Original Article

Characteristics of Central Serous Chorioretinopathy without Leakage

Deepika C. Parameswarappa[1,2], Dmitrii S. Maltsev[3], Abhilash Goud[1], Sumit Randhir Singh[1,4], Jay Chhablani[1]

[1]Smt. Kanuri Santhamma Centre for Vitreo-Retinal Diseases, L V Prasad Eye Institute, Hyderabad, Telangana, India, [2]Department of Ophthalmology, Military Medical Academy, St. Petersburg, Russian Federation, Academy for Eye Care Education, L V Prasad Eye Institute, Hyderabad, Telangana, India, [3]Department of Ophthalmology, Military Medical Academy, Saint Petersburg, Russia, [4]Department of Retina and Uveitis, L V Prasad Eye Institute, GMR Varalakshmi Campus, Visakhapatnam, Andhra Pradesh, India

Abstract

Purpose: To describe optical coherence tomography (OCT) characteristics of central serous chorioretinopathy (CSCR) without any hyperfluorescent leakage on fundus fluorescein angiography (FFA).

Methods: This was a multicentric, retrospective, observational study of ten eyes of ten patients with CSCR without any hyperfluorescence leakage on FFA. Baseline patient characteristics, best corrected visual acuity, and OCT parameters like relative retinal pigment epithelium (RPE) reflectivity at the presumed leak site and control site were measured.

Results: Increased macular thickness, neurosensory detachment, and choroidal thickness were seen at the site of maximum subretinal fluid (SRF). Out of ten eyes, nine had photoreceptor outer segment (PROS) disruption (46% ± 26.33%) at the site of SRF pocket, and five had presumed former leak site characterized by PROS thinning. The presumed leak site demonstrated higher RPE reflectivity compared to the control site (0.92 ± 0.04 vs. 0.87 ± 0.04; $P = 0.0058$).

Conclusion: CSCR without hyperfluorescent leakage on FFA may have PROS damage and changes in RPE hyperreflectivity.

Keywords: Central serous chorioretinopathy, Fundus fluorescein angiography, Optical coherence tomography, Photoreceptor outer segment, Retinal pigment epithelium hyperreflectivity

Address for correspondence: Jay Chhablani, Smt. Kanuri Santhamma Centre for Vitreo-Retinal Diseases, L V Prasad Eye Institute, Banjara Hills, Hyderabad - 500 034, Telangana, India.
E-mail: jay.chhablani@gmail.com
Submitted: 18-Jul-2020; **Revised:** 20-Dec-2020; **Accepted:** 25-Dec-2020; **Published:** 05-Jul-2021

Introduction

Central serous chorioretinopathy (CSCR) is primarily a disease of choroid and retinal pigment epithelium (RPE) characterized by serous neurosensory and RPE detachments. It is characterized by leakage of fluid from the RPE and its accumulation in the subretinal space due to loss of barrier function of RPE.[1] Barrier function of RPE is lost due to hyperpermeable choroidal vessels which increases the hydrostatic pressure leading to RPE detachments.[1,2] Finding the site of the leak and the treatment of the leak are important, especially in cases of persisting fluid, to reduce the photoreceptor damage and vision loss. The leakage, i.e., hyperfluorescence, can be characterized on fundus fluorescein angiography (FFA) as inkblot, smokestack, and as multifocal pattern.[3] Accurate identification of hyperfluorescence can help decide the site for laser photocoagulation to achieve closure of the leak and subsequent resolution of subretinal fluid (SRF).

