirmed based on diagnostic

tests performed at baseline and revision of the patient's medical history. The diagnostic criteria for CSCR used in the study were adopted from the CSCR International Group, which published modern, multimodal imaging-based criteria for CSCR diagnosis and classification in 2020.[28] Among these, the current or past presence of SRF and alterations of the RPE present on fundus autofluorescence (FAF) were of primary importance. Other criteria, of which only one was necessary for a diagnosis, included leakage on fluorescein angiography (FA), the hyperpermeability of the choriocapillaris on indocyanine green angiography (ICGA), and increased choroidal thickness.

All patients underwent the following examinations at baseline: BCVA, spectral domain optical coherence tomography (SD-OCT), and OCT-angiography (REVO FC 130, 2023, Optopol Technology, Zawiercie, Poland), FAF (Visucam 524, 2018, Carl Zeiss Meditec AG, Jena, Germany), and FA (Visucam 524, 2018, Carl Zeiss Meditec AG, Jena, Germany) either performed on site or evaluated if the patient underwent these procedures outside the center. ICGA (Visucam 524, 2019, Carl Zeiss Meditec AG, Jena, Germany) was performed on every patient directly before each PDT session. SD-OCT measurements included central subfoveal thickness (CST), macular volume (MV), and subfoveal choroidal thickness (SFCT). CSCR cases complicated by MNV were excluded from the study. The assessment of MNV presence was based on the result of OCT-angiography. PDT was performed with half of the standard dose: 3 mg/m² and 50 J/cm² laser fluence (Vitra 689, 2020, Quantel Medical, Cournon d'Auvergne Cedex, France). The amount of verteporfin that was injected was calculated to achieve the above parameters from each patient's body weight and height. The verteporfin was dissolved in 30 ml of 5% glucose solution and automatically injected for 15 min. Five minutes later, the 689 laser was applied using the Mainster wide-field 1.5 × ocular lens. The treatment area was defined based on ICGA results as the area of hyperpermeability of the choriocapillaris. In cases with diffuse hyperpermeability of the choriocapillaris, the whole area of hyperfluorescence was covered with laser spot (available maximum of 8000 μm) with a 500 μm margin and irradiated for a standard 83 s. In cases, when the target area was larger or irregular, the second irradiation to the remaining surface was performed immediately after the first one.

Table 2
Spearman's rank correlation coefficients as regards the numerical traits assessed in the study cohort at baseline.

Analyzed trait	logMAR	Central subfoveal thickness	Subfoveal choroidal thickness	Macular volume
Age	0.19	−0.15	−0.13	−0.12
	0.3470	0.4555	0.5245	0.5582
Disease duration	0.25	0.15	0.08	−0.20
	0.2264	0.4700	0.6788	0.3350
Best corrected visual acuity (logMAR)		0.14	**0.41**	0.05
		0.4861	**0.0380**	0.7918
Central subfoveal thickness			0.06	**0.62**
			0.7854	**0.0007**
Subfoveal choroidal thickness				−0.02
				0.9273

First row: Spearman's rho correlation coefficient; second row: *P*-value.

After the procedure, patients were advised to avoid sunlight and wear sunglasses for 48 h. The first follow-up visit was scheduled 1 month after the PDT procedure. In cases with complete resolution of fluid, the subsequent visit was arranged after the next 2 months, that is, 3 months after treatment. After that, patients were followed up regularly, and the final follow-up visit was recorded 12 months after PDT. At each follow-up visit, the following diagnostic tests were performed: BCVA measurement, SD-OCT and angio-OCT scans, color fundus photography, and FAF. In cases that did not respond to PDT, other treatment modalities were tried, namely, SML 810 nm or thermotherapy with a 689 nm laser; alternatively, patients were followed by their local ophthalmologists.

2.1. Statistical analysis

Analysis of the results of PDT crossover included the percentage of patients with complete resorption of fluid, number of recurrences after successful PDT, and changes in BCVA, CST, MV, and choroidal thickness. The correlations between patient age, the number of preceding SML sessions, SFCT, CST, MV, and response to PDT were also analyzed.

