Funduscopy-guided fluorescein angiography-free focal laser photocoagulation for central serous chorioretinopathy

Anuja Mohanty, Santosh K Mahapatra

Purpose: To identify and correlate hypopigmented spots on funduscopy with the leakage points on fluorescein angiography (FA) in patients with central serous chorioretinopathy (CSCR) to provide criteria for FA-free focal laser photocoagulation (FLP). Methods: Fifty consecutive patients of acute CSCR were evaluated between March and October 2019 confirming the inclusion and exclusion criteria. Colocalization of leakage points with discrete hypopigmented spots on clinical funduscopy was evaluated using FA. Positive predictive value (PPV) was calculated to identify the status of association between these to formulate criteria for FA-free FLP of CSCR patients in future. Results: Out of the 50 eyes, 38 (76%) had a discrete hypopigmented spot on funduscopy which coincided with the leakage point on FA. The PPV of finding a leakage point at the area of discrete hypopigmented spot is 95%. Colocalization with a pigment epithelial detachment was found in 25 (65.7%) of these 38 eyes. Retinal pigment epithelial irregularities were found associated in all of these 38 eyes, Subretinal homogenously hyperreflective material was found in 8 (21.05%) of 38 eyes. optical coherence tomography following FLP of leakage point in all cases showed complete resolution of CSCR in 47 (94%) eyes. Conclusion: This study demonstrates that hypopigmented spots on clinical fundus examination in CSCR patients, when present, coincide with the leakage point of FA. This may aid to undergo FA-free FLP treatment in CSCR patients.

Key words: Central serous chorioretinopathy, fluorescein angiography-free, focal laser photocoagulation, hypopigmented spot, pigment epithelial detachment

Central serous chorioretinopathy (CSCR) is a multifactorial disease characterized by localized neurosensory detachment (NSD) with or without focal pigment epithelial detachments (PEDs) and altered retinal pigment epithelium (RPE).\[1\] It most commonly occurs in young men between 20 and 45 years of age.\[2\] Patients with CSCR mostly complain of central scotoma and blurred vision. The primary pathophysiology is believed to be underlying choroidal abnormalities: choroidal thickening and hyperpermeability with increased tissue hydrostatic pressure and breakdown of the outer blood retina barrier (microdefects in RPE) that leads to fluid accumulation in the subretinal space.\[3-5\]

CSCR can be acute or chronic although there is no clear distinction. In the acute stage, a serous macular detachment is classically seen with/without associated PEDs; occasionally yellowish subretinal fibrin deposits may be seen. The chronic (4–6 months) presence of subretinal fluid (SRF) can cause RPE damage which can be visualized fundoscopically as RPE mottling, gravitational RPE atrophic tracks, sometimes associated with schitic retinal edema.\[6\]

Multimodal imaging including swept-source optical coherence tomography (SS-OCT), OCT angiography (OCTA), fundus autofluorescence (FAF), fluorescein angiography (FA), indocyanine green angiography (ICGA) have led to better understanding of the disease and monitoring the response to treatment. OCT can demonstrate the NSD, PED, thickened choroid (SS-OCT). ICGA shows the dilated choroidal vasculature and choroidal hyperpermeability. FAF may be helpful to detect chronicity of the disease. FA shows ink-blot or smoke-stack pattern of leakage in acute CSCR and demarcates PED.

Although CSCR is an idiopathic condition with spontaneous resolution on lifestyle modifications and discontinuing exogenous corticosteroid intake in any form; different treatment methods exist, which are usually reserved for chronic and recurrent CSCR. The SRF accumulation in acute CSCR causes photoreceptor damage, which is persistent and manifests as decreased contrast sensitivity, micropsia, persistent scotomas even after SRF resolution.\[7,8\] Chronic CSCR has a poor long-term visual prognosis due to accompanying RPE atrophy and persistent NSD.\[9,10\] Hence, it is crucial to treat CSCR in the acute phase.

The different modalities of treatment include laser photocoagulation (argon, micropulse diode laser, transpupillary thermotherapy), photodynamic therapy (standard, reduced...
dose, reduced fluence), intravitreal anti-vascular endothelial growth factors (anti-VEGFs), and pharmacotherapy.

Even though OCT findings allow confirmation of CSCR without invasive FA, FA is used to localize the leakage point in order to facilitate focal laser photocoagulation (FLP). Application of FLP to the RPE leakage point hastens the resolution of NSD in CSCR. Therefore, argon laser photocoagulation to focal leakage point on FA is an effective treatment for acute CSCR, provided the leak is not subfoveal or juxtafoveal.\[10\]

The purpose of this study is to identify and correlate hypopigmented spots on funduscopy with the leakage points on fluorescein angiography (FA) in patients with central serous chorioretinopathy (CSCR) to provide criteria for FA-free focal laser photocoagulation (FLP).