Previous studies have shown the changes in optical coherence tomography (OCT) at the leakage site such as coincidence of leakage point in the upper half of pigment

Access this article online

Quick Response Code:

Website: www.jcurrophthalmol.org

DOI: 10.4103/joco.joco_35_20

How to cite this article: Parameswarappa DC, Maltsev DS, Goud A, Singh SR, Chhablani J. Characteristics of central serous chorioretinopathy without leakage. J Curr Ophthalmol 2021;33:152-7.

epithelial detachment (PED), area of photoreceptor outer segment (PROS) thinning, dipping of the outer retinal layers, microrip of RPE, and hyporeflective subretinal lucency at the leakage site.[4] However, there are few instances wherein SRF accumulation is seen without any hyperfluorescence on FFA. There is no literature available about OCT findings in eyes without any hyperfluorescence on FFA.

The present study is intended to understand OCT characteristics with regard to RPE reflectivity and PROS integrity of eyes with persistent SRF without any hyperfluorescence on FFA.

Methods

We performed a multicentric, retrospective, observational study of ten eyes of ten patients who were diagnosed as CSCR without any hyperfluorescence on FFA. The local ethics committee approved the study at each center, and a written informed consent was obtained from each participant. CSCR without any leaking was defined as the presence of SRF with no hyperfluorescence which would suggest leakage on FFA in the area of SRF and in other parts of the retina as well. Clinically, neurosensory detachment (NSD) was measured in terms of disc diameters by using fundus photographs. Eyes with signs of chronic RPE damage, double-layer sign, punctate hyperfluorescence on FFA, or the presence of any type of hyperfluorescence were excluded. Baseline patient characteristics, best corrected visual acuity (BCVA), and OCT parameters were analyzed at presentation and at the last follow-up visit. Patients received either treatment in the form of micropulse laser, oral eplerenone, or were observed. OCT volume scans were obtained using swept-source OCT (DRI OCT Triton, Topcon, Tokyo, Japan). FFA was performed using Heidelberg HRA2 (Heidelberg Engineering, Inc., Vista, CA, USA). FFA images were captured till 10 min of late frames.

Optical coherence tomography parameters

Various OCT parameters were analyzed such as central macular thickness (CMT), maximum height of SRF, the presence of PED, maximum height of PED and height of PED at the site of SRF pocket, sub-foveal choroidal thickness (SFCT), and choroidal thickness (CT) at the site of maximum SRF pocket. PROS thickness was measured over the area of SRF pocket in cross-sectional images with the help of inbuilt caliper and analyzed in terms of percentages (from 0% to 100%).[4] Based on previous studies, the area of PROS thinning was adopted as an indicator corresponding to the former leak, and the RPE reflectivity was measured at the site of RPE abnormalities under the area of PROS disruption.[4] PROS thickness was measured from cross-sectional OCT B-scan images at the site of maximum SRF as distance from the inner surface of the inner segment/outer segment band and the outer border of the PROS layer.[4,5] The percentage of PROS thinning was calculated by considering the total area of PROS above the area of SRF and the area of the PROS thinning inside that. PROS thinning referred to reduced thickness of PROS, whereas PROS disruption was referred to total loss PROS. Other features analyzed were the presence of subretinal exudation and choroidal hyperreflective dots.

CMT was measured manually as the distance between internal limiting membrane and anterior border of RPE-Bruch's membrane complex at the fovea. The maximum height of SRF was measured as the distance between outer border of photoreceptor layer and anterior border of RPE-Bruch's membrane complex. SFCT was measured as the distance between Bruch's membrane and choroid–scleral interface.

Reflectivity of RPE at baseline was analyzed by ImageJ software [Figure 1]. Line of 100 ± 10 pixels (approximately 600 μm) was created using a line tool at the level of inner ½