Numerical traits were depicted through their mean, standard deviation, median, and lower-to-upper quartile values. The normality of the data distribution was assessed using the Shapiro–Wilk W test. A mixed model with repeated measures was fitted to estimate the significance of changes in the investigated traits throughout the 12-months observation period. Spearman's rank correlation *rho* coefficients were computed when assessing the relationships between selected variables measured on different scales. A *P*-value <0.05 was deemed statistically significant. All the computational procedures were performed using NCSS 2023 Statistical Software (NCSS, LLC. Kaysville, Utah, U.S.A.)

3. Results

The basic baseline parameters of the study group are provided in Table 1. All patients presented with SRF at baseline but also with other retinal alterations: cystic changes in the neurosensory retina were noted in 7/26 eyes, fibrin in the SRF in 7/26 eyes, and pigment epithelial detachment (PED) within the SRF cavity in 7/26 eyes (all 26.9%). At least one such alteration was noted in 17/26 eyes (65.38%).

Fluorescein angiography photographs in all cases revealed ill-defined areas of hyperfluorescence corresponding to leakage or staining, window defects of the RPE and sometimes areas of PED. There were no localized points of leakage that could be possible a subject to classic photocoagulation.

Results of the ICGA in all cases showed placoid areas of diffuse hyperpermeability of choriocapillaris of different size, which was reflected in the adjustment of the laser spot diameter used for treatment: it ranged from 3000 to 7000 μm. In two cases it was necessary to perform additional irradiation to the area extending beyond the first applied laser spot during the same session.

At the first post-treatment visit at 1-month, complete resorption was observed in 21/26 eyes (80.77%). Non-responders to PDT treatment were statistically significantly older than patients in whom complete resolution of SRF was noted (67.60 ± 8.76 versus 44.86 ± 9.41 years, *P* = 0.0016) and had a higher mean number of unsuccessful SML treatments before switching to PDT (4.8 ± 1.92 versus 3.19 ± 1.47). There were no significant differences between responders and non-responders regarding disease duration, CST, MV, SFCT, and PDT laser spot diameter. Analysis of the correlation between SD-OCT measurements and age, BCVA, and disease duration revealed that poorer BCVA values were associated with higher SFCT measurements, and lower CST values were strongly associated with lower MV values (Table 2). After PDT treatment, BCVA and all SD-OCT parameters significantly improved (Table 3) (see Fig. 1).

Complete resolution of CSCR after PDT was maintained throughout the study in 18 cases (69.23%). The results of the BCVA and SD-OCT measurements of these patients throughout the study are provided in Table 4. It should be noted that BCVA in that group improved significantly from 0.39 ± 0.18 to 0.19 ± 0.2 logMAR (*P* = 0.01). Recurrence was noted in three eyes at the 3-months follow-up visit. These patients, and remaining 5 non-responders to PDT, were treated with oral 50 mg Eplerenon (8 cases), another session of SML 810 nm (7 cases) and 689 nm thermotherapy with laser set at 150 J/cm2 without Verteporfin (1 case). Three eyes out of the eight eyes responded: one recurred eye treated with 689 nm thermotherapy and two PDT non-responders that improved after another SML 810 nm session. Thus, 21 eyes presented with CSCR remission at the end of the study (Fig. 2). Examples of successful PDT treatment in complex CSCR cases visualized by the total resorption of SRF and intraretinal fluid is presented at the SD-OCT scans in Fig. 3 A and B.

No adverse events related to the treatment were noted in the treated eyes during the follow-up.

Table 3
Repeated measurements of the investigated ophthalmological parameters in the study cohort from baseline to 1-month follow-up (n = 26).

Analyzed trait	Time point	Statistical parameter				
		M	SD	Me	Q₁-Q₃	*P*-value
Best corrected visual acuity (logMAR)	**Baseline**	0.42	0.20	0.40	0.27–0.53	**0.0005**
	1 month	0.29	0.22	0.25	0.16–0.40	
Central subfoveal thickness (μm)	**Baseline**	310.23	80.87	288.00	240.25–364.00	**<0.0001**
	1 month	225.11	62.05	191.25	191.25–243.50	
Subfoveal choroidal thickness (μm)	**Baseline**	572.11	116.21	567.50	505.25–650.00	**0.0001**
	1 month	480.38	103.85	490.00	388.00–547.75	
Macular volume (mm³)	**Baseline**	8.40	0.75	8.36	7.82–8.76	**00001**
	1 month	7.80	0.52	7.74	7.53–8.12	

M – mean; Me – median; SD – standard deviation; Q – quartile.