Methods

The study was conducted after approval from the institutional ethics committee. Written informed consent was obtained from all patients after being informed about the procedure.

In this study, we prospectively studied 50 eyes of 50 consecutive symptomatic patients of acute CSCR from March and October 2019. We have included patients presenting with first episode of CSCR and considered treatment for any patients having metamorphopsia or black shadow in the central visual field for more than 1 month despite medical management. Patients who had undergone any previous treatment for CSCR (including FLP, micropulse laser therapy and photodynamic therapy or have signs of any other active retinal disease in the study eye were excluded from the study. In cases of bilateral CSCR, only one eye was included in the study. All patients underwent standard ophthalmic examinations: best-corrected visual acuity (BCVA), anterior segment evaluation with slit lamp, and dilated fundoscopy with +90D examination with slit lamp and/or indirect ophthalmoscopy. Following this, they underwent evaluation with SS-OCT and FA. The data included age and sex of the patient, BCVA, duration of symptoms, findings on fundoscopy, SS-OCT, and FA which were recorded in the first visit, and patients underwent FLP. All patients who were not willing to continue further medical management and had occupational demands were our indication for FLP. The laser parameters used were argon green laser (wavelength 514 nm), 10 µm spot size, <100 MW power, <100 ms duration. Direct focal laser photocoagulation to juxtafoveal and extrafoveal leaks was applied to cause mild blanching and taking care not to disrupt areas of PED. They were followed up at 2 weeks and 1 month after FLP with SS-OCT.

The SS-OCT and FA system used was the deep range imaging OCT Triton plus (Topcon, Japan). For OCT, in addition to enhanced depth retinal cross-sectional images centered on the fovea, three-dimensional macular scans were also obtained. The OCT findings in the outer retinal layers and the subretinal fluid at the leakage point were evaluated in each case with special attention to findings like: 1) presence of PEDs, 2) photoreceptor outer segment (PROS) layer thinning, 3) dipping of the outer retinal layers, 4) presence of subretinal fibrin, and 5) RPE irregularities.

All patients underwent standard FA with an intravenous injection of 3 ml of 20% sodium fluorescein solution (FLURES, Aurolab, India) at the first visit. The colored fundus photo of FA and OCT of each patient was superimposed manually in the system by tracing the retinal vessel branching pattern with respect to the leakage point to obtain a spatial overlap. This was done to study the OCT findings at the leakage point and facilitate FLP.

The possibility to perform FA-free FLP was evaluated in all patients included in the study and presenting with discrete hypopigmented spot on funduscopy, which allows clear identification of the leakage point.

Results

We analyzed the findings of 50 eyes of 50 patients with CSCR. The mean age was 35.2 ± 7.4 years. There were 44 (88%) males and only 6 (12%) females.

Out of the 50 eyes, 38 (76%) had a discrete hypopigmented spot on funduscopy which coincided with the leakage point on FA [Fig. 1]. Only two eyes out of the 50 eyes had hypopigmented spot which did not correspond to the leakage point on FA. The PPV of finding a leakage point at the area of discrete hypopigmented spot is 95%. Of the 50 eyes, 5 eyes (10%) had more than one leaks; 2 out of these 5 eyes had hypopigmented spot on funduscopy (one patient had multiple leaks within the hypopigmented spot, while one had a leak within the spot and one leak elsewhere).

PED was present in 42 (84%) of 50 eyes. A PED colocalized with the hypopigmented spot in 25 of 38 eyes (65.7%) [Fig. 2].

PROS layer thinning was observed in 23/50 eyes (46%), PROS thinning in 3/38 eyes (7.89%) over the NSD coincided with the leakage point but was not associated with a PED, whereas in 8/38 eyes (21.05%) PROS thinning was overlying the PED [Fig. 3].

Subretinal homogenously hyperreflective material suggestive of subretinal fibrin was found in 8 (21.05%) of 38 eyes [Fig. 4].

Figure 1: A discrete hypopigmented spot on funduscopy coincided with the leakage point on FA
Dipping of outer retinal layers was seen in 5/38 eyes (13.15%), of which one patient had an area of outer retinal layers dipping on the summit of PED, which coincided with the leakage point on FA [Fig. 5].

Retinal pigment epithelial (RPE) irregularities were seen in 28/38 eyes (73.68%). OCT following FLP of leakage point in these cases showed complete resolution of CSCR in 47 (94%) eyes within a month.

**Figure 2:** PED colocalized with the hypopigmented spot corresponding to the leakage point on FA

**Figure 3:** PROS thinning overlying the PED

Discussion

The various morphologic changes associated with CSCR such as PED, PROS thinning, subretinal fibrinous exudates, and outer retinal layer dipping could be well defined with the advent of SS-OCT.

Maltsev et al. showed that the presence of both PEDs and PROS thinning coinciding with the leakage point was found in a significant number of eyes with CSCR.

