Peripheral retinal avascularity and capillary leakage in central serous chorioretinopathy

V.G. Madanagopalan*, Karan Shah, C.K. Nagesha, Prabu Baskaran

Aravind Eye Hospital and Postgraduate Institute, Pondicherry, India

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Abstract

Purpose: To report a novel finding of peripheral retinal avascularity (PRA) and peripheral capillary leakage (PCL) on wide-field fluorescein angiography (WFA) in non-dependent quadrants, in eyes with bilateral chronic central serous chorioretinopathy (CSCR).

Methods: Forty six patients with bilateral CSCR were studied. Four patients had PRA and PCL, and 42 patients did not. The demographic profile, clinical findings, and imaging characteristics of the two groups were compared.

Results: There was no significant difference between those patients with and without PRA and PCL with respect to the demographic profile, clinical findings, and imaging characteristics. Laser photocoagulation to extrafoveal points of leakage seen on fluorescein angiography (FA) was sufficient to cause complete resolution of CSCR in these 4 patients. PRA areas were not treated.

Conclusion: The PRA and PCL in CSCR are novel findings, which have not been previously described.

Keywords: Central serous chorioretinopathy; Peripheral retinal avascularity; Peripheral capillary leakage; Wide field fluorescein angiography; Intraocular inflammation

Introduction

Chronic central serous chorioretinopathy (CSCR) arises due to choroidal congestion and hyperpermeability along with retinal pigment epithelial (RPE) dysfunction. Peripheral changes of the fundus in CSCR with clinical examination and imaging systems including fundus photography, autofluorescence, and indocyanine green angiography have been described.

However, the fluorescein angiographic (FA) features of the retinal periphery in patients with chronic CSCR are not widely discussed. This report presents four patients with bilateral chronic CSCR who had novel findings of peripheral retinal avascularity (PRA) and peripheral capillary leakage (PCL) on FA in non-dependent quadrants.

Methods

A retrospective study was done at a tertiary level eye hospital in South India after Institutional Review Board and ethical committee approval. The study adhered to the tenants of Declaration of Helsinki. 46 patients with chronic CSCR in both eyes were studied. Spectral domain optical coherence tomography, fundus autofluorescence, and FA performed with Spectralis (Heidelberg, Germany) were analyzed.

Results

We identified 4 males (Figs. 1–4) in whom bilateral PCL and adjacent PRA were seen in non-dependent quadrants on wide-field FA (WFA). There were no features suggestive of systemic illness, myopia, uveitis, or inherited retinal
Fig. 1. In a 37-year-old male with central serous chorioretinopathy (CSCR), macular leaks (arrows), peripheral avascular zones (arrow heads), and late leakage from small peripheral vessels (asterisks) are seen.

Fig. 2. In a 45-year-old male with central serous chorioretinopathy (CSCR), macular leak (arrows), peripheral capillary loss (arrow heads), and neovascularization over the detached retina are seen in the right eye (asterisk).
pathology. Vasculitis work-up which included complete blood counts, hemoglobin assay, erythrocyte sedimentation rate, peripheral smear examination, serum angiotensin converting enzyme assay, Venereal Disease Research Laboratory test for syphilis, Mantoux tuberculin skin test for tuberculosis, perinuclear Anti-neutrophil Cytoplasmic Antibodies, cytoplasmic Anti-neutrophil Cytoplasmic Antibodies, Anti Nuclear Antibodies, Tridot test for Human Immunodeficiency Virus, Hepatitis B antigen assay, Toxoplasma IgG and IgM, and chest roentgenogram were unremarkable in these 4 patients. FA showed distinct PRA and PCL in non-dependent quadrants (Figs. 1–4). Laser photocoagulation of extrafoveal leakage points lead to resolution of CSCR in these 4 patients.

There was no significant difference between the patients who had PRA (4) and those who did not have PRA (42) with respect to age, gender, duration of symptoms, history of past focal laser therapy, number of quadrants of autofluorescence changes, and presence of subretinal fibrin or inferior retinal detachment (RD) (P > 0.05 for all) (Table 1).