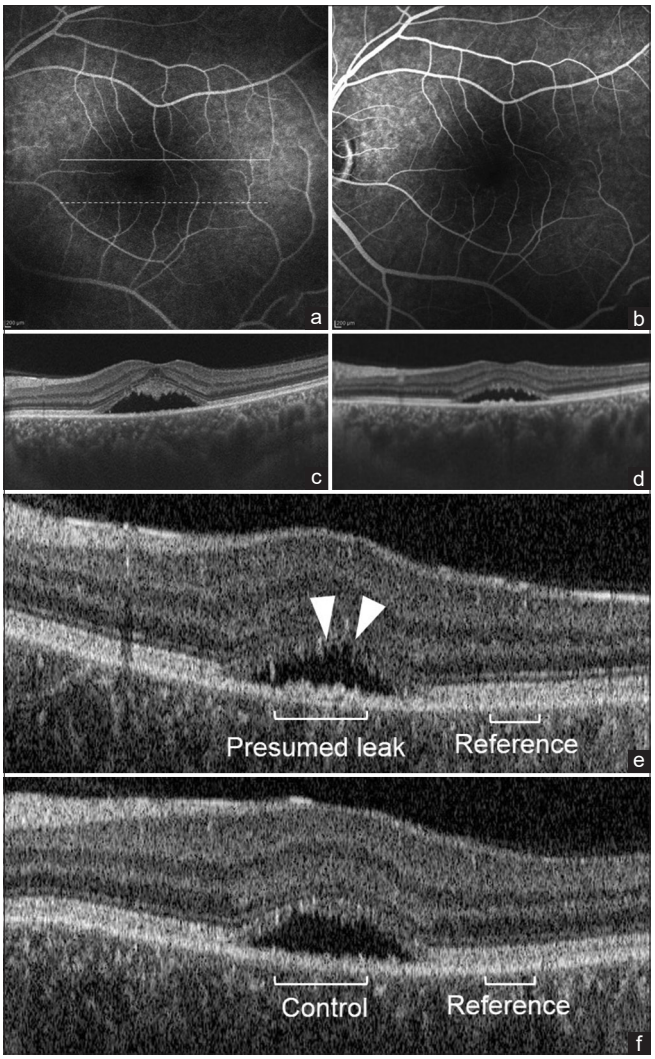

Figure 1: Representative for evaluation of retinal pigment epithelium (RPE) reflectivity in central serous chorioretinopathy without any hyperfluorescence. Fluorescein angiography shows no hyperfluorescence initially (a) and at 6 months (b). Optical coherence tomography (OCT) showed central neurosensory detachment at presentation (c) which persists at 6 months (d). OCT (corresponds to the dashed white line) through the presumed former leak shows RPE abnormalities and photoreceptor outer segment thinning (arrowheads) (e). Mean RPE reflectivity was 178.1 at presumed leak and 195.1 reference area. OCT scan (corresponds to the solid white line) through the control area (f). Mean RPE reflectivity was 170.6 at control area and 197.3 at reference area

height of RPE band within the area of NSD and adjacent to it. A mean length of the line was 600 micrometers (or 100 pixels).

The line tool of ImageJ measures reflectivity along one-pixel line. If the PED or RPE irregularities were presented, the line tool traced the shape of the PED/RPE irregularities at the level of ½ of RPE band thickness. A plot profile was constructed and further analysis was performed followed by the export of numerical data.

The effect of individual factors, such as optical media clarity and RPE pigmentation on the evaluation of RPE reflectivity, was removed by using a relative reflectivity index, which was calculated as the ratio of RPE reflectivity in the area of interest (i.e., site of SRF) to the control site in the reference area. The reference area was defined as an area of unaffected RPE outside the NSD but not closer than 1 mm to the scan border.

For the SRF site and control site, the relative reflectivity was calculated for: (1) mean reflectivity (MR), (2) minimum reflectivity (Rmin), and (3) maximum reflectivity (Rmax). We measured maximum and minimum RPE reflectivity to ascertain that the increase of the mean RPE reflectivity is the main feature of the leak. The decreased Rmin may indicate the presence of RPE defects (specifically in the eyes with previous focal leak) and may secondarily reduce MR despite local increase. The relative RPE reflectivity was evaluated at the presumed leak site with PROS thinning and control site sharing similar morphological characteristic (height of SRF and RPE abnormalities). A review of all cross-sectional scans was done by a blinded grader (D.M.) for the presence of a visible RPE defect and a hypertransmissive track in the underlying choroid.