In a study conducted by Kim et al., OCT images of the leakage sites showed PED in 31.9%, whereas in our study, PED colocalized to the leakage point in 65.7%. Maltsev et al. showed PED coinciding with leakage point in 80%.

PROS thinning was found in 90.4% of the PEDs coinciding with leakage points in the study by Maltsev et al. In our study PROS thinning was seen only in 46%. We have included acute CSCR, whereas Maltsev et al. had included only chronic CSCR cases. An active flow through the leakage point causing PROS washout may result in its thinning even in acute cases. Prolonged NSD causes degenerative manifestations in the outer
retina, especially PROS thinning, which may account for the difference observed.

Kim et al.\(^\text{[12]}\) observed a hyperreflective area suggesting fibrinous exudate in the subretinal space around the leakage site in 20.3%. We reported similar subretinal hyperreflective material in 21.05%. In 13.0%, sagging or dipping of the posterior layer of the neurosensory retina over the leakage site was reported by Kim et al.\(^\text{[12]}\); we observed a similar finding in 13.15%. This seems to arise from the swelling of the outer nuclear layer due to the traction by fibrinous exudates [Table 1].\(^\text{[12]}\)

Different hypotheses regarding multiple, dot-like, yellow precipitates and subretinal yellow material within the area of NSD in patients with CSCR have been proposed, which correlate with high reflective deposits on SS-OCT. These include the accumulation of shed PROS, fibrin or lipids, or macrophages clearing the subretinal space. However, the exact nature of these deposits and their origin is yet to be determined.\(^\text{[13,14]}\)

We also report the finding of presence of a well-defined and discrete hypopigmented spot on fundus examination in CSCR patients, which when present coincides with the leakage point on FA, which was observed in 38/50 eyes (76%). This fundoscopic appearance could be due to the RPE disintegrity at the point of leak. Thus, hypopigmented spot appears to be a significant finding for the precise localization of presumed leakage points without FA and/or OCT. A thorough PubMed

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**Figure 4:** Subretinal homogenously hyperreflective material suggestive of subretinal fibrin

**Figure 5:** An interesting case of outer retinal layers dipping on the summit of PED which coincided with the leakage point on FA. The retinal thickness at the point of leak is 792 µm
search yielded no articles conforming to this finding. To the best of our knowledge, this is the first study citing the importance of fundus examination in CSCR eyes highlighting the presence of a hypopigmented spot which is of great significance in formulating guidelines for FA free FLP as the PPV for finding a discrete hypopigmented spot is as high as 95%. The presence of discrete hypopigmented spot over or near the area of NSD detachment in cases of CSCR can be considered as a direct evidence of leak point on FA and can be used for FA free FLP in cases of CSCR. Based on our findings we feel fundoscopy-guided FA free FLP will be a better method at this point of time. Further studies to find specific OCT characteristics can be undertaken to answer this question in a more specified manner.

FA-free identification of the leakage point can help to manage at least some patients with CSCR without FA completely (especially in whom FA is contraindicated). It also would increase the safety of CSCR management since FA is an invasive procedure, that is associated more frequently with mild adverse effects like nausea and vomiting and rarely with a variety of allergic reactions. Also, it bypasses the imaging modalities required for FLP and cuts down the cost of treating CSCR.

**Conclusion**

CSCR is a common cause of visual impairment, especially in the middle-aged men. Identification of the leakage point is a critical step for FLP, which is a relatively easy and effective treatment option for CSCR. While imaging is evolving rapidly, this study demonstrates that hypopigmented spot on clinical fundus examination in CSCR patients, when present almost always coincides with the leakage point on FA, and can facilitate FA free focal laser photocoagulation in future.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

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**Table 1: Comparison of findings across other studies showing similar results**

| Characteristics                                      | Kim et al.[12] | Maltsev et al.[11] | Our study |
|-------------------------------------------------------|----------------|--------------------|-----------|
| Sample size                                           | 63 eyes        | 48 eyes            | 50 eyes   |
| RPE bump/irregularities                               | 68.1%          | 80%                | 73.68%    |
| PED coinciding with leak                              | 31.9%          | 20.3%              | 65.7%     |
| Sub-retinal fibrin                                    | 13%            | 12.5%              | 21.05%    |
| Dipping of outer retinal layers                       | 13%            | 2.1%               | 13.15%    |
| RPE microrip                                          | 1.58%          | 27.3% ± 13.0%      | Fundoscopy guided-76% |
| Others                                                |                |                    | 21.05%    |
| PROS thinning over PED                                | 90.4%          |                    | Fundoscopy guided-54.2% |
| Mean distance from upper border of NSD to leak         |                |                    | 21.05%    |
| FA-free FLP                                           |                |                    | Fundoscopy guided-76% |
| OCT guided-54.2%                                      |                |                    | Fundoscopy guided-76% |

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