Discussion

Bullous RD in CSCR is usually present in the dependent quadrant and, as a consequence, avascular retina and peripheral neovascularization has been described inferiorly.5,6 However, unlike previous case reports, in our series, we noted avascular areas and vascular leaks not just in the inferior dependent quadrant but in other “non-dependent” quadrants as well.

Normal eyes have no frank PCL.7 WFA in uveitis shows areas of PRA and leakage that are not identifiable with clinical examination.8 In a series by Lu et al., few eyes without any other clinical signs had peripheral vascular leakage.9 It was inferred that these eyes had some form of intraocular inflammation, most likely intermediate uveitis, not detectable clinically. We postulate that a similar mechanism operates in our series of eyes. These patients had no clinical sign of active uveitis. There is evidence in literature to suggest that CSCR and uveitis may co-exist.10 Normal RPE function contributes to the immune privileged microenvironment of the eye and plays a role in prevention of intraocular inflammation.11 In CSCR, there is widespread RPE damage, and the presence of chronic fluid leads to photoreceptor death.1 When cells die in vivo, an inflammatory response is triggered.12,13 Molecules liberated by injured cells stimulate generation of proinflammatory mediators in other cells or extracellular sources.12 Proteome and metabolome study of subretinal fluid obtained from eyes with CSCR revealed that, besides other changes, proteins and metabolites
related to inflammation and alternate complement pathway were deregulated.\textsuperscript{14} Based on existing literature that provides evidence linking cell death with inflammation and based on the peculiar angiographic findings in our series of eyes with CSCR, we speculate that chronic and widespread RPE dysfunction, along with photoreceptor death, could cause an indolent intraocular inflammation. As a consequence, peripheral vascular channels are affected with low-grade vasculitis. On FA, we hypothesize that this inflamed peripheral vasculature manifests with PCL and hyperfluorescence. Inflammation of these peripheral small caliber vessels will lead to their closure explaining the PRA seen on FA.

However, given that there was no difference in demographic and fundus characteristics of patients with PRA and patients without PRA, we believe there may be other factors or mechanisms that contribute to these peripheral angiographic abnormalities. A control group of normal patients would also help to validate these results. Since ours was a retrospective study, enhanced depth imaging (EDI) of the choroid was not available to estimate choroidal thickness.

Table 1
Demographic and ocular characteristics of central serous chorioretinopathy (CSCR) patients with and without peripheral retinal avascularity (PRA) and peripheral capillary leakage (PCL).

| Characteristic                                | Group A (PRA and PCL present) | Group B (PRA and PCL absent) | P     |
|-----------------------------------------------|-------------------------------|------------------------------|-------|
| Age, in years, mean (range, SD)               | 41 (32–50; 8.04)              | 41.6 (30–58; 8.76)           | 0.89  |
| Males, number of patients (%)                 | 4 (100)                       | 38 (90)                      | 0.99  |
| Duration of symptoms, in days, mean (range, SD)| 378.75 (150–730; 250.14)     | 258.33 (90–730; 196.67)      | 0.25  |
| Past focal laser photocoagulation, number of patients (%) | 1 (25) | 3 (7) | 0.31 |
| Subretinal fibrin, number of patients (%)     | 2 (50)                        | 19 (45)                      | 0.99  |
| Inferior retinal detachment, number of patients (%) | 1 (25) | 7 (17) | 0.54 |
| Number of quadrants of autofluorescence changes, mean (range, SD) | 4.5 (3–6; 1.29) | 4.26 (3–8; 1.32) | 0.73 |

PRA: Peripheral retinal avascularity; PCL: Peripheral capillary leakage; N: Number of patients; SD: Standard deviation.

Fig. 4. In 32-year-old male with central serous chorioretinopathy (CSCR), macular leaks (arrows), peripheral non-perfusion areas (arrow heads), and inferior retinal detachment (asterisks) are seen.
Further studies with EDI or swept source optical coherence tomography (OCT) along with analysis of vitreous or aqueous samples for the presence of inflammatory mediators may help us in understanding the pathology of this unique angiographic feature better.

To conclude, this is the first report describing an association of PRA and PCL with chronic CSCR. Although they do not appear causal and do not influence the natural course of CSCR, clinicians need to be aware of this entity, as treatment of these peripheral retinal changes is not necessary when resolution of CSCR is desired.

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