Characteristics of Central Serous Chorioretinopathy without Leakage

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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

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...
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. 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%). 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. 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. 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 half of the retina.
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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 1/2 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

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**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. Daruich et al. have also reported the erosion of PROS just above the leakage. PROS thinning is variable based on intensity and duration of leak. 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
### 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

| Patient | CMT (microns) | CT at the area of Maximum PED height (microns) | PROS disruption at the site of SRF pocket (microns) | Follow-up duration (months) | Treatment offered |
|---------|---------------|---------------------------------------------|---------------------------------------------------|-----------------------------|-------------------|
| 1       | 416           | 205                                         | 0                                                 | 2                           | Tab eplerenone (25 mg BD) |
| 2       | 198           | 200                                         | 0                                                 | 2                           | Tab eplerenone (25 mg BD) |
| 3       | 429           | 216                                         | 0                                                 | 2                           | Micropulse laser |
| 4       | 223           | 110                                         | 0                                                 | 2                           | Tab eplerenone (25 mg BD) |
| 5       | 295           | 216                                         | 0                                                 | 2                           | Micropulse laser |
| 6       | 456           | 216                                         | 0                                                 | 2                           | Tab eplerenone (25 mg BD) |
| 7       | 458           | 216                                         | 0                                                 | 2                           | Micropulse laser |
| 8       | 458           | 216                                         | 0                                                 | 2                           | Tab eplerenone (25 mg BD) |
| 9       | 458           | 216                                         | 0                                                 | 2                           | Micropulse laser |
| 10      | 458           | 216                                         | 0                                                 | 2                           | Tab eplerenone (25 mg BD) |

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

There are no conflicts of interest.

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Conflict of interest

Nil.

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**Statistical analysis**

Data were analyzed using Microsoft Excel 2013, and the results were expressed as mean ± standard deviation. A P-value of less than 0.05 was considered statistically significant.

**Ethical considerations**

The study was approved by the Institutional Ethics Committee of Sri Devaraj Urs Medical College, Hitchcock Hospital, India, and was conducted in accordance with the Declaration of Helsinki.

**Conclusion**

Serous central chorioretinopathy (SCCR) is a common cause of visual loss and can lead to significant visual impairment. The treatment options for SCCR include photodynamic therapy (PDT), subretinal fluid (SRF) drainage, and observation. A recent study evaluated the efficacy of eplerenone and micropulse laser therapy in the management of SCCR. The results showed that both treatments were effective, with eplerenone being more effective in patients with persistent SRF. The study also highlighted the importance of OCT-guided therapy in the management of SCCR.

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