Table 4
Repeated measurements of the investigated ophthalmological parameters in the study cohort that responded to PDT from baseline to 12-months follow-up (n = 18).

Analyzed trait	Time point	Statistical parameter				
		M	SD	Me	Q₁-Q₃	*P*-value
Best corrected visual acuity (logMAR)	Baseline	0.39	0.18	0.40	0.27–0.42	**0.0108**
	1 month	0.22	0.17	0.20	0.10–0.30	
	3 months	0.21	0.21	0.18	0.07–0.23	
	12 months	0.19	0.20	0.10	0.05–0.25	
Central subfoveal thickness (μm)	Baseline	316.44	75.83	298.00	260.50–376.50	**< 0.0001**
	1 month	204.44	45.64	198.50	169.75–218.25	
	3 months	195.11	23.77	191.00	180.00–214.50	
	12 months	197.67	22.99	198.00	183.25–216.75	
Subfoveal choroidal thickness (μm)	Baseline	579.28	118.56	586.00	499.75–661.75	**< 0.0001**
	1 month	464.50	106.26	451.00	365.00–542.50	
	3 months	444.56	100.20	445.00	353.75–536.50	
	12 months	446.78	89.16	455.00	360.00–503.25	
Macular volume (mm³)	Baseline	8.44	0.77	8.42	8.04–8.76	**< 0.0001**
	1 month	7.65	0.42	7.66	7.50–7.95	
	3 months	7.61	0.37	7.67	7.47–7.88	
	12 months	7.67	0.35	7.70	7.47–7.92	

M – mean; Me – median; SD – standard deviation; Q – quartile.
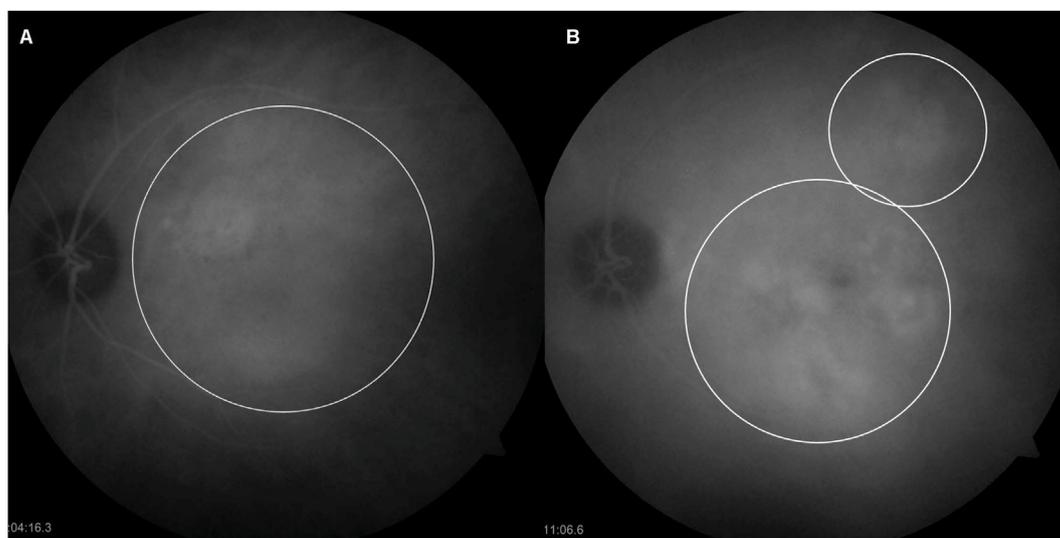
Fig. 1. (A) ICGA with areas of hyperpermeability of choriocapillaris and marked boundaries of the PDT laser spot. In case (B) additional irradiation was performed (smaller circle).
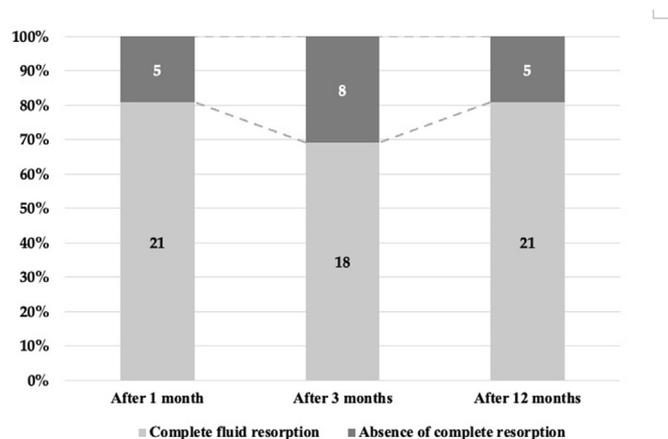

Fig. 2. Complete fluid resorption during the observation period in all subjects (Cochran's Q test; *P* = 0.1738).

