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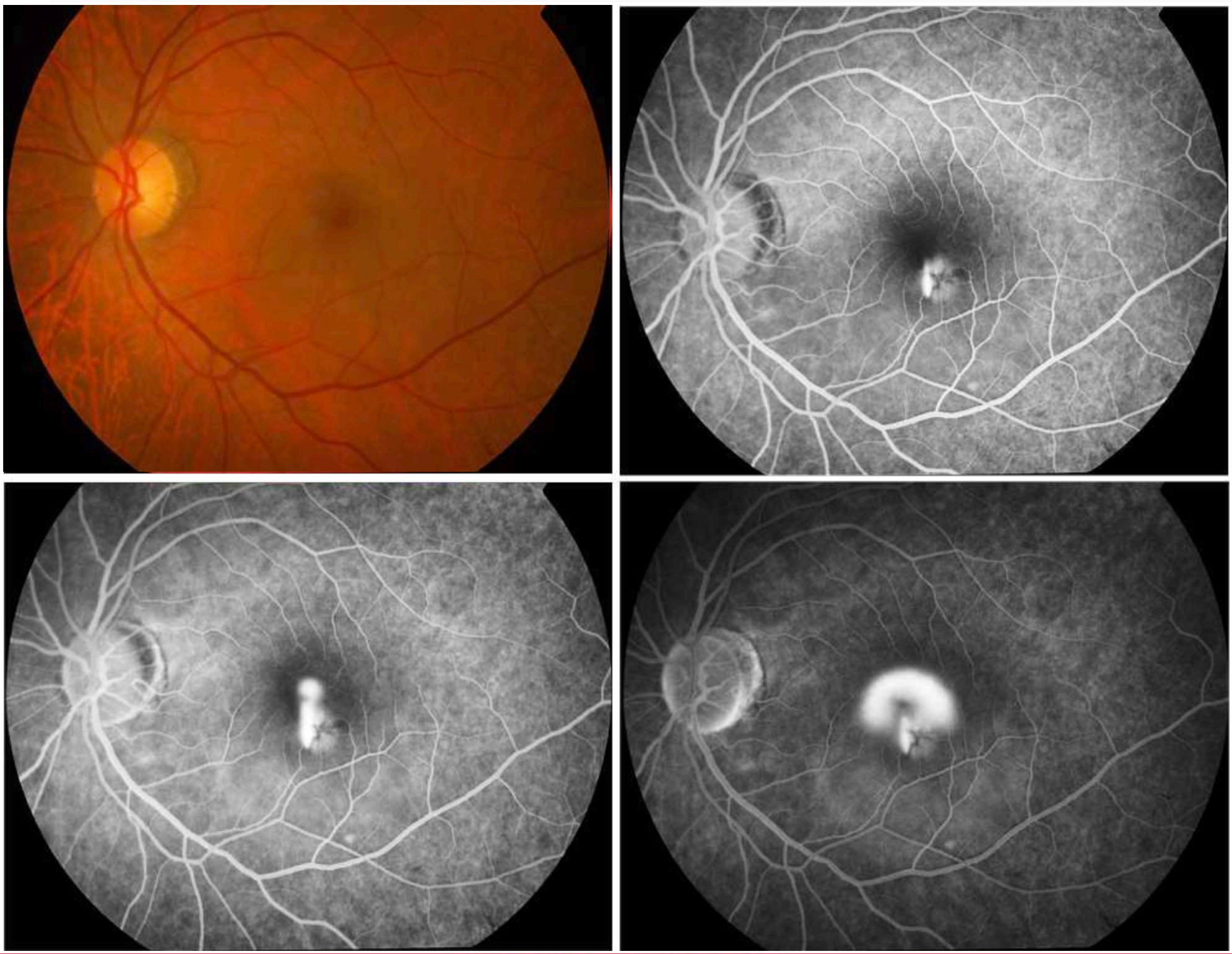
The Official Newsletter of the

VITREORETINAL SOCIETY-INDIA



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FROM THE PRESIDENT'S DESK

Dear Friends

Another issue of our newsletter is in your hands. This issue is focused on CSR and just like the previous issues, is worth preserving for reference. I congratulate the editorial team for the excellent job.

The next VRSI meeting will be held in Trivandrum. The preparations have already been started by Dr Unni and the team. The venue is set amidst picturesque surroundings and the Arabian Sea beckons you! Please plan to attend and enjoy the place and the meeting!!

Diabetic retinopathy related activities are going on in full swing. Dr Manisha Agarwal has detailed the various activities in this regard.

Lastly, the ASRS has requested VRSI to participate in the PAT survey. We urge all the members to take part in this in large numbers to reflect the current practice trends of our members.

Dr N S Muralidhar

FROM THE HONORARY SECRETARY'S DESK

Dear Friends,

Hope you had a great experience of attending the annual VRSI conference at Nagpur from 1-3rd Dec 2022. A great scientific program had been put up by our Scientific Chair-Dr Mahesh P Shanmugam with a great hospitality by Dr. Sulabha Deshpande-President LOC, Prashant Bawankule-Organizing Secretary and their entire team. We had the highest number of registrations this year in the annual conference with a great participation by both national and international faculty.

Various activities are being conducted by the society to spread awareness for blindness secondary to Diabetic retinopathy including skill transfer workshops and formulation of the screening guidelines for the Diabetologists.

This newsletter is focused on a very common retinal pathology – CSCR and hope all of you enjoy reading the issue as a lot of effort has been put by the editorial team.

This year annual conference is being hosted by Dr Unnikrishnan Nair at Trivendrum