Statistical analysis was done using SPSS statistical software version 23 (SPSS Inc., Chicago, IL, USA). The data were tabulated as mean ± standard deviation. Statistical significance of the differences in MR, Rmin, and Rmax between the leak site and control site was calculated by repeated measures analysis of variance in view of similar baseline variance of both the sites in the same eye. $P < 0.05$ was considered statistically significant.

Results

The study included ten eyes of ten patients (nine males and one female) of CSCR with no leak. The mean age of patients was 44.5 ± 7.1 years (range, 38–57 years). None of the patients were on any form of steroid treatment at the initial presentation. The mean duration of symptoms was 104.5 ± 79.70 days (range, 10–210 days). The mean BCVA at presentation was 0.20 ± 0.18 logMAR (Snellen equivalent 20/30). All ten eyes had SRF in macular region with foveal involvement. The mean size of SRF pocket, mean CMT, CT, and PED at the height of SRF pocket were compared at baseline and last visit [Table 1]. Out of ten eyes, five eyes had PED at presentation with a mean PED height of 164.4 ± 99.57 µm. Nine eyes had PROS disruption at the site of SRF pocket, and the mean PROS disruption was 46% ± 26.33% [Table 1]. Subretinal deposits were seen in four out of ten eyes, and one eye showed choroidal hyperreflective dots. Representative case is shown as Figure 1.

Out of ten eyes of ten patients, five patients were observed without any treatment. Two patients received micropulse laser (5% duty cycle) with resolution in one patient [Figure 2]. Three patients were treated with oral eplerenone (25 mg BD), among which only one patient showed partial resolution [Figure 3]. The mean follow-up duration was 3.2 months [Table 1]. Among seven eyes with follow-up visits, three had resolution in SRF whereas the other four did not resolve. The mean BCVA of seven eyes at the last follow-up was 0.17 ± 0.17 logMAR (20/30). Seven eyes had follow-up visits, but one among them did not have the OCT scans at the last visit. Out of seven eyes who had

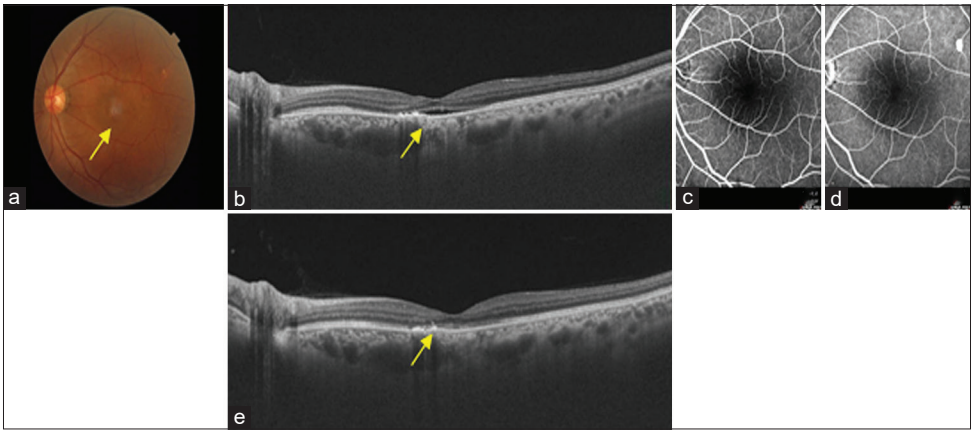

Figure 2: A-35-year-old male with left eye diminution of vision, best corrected visual acuity (BCVA) of 20/40, left eye fundus showed neurosensory detachment (NSD) at the foveal region (a). Optical coherence tomography showed subretinal fluid (SRF) with hyperreflectivity of retinal pigment epithelium (RPE) (arrow). (b) Fundus fluorescein angiography showed no evidence of hyperfluorescence in early phase (c) and in late phase (d) at the site of NSD. The patient was treated with 5% micropulse laser in the NSD area. Three months post 5% micropulse, his BCVA was 20/20, and OCT showed resolution of the SRF and RPE hyperreflectivity (arrow)(e)