4. Discussion

The results of our study showed the high effectiveness of PDT in eyes unresponsive to SML treatment. PDT was effective in providing absolute resorption of subretinal and intraretinal fluid in the majority of patients (80% at 1 month), with durability of the effect in 70% at 12 months post-treatment. BCVA improved significantly in the responders by mean 0.2 logMAR to a value of about 0.63 on the Snellen chart. However, this still leaves a substantial deficit in visual acuity, which can be attributed to alterations of the retinal architecture (retinal thinning) observed after the resorption of fluid. The mean CST of 197.67 μm and mean MV of 7.67 mm³ measured at 12 months post-treatment were much below the normal values in the matched control group reported by the same authors in a previous study (238.6 μm and 8.06 mm³, respectively).[1] It must be emphasized that exactly the same visual deficit was reported following the resolution of chronic CSCR in other studies.[1,2] PDT enabled a significant reduction of SFCT; however, the final choroidal thickness remained high (446.78 μm). Obviously, this moderate reduction was sufficient for the therapeutic success of the procedure.

PDT has been used for the treatment of CSCR for about 20 years. Since its first off-label use for the management of CSCR in 2003, the hypothesis
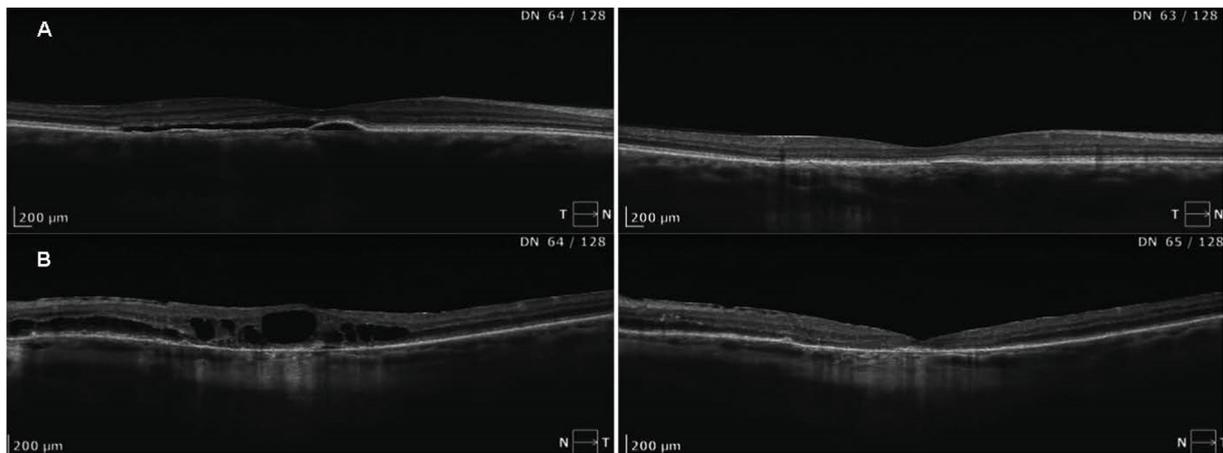
Fig. 3. Examples of successful treatment with PDT in patients unresponsive to SML (SD-OCT scans). (A) present a complex CSCR case complicated by pigment epithelial detachment despite absence of subretinal neovascularization. (B) shows a case with predominant intraretinal alterations and just a subtle presence of subretinal fluid. It might be assumed, that larger amount of SRF was present at earlier stage, but with chronicity of the disease it migrated to the neurosensory retina through the compromised RPE.

of its action has not much changed. PDT is believed to promote choriocapillaris hypoperfusion through direct interaction with vessels' endothelium, reduction of vascular hyperpermeability and decrease of choroidal congestion.[29–32] SML, on the other hand, works through direct thermal stimulation of the RPE. It evokes the production of heat shock proteins, which have anti-inflammatory and *anti*-vasogenic properties, restores anti-oxidative cellular balance and improves RPE function as a pump.[33,34] Hence, RPE integrity is required to obtain therapeutic effect. With the target set at the choroid, PDT seems to work better than SML in patients with compromised RPE – impairment characteristic for long-lasting and complex CSCR cases, such as analyzed in our study group.

Patients unresponsive to PDT were significantly older compared to responders. That fact, naturally inclines to think of them as patients with neovascular form of CSCR or even benign form of wet age-related macular degeneration (AMD). Nevertheless, neovascularization was not detected in these cases neither by routinely performed OCTA nor by ICGA examination. We think that poor response may be attributed to impaired function of the choroid associated with older age and its insufficiency to eliminate SRF and IRF. In such patients, transient hypoperfusion at the level of choriocapillaris elicited by the PDT does not effect in resorption of the fluids typical for CSCR, contrary to younger patients without impaired choroidal function.

The topic of crossover to PDT after unsuccessful SML was directly addressed only in one study: the REPLACE trial.[35] The study, which was an extension of the large-scale PLACE trial,[36] showed the efficacy of such a switch, regarded as the complete resolution of SRF, in 81% of cases (32 eyes were included). Our study revealed similar results regarding morphological retinal response after crossover to PDT. Interestingly, contrary to REPLACE, we noted significant mean BCVA improvement in our group, despite the very long duration of symptoms and low initial visual acuity. Moreover, the cohort that we analyzed underwent SML more than once; thus, the unresponsiveness to this treatment was definitively ascertained.

CSCR therapy remains problematic in complex cases. Different treatment modalities have been tried, but precise recommendations regarding the order or line of therapy are lacking.[37,38] The problem with the validation of the effectiveness of different therapeutic modalities in CSCR may be linked to the methodology of clinical trials. Usually, analysis of the results of treatment is conducted for the whole cohort of CSCR patients. Although only acute/chronic cases are evaluated separately sometimes, the assessment of specific morphological subtypes is rare. It is plausible that some treatment options could prove effective for certain CSCR subtypes but not for the whole population of CSCR patients.

We believe that defining the clinical features of CSCR subtypes responsive to available therapies is crucial for successful treatment. We realize that small sample size in our study limits the possibility to draw unequivocal conclusions, however it has to be noted, that patients unresponsive to SML present with duration of symptoms longer than usually reported for chronic CSCR (more than 4 years in our sample)[2,39,40] and SFCT higher than mean numbers reported in other studies (close to 600 μm in our sample).[26,41,42] In this group, higher choroidal thickness is also strongly correlated with poorer visual acuity, so it is plausible that the choroidal changes are predominantly responsible for disease persistence and visual loss, with retinal alterations developing secondarily. We believe that these eyes present as the choroidal CSCR type and should be treated with choroid-oriented therapies. At the early stage of CSCR, pure-choroidal types of CSCR have intact RPE and better visual prognosis[43] and the delay of therapy targeted at the choroid might lead to development of RPE and photoreceptor changes and subsequent visual loss.[44]

The main study limitation is relatively small sample size. This is mainly due to Verteporfin shortage, as it was impossible to obtain larger number of the vials and perform crossover to PDT in higher number of eyes.

5. Conclusions

PDT provides an opportunity for the successful treatment of CSCR unresponsive to SML. Improvements are possible even with a long duration of symptoms and significant alterations in retinal morphology. Thus, PDT should be considered for patients with prominently increased choroidal thickness.

Study approval

The study was approved by the local bioethics committee of Okręgowa Izba Lekarska w Gdańsku (approval no. KB-35/23) on August 16, 2023 and conducted according to the guidelines of the Declaration of Helsinki.

Author contributions

Conceptualization MG, methodology MG, AG, KK, software: KK, validation: MG, KK, AG, formal analysis MG, KK, investigation MG, KK, resources MG, KK, data curation KK, writing- original draft preparation MG, writing – review and editing AG, MG, KK, All authors have read and agreed to the published version of the manuscript.