follow-up visits, one eye had persistent PED with PED height of 49 µm. PROS disruption at the site of SRF pocket was seen in six eyes at the last visit with a mean PROS disruption of 30.0% ± 31.62% [Table 1]. Subretinal hyperreflectivity was persistent in one patient. Out of six patients who had follow-up scans, five patients showed hyperreflectivity of the RPE at the site of SRF in OCT scans.

In one case with no PROS thinning and RPE abnormalities suggestive for former leak, we found significant area of ellipsoid zone attenuation which encompassed surrounding attached neuroepithelium. Out of ten fellow eyes, two had CSCR with one having leakage site showing hyperfluorescence, and the remaining eight eyes had chronic CSCR changes.

The suspected leak site demonstrated significantly higher mean RPE reflectivity compared to the control site, 0.92 ± 0.04 and 0.87 ± 0.04, respectively (P = 0.0058). There were no statistically significant differences between the suspected leak site and control site in MinR (0.59 ± 0.06 and 0.45 ± 0.07, respectively [P = 0.058]) and MaxR (1.21 ± 0.01 and 1.15 ± 0.05, respectively [P = 0.27]) [Figure 4].

Discussion

CSCR without any leakage/hyperfluorescence on FFA is a rare finding. Previous studies have correlated the site of leakage with PROS thinning; however, there are no reports on CSCR without leakage. Maltsev *et al*. have reported previously that PROS thinning coincided with the leakage points in 88.9% of their patients and suggested that the PROS thinning may result from the washout of the PROS by an active flow through the leakage point.[4] Daruich *et al*. have also reported the erosion of PROS just above the leakage.[5] PROS thinning is variable based on intensity and duration of leak.[4,5] In our study, PROS thinning was seen at the peak of SRF pocket and close to small PEDs. We analyzed OCT parameters of ten eyes of CSCR with no hyperfluorescence on FFA. PROS disruption at the site of SRF pocket was seen in nine eyes with a mean PROS disruption of 46 ± 26.33%.

From previous studies, we learned that RPE abnormalities (small PRE detachments and bumps as well as RPE defects) are typical OCT characteristics for leaks in CSCR. All of this justifies the location of former leaks at the site of RPE abnormalities under the area of PROS thinning. In addition, we analyzed RPE reflectivity within these suspicious areas since it was noticed in acute CSCR cases that RPE adjacent