Funding

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

References

1. Gawęcki M, Grzybowski A. Ganglion cell loss in the course of central serous chorioretinopathy. *Ophthalmol Ther.* 2023 Feb;12(1):517–533. https://doi.org/10.1007/s40123-022-00625-5.
2. Gawęcki M, Jaszczuk-Maciejewska A, Jurska-Jaśko A, et al. Impairment of visual acuity and retinal morphology following resolved chronic central serous chorioretinopathy. *BMC Ophthalmol.* 2019 Jul 25;19(1):160. https://doi.org/10.1186/s12886-019-1171-5. PMC6659242.
3. Gawęcki M, Grzybowski A, Pompein-Batkiewicz M. Significant visual impairment after short-lasting central serous chorioretinopathy. *Case Rep Ophthalmol.* 2022 Sep 19;13(3):678–685. https://doi.org/10.1159/000525924.
4. Gawęcki M, Jaszczuk A, Grzybowski A. Short term presence of subretinal fluid in central serous chorioretinopathy affects retinal thickness and function. *J Clin Med.* 2020 Oct 26;9(11):3429. https://doi.org/10.3390/jcm9113429.
5. Leaver P, Williams C. Argon laser photocoagulation in the treatment of central serous retinopathy. *Br J Ophthalmol.* 1979 Oct;63(10):674–677. https://doi.org/10.1136/bjo.63.10.674.
6. Robertson DM, Ilstrup D. Direct, indirect, and sham laser photocoagulation in the management of central serous chorioretinopathy. *Am J Ophthalmol.* 1983 Apr;95(4):457–466. https://doi.org/10.1016/0002-9394(83)90265-9.
7. Frankhauser F, Kwasniewska S. *Lasers in Ophthalmology.* Kugler Publications; 2003:269.
8. Işık MU, Değirmenci MFK, Sağlık A. Efficacy of the subthreshold micropulse yellow wavelength laser photostimulation in the treatment of chronic central serous chorioretinopathy. *Int J Ophthalmol.* 2020 Sep 18;13(9):1404–1410. https://doi.org/10.18240/ijo.2020.09.11.
9. Gawęcki M. Subthreshold diode micropulse laser combined with intravitreal therapy for macular edema-A systematized review and critical approach. *J Clin Med.* 2021 Mar 31;10(7):1394. https://doi.org/10.3390/jcm10071394.
10. Gawęcki M. Micropulse laser treatment of retinal diseases. *J Clin Med.* 2019 Feb 13;8(2):242. https://doi.org/10.3390/jcm8020242.
11. Goté JT, Singh SR, Chhablani J. Comparing treatment outcomes in randomized controlled trials of central serous chorioretinopathy. *Graefes Arch Clin Exp Ophthalmol.* 2023 Aug;261(8):2135–2168. https://doi.org/10.1007/s00417-023-05996-4. Epub 2023 Mar 2.
12. Zhao T, Li J, Wang Y, et al. Intravitreal injections with anti-VEGF agent aflibercept versus subthreshold micropulse laser for chronic central serous chorioretinopathy: the alternative treatment regimens for verteporfin-shortage in China. *Ann Med.* 2023 Dec;55(1):2227424. https://doi.org/10.1080/07853890.2023.2227424.
13. Gawęcki M, Jaszczuk-Maciejewska A, Jurska-Jaśko A, et al. Functional and morphological outcome in patients with chronic central serous chorioretinopathy treated by subthreshold micropulse laser. *Graefes Arch Clin Exp Ophthalmol.* 2017 Dec;255(12):2299–2306. https://doi.org/10.1007/s00417-017-3783-x. Epub 2017 Aug 22.
14. Scholz P, Ersoy L, Boon CJ, et al. Subthreshold micropulse laser (577 nm) treatment in chronic central serous chorioretinopathy. *Ophthalmologica.* 2015;234(4):189–194. https://doi.org/10.1159/000439600. Epub 2015 Sep. 26.
15. Altınel MG, Acikalin B, Gunes H, et al. Optical coherence tomography parameters as predictors of treatment response to a 577-nm subthreshold micropulse laser in chronic central serous chorioretinopathy. *Laser Med Sci.* 2021 Sep;36(7):1505–1514. https://doi.org/10.1007/s10103-020-03225-6.