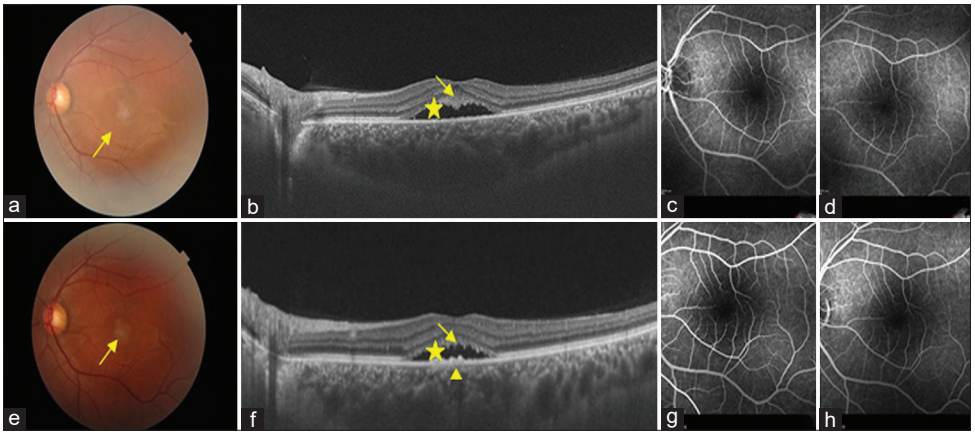

Figure 3: A-38-year-old male with left eye blurred vision for 6 months, best corrected visual acuity (BCVA) of 20/20, left eye fundus showed neurosensory detachment (NSD) at the fovea (a). Optical coherence tomography (OCT) showed subretinal hyperreflectivity (arrow) and subretinal fluid (SRF) (asterisk). (b) There was no hyperfluorescence fluorescein angiography (FA) in early (c) and late phases (d). The patient was treated with oral eplerenone 25 mg BD. Five months posttreatment, BCVA was 20/20. Fundus showed reduction in NSD (e). OCT showed reduction of subretinal hyperreflectivity (arrow) and SRF (asterisk) with retinal pigment epithelium hyperreflectivity (arrowhead) (f). There was no hyperfluorescence in FA in early (g) and late phase (h)

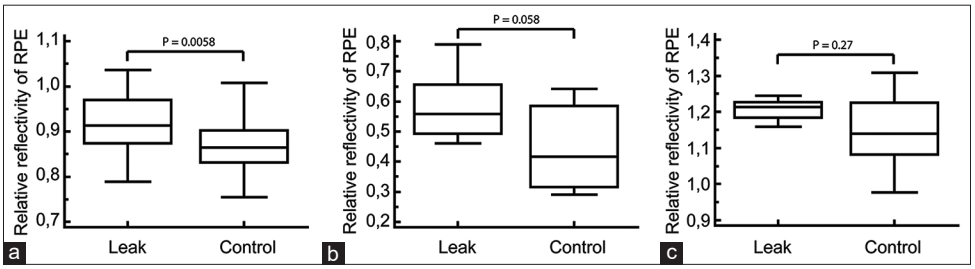

Figure 4: Box-and-whisker plots demonstrating differences in mean reflectivity (a), minimum reflectivity (b), and maximum reflectivity (c) of retinal pigment epithelium in leak site and control site

Table 1: Comparison of optical coherence tomography parameters at baseline and last follow-up visit also duration of follow-up and treatment received by patient

	CMT (microns)		Maximum height of the SRF (microns)		CT at the area of maximum SRF pocket (microns)		Maximum PED height if any at the site of SRF pocket (microns)		PROS disruption at the site of SRF pocket (%)		Follow-up duration (months)	Treatment offered
	Baseline	Last follow-up	Baseline	Last follow-up	Baseline	Last follow-up	Baseline	Last follow-up	Baseline	Last follow-up		
Patient 1	419	198	279	0	425	400	136	0	0	10	2	Observed
Patient 2	368	NA	216	NA	402	NA	No PED	No PED	70	NA	NA	Tab eplerenone (25 mg BD)
Patient 3	464	NA	210	NA	471	NA	57	NA	60	NA	NA	Tab eplerenone (25 mg BD)
Patient 4	177	153	79	0	295	381	No PED	No PED	20	10	2	Micropulse laser
Patient 5	323	NA	162	NA	456	NA	307	NA	20	NA	3	Observed
Patient 6	732	NA	516	NA	306	NA	No PED	No PED	70	NA	NA	Observed
Patient 7	570	148	426	29	359	353	220	0	30	10	5	Tab eplerenone (25 mg BD)
Patient 8	346	284	198	150	534	618	No PED	No PED	70	60	2	Observed
Patient 9	270	198	110	0	310	300	102	42	50	10	4	Observed
Patient 10	491	249	329	125	250	363	No PED	No PED	70	80	5	Micropulse laser
Mean	416	205	252.5	50.66666667	380.8	402.5	164.4	14	46	30	3.2	
SD	158.394725	53.34416557	137.758444	68.64886501	91.4194241	110.83817	99.5755994	24.2487113	26.3312235	31.6227766	1.2	

CMT: Central macular thickness, SRF: Subretinal fluid, CT: Choroidal thickness, PED: Pigment epithelial detachment, PROS: Photoreceptor outer segment, NA: Not available, SD: Standard deviation

to a hyperfluorescent leakage point often demonstrated increased reflectivity.[4] We found that reflectivity of the RPE at the suspicious leak site coincided with PROS thinning and RPE reflectivity which was significantly increased compared to the control area. Although pathophysiological significance for increased RPE reflectivity at the suspected leak is not understood, it may suggest RPE decompensation at the cellular level. Both PROS thinning and RPE reflectivity changes represent a reparative process during the closure of the leak.

CSCR without any hyperfluorescence can be either observed or treated with eplerenone or micropulse laser. As the hyperfluorescent leakage site is not identified, eplerenone is a good option. Micropulse laser is also a good option to treat the area of SRF with high-density confluent burns with 5% duty cycle. Luttrull has reported good clinical results by treating a larger area of CSCR with subthreshold micropulse laser.[6] Subthreshold micropulse laser is also more appropriate when SRF is involving the fovea.[7]

OCT-guided analysis of PROS thickness helps us in the identification of the probable site of leak corresponding to the area of PROS disruption. Thus, identification of PROS disruption site from OCT might help us in FFA-free laser.[5] Furthermore, the identification of RPE hyperreflectivity site in OCT can help in FFA-free laser. However, we were unable to compare the efficacy in this small case series between the available treatment options.

Our study was limited with small sample and the absence of indocyanine green angiography images. However, CSCR without any hyperfluorescence is a very rare finding. We were unable to compare the different modalities due to relatively smaller number in each group. Strengths of the study are that we excluded eyes with Drusen Laser study to exclude any possibility of choroidal neovascularization as well as eyes with diffuse RPE atrophic changes suggestive of chronic central serous chorioretinopathy.

In conclusion, CSCR with no hyperfluorescent leakage has PROS thinning and changes in RPE hyperreflectivity over the SRF pocket. Treatment with either eplerenone or micropulse laser may be done to prevent photoreceptor damage and visual loss. We believe that this finding could be a transient phase where spontaneous closure of the leakage might have occurred leading to no leakage in the angiography. OCT indicators such as PROS thinning and changes in RPE hyperreflectivity can help in these cases. Further studies with newer biomarkers on OCT, various treatment options, and long-term outcomes are warranted in cases of persistent SRF in CSCR without any leakage.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Nicholson B, Noble J, Forooghian F, Meyerle C. Central serous chorioretinopathy: Update on pathophysiology and treatment. Surv Ophthalmol 2013;58:103-26.
2. Prünte C, Flammer J. Choroidal capillary and venous congestion in central serous chorioretinopathy. Am J Ophthalmol 1996;121:26-34.
3. Turchetti R, de Moraes HV Jr., Maia HS. Number, shape, and topography of leakage points in patients with central serous chorioretinopathy. Arq Bras Oftalmol 2005;68:317-20.
4. Maltsev DS, Kulikov AN, Chhablani J. Topography-guided identification of leakage point in central serous chorioretinopathy: A base for fluorescein angiography-free focal laser photocoagulation. Br J Ophthalmol 2018;102:1218-25.
5. Daruich A, Matet A, Dirani A, Bousquet E, Zhao M, Farman N, *et al*. Central serous chorioretinopathy: Recent findings and new physiopathology hypothesis. Prog Retin Eye Res 2015;48:82-118.
6. Luttrull JK. Low-intensity/high-density subthreshold diode micropulse laser for central serous chorioretinopathy. Retina 2016;36:1658-63.
7. Hanumunthadu D, Tan AC, Singh SR, Sahu NK, Chhablani J. Management of chronic central serous chorioretinopathy. Indian J Ophthalmol 2018;66:1704-14.