16. Arsan A, Kanar HS, Sonmez A. Visual outcomes and anatomic changes after sub-threshold micropulse yellow laser (577-nm) treatment for chronic central serous chorioretinopathy: long-term follow-up. *Eye (Lond).* 2018 Apr;32(4):726–733. https://doi.org/10.1038/eye.2017.293. Epub 2018 Jan 5.
17. Gorhe S, Chugh MK, Goel N, et al. Clinical feature of cystoid macular degeneration in central serous chorioretinopathy. *Indian J Ophthalmol.* 2023 Nov;71(11):3489–3493. https://doi.org/10.4103/IJO.IJO_255_23.
18. Battaglia Parodi M, Arrigo A, Iacono P, et al. Central serous chorioretinopathy: treatment with laser. *Pharmaceuticals.* 2020 Nov 2;13(11):359. https://doi.org/10.3390/ph13110359.
19. Ruiz-Moreno JM, Lugo FL, Armadá F, et al. Photodynamic therapy for chronic central serous chorioretinopathy. *Acta Ophthalmol.* 2010 May;88(3):371–376. https://doi.org/10.1111/j.1755-3768.2008.01408.x. Epub 2009 Nov 27.
20. Iacono P, Da Pozzo S, Varano M, et al. Photodynamic therapy with verteporfin for chronic central serous chorioretinopathy: a review of data and efficacy. *Pharmaceuticals.* 2020 Oct 29;13(11):349. https://doi.org/10.3390/ph13110349.
21. Ruiz-Del-Tiempo MP, Calvo P, Ferreras A, et al. Anatomical retinal changes after photodynamic therapy in chronic central serous chorioretinopathy. *J Ophthalmol.* 2018 Feb 6;2018:4081874. https://doi.org/10.1155/2018/4081874.
22. Lai FH, Ng DS, Bakthavatsalam M, et al. A multicenter study on the long-term outcomes of half-dose photodynamic therapy in chronic central serous chorioretinopathy. *Am J Ophthalmol.* 2016 Oct;170:91–99. https://doi.org/10.1016/j.ajo.2016.07.026. Epub 2016 Aug 9.
23. Tseng CC, Chen SN. Long-term efficacy of half-dose photodynamic therapy on chronic central serous chorioretinopathy. *Br J Ophthalmol.* 2015 Aug;99(8):1070–1077. https://doi.org/10.1136/bjophthalmol-2014-305353. Epub 2015 Feb 13.
24. Flores-Moreno I, Arcos-Villegas G, Sastre M, et al. Changes in choriocapillaris, sattler, and haller layer thicknesses in central serous chorioretinopathy after half-fluence photodynamic therapy. *Retina.* 2020 Dec;40(12):2373–2378. https://doi.org/10.1097/IAE.0000000000002764.
25. Alovisi C, Piccolino FC, Nassisi M, et al. Choroidal structure after half-dose photodynamic therapy in chronic central serous chorioretinopathy. *J Clin Med.* 2020 Aug 24;9(9):2734. https://doi.org/10.3390/jcm9092734.
26. Alovisi C, Piccolino FC, Nassisi M, et al. Choroidal structure after half-dose photodynamic therapy in chronic central serous chorioretinopathy. *J Clin Med.* 2020 Aug 24;9(9):2734. https://doi.org/10.3390/jcm9092734.
27. Keunen JEE, Battaglia-Parodi M, Vujosevic S, et al. International retinal laser society guidelines for subthreshold laser treatment. *Transl Vis Sci Technol.* 2020 Aug 7;9(9):15. https://doi.org/10.1167/tvst.9.9.
28. Chhablani J, Cohen FB, Central Serous Chorioretinopathy International Group. Multimodal imaging-based central serous chorioretinopathy classification. *Ophthalmol Retina.* 2020 Nov;4(11):1043–1046. https://doi.org/10.1016/j.oret.2020.07.026.
29. Battaglia Parodi M, Da Pozzo S, Ravalico G. Photodynamic therapy in chronic central serous chorioretinopathy. *Retina.* 2003 Apr;23(2):235–237. https://doi.org/10.1097/00006982-200304000-00016.
30. Chan WM, Lam DS, Lai TY, et al. Choroidal vascular remodelling in central serous chorioretinopathy after indocyanine green guided photodynamic therapy with verteporfin: a novel treatment at the primary disease level. *Br J Ophthalmol.* 2003 Dec;87(12):1453–1458. https://doi.org/10.1136/bjo.87.12.1453.
31. Yannuzzi LA, Slakter JS, Gross NE, et al. Indocyanine green angiography-guided photodynamic therapy for treatment of chronic central serous chorioretinopathy: a pilot study. *Retina.* 2003;23:288–298. https://doi.org/10.1097/00006982-200306000-00002.
32. Hara C, Maruyama K, Wakabayashi T, et al. Choroidal vessel and stromal volumetric analysis after photodynamic therapy or focal laser for central serous chorioretinopathy. *Transl Vis Sci Technol.* 2023 Nov 1;12(11):26. https://doi.org/10.1167/tvst.12.11.26.
33. Luttrull JK, Sramek C, Palanker D, et al. Long-term safety, high-resolution imaging, and tissue temperature modeling of subvisible diode micropulse photocoagulation for retinovascular macular edema. *Retina.* 2012 Feb;32(2):375–386. https://doi.org/10.1097/IAE.0b013e3182206f6c.
34. Kozak I. Editorial to: the effect of nondamaging subthreshold laser therapy in patients with chronic central serous chorioretinopathy. *Graefes Arch Clin Exp Ophthalmol.* 2023 Dec 1. https://doi.org/10.1007/s00417-023-06316-6.
35. van Rijssen TJ, van Dijk EHC, Scholz P, et al. Crossover to photodynamic therapy or micropulse laser after failure of primary treatment of chronic central serous chorioretinopathy: the REPLACE trial. *Am J Ophthalmol.* 2020 Aug;216:80–89. https://doi.org/10.1016/j.ajo.2020.04.007. Epub 2020 Apr 11.
36. van Dijk EHC, Fauser S, Breukink MB, et al. Half-dose photodynamic therapy versus high-density subthreshold micropulse laser treatment in patients with chronic central serous chorioretinopathy: the PLACE trial. *Ophthalmology.* 2018 Oct;125(10):1547–1555. https://doi.org/10.1016/j.ophtha.2018.04.021. Epub 2018 Jun 14.
37. Zhang X, Lim CZF, Chhablani J, et al. Central serous chorioretinopathy: updates in the pathogenesis, diagnosis and therapeutic strategies. *Eye Vis (Lond).* 2023 Jul 11;10(1):33. https://doi.org/10.1186/s40662-023-00349-y.
38. van Dijk EHC, van Rijssen TJ, Subhi Y, et al. Photodynamic therapy for chorioretinal diseases: a practical approach. *Ophthalmol Ther.* 2020 Jun;9(2):329–342. https://doi.org/10.1007/s40123-020-00250-0. Epub 2020 Apr 11.
39. Toto L, D'Aloisio R, De Nicola C, et al. Short-term comparison between navigated subthreshold microsecond pulse laser and oral eplerenone for chronic central serous chorioretinopathy. *Sci Rep.* 2022 Mar 18;12(1):4727. https://doi.org/10.1038/s41598-022-08764-2.
40. Ersoz MG, Arf S, Hocaoglu M, et al. Patient characteristics and risk factors for central serous chorioretinopathy: an analysis of 811 patients. *Br J Ophthalmol.* 2019 Jun;103(6):725–729. https://doi.org/10.1136/bjophthalmol-2018-312431. Epub 2018 Jul 12.
41. Dhirani NA, Yang Y, Somani S. Long-term outcomes in half-dose verteporfin photodynamic therapy for chronic central serous retinopathy. *Clin Ophthalmol.* 2017 Dec 6;11:2145–2149. https://doi.org/10.2147/OPTH.S151933.

42. Lee SH, Lee J, Kim M, et al. The effect of nondamaging subthreshold laser therapy in patients with chronic central serous chorioretinopathy. *Graefes Arch Clin Exp Ophthalmol.* 2023 Nov 27. https://doi.org/10.1007/s00417-023-06315-7. Epub ahead of print.

43. Arrigo A, Aragona E, Bordato A, et al. Acute central serous chorioretinopathy subtypes as assessed by multimodal imaging. *Transl Vis Sci Technol.* 2021 Nov 1; 10(13):6. https://doi.org/10.1167/tvst.10.13.6.

44. Gawęcki M, Jaszczuk-Maciejewska A, Jurska-Jaśko A, et al. Transfoveal micropulse laser treatment of central serous chorioretinopathy within six months of disease onset. *J Clin Med.* 2019 Sep 6;8(9):1398. https://doi.org/10.3390/jcm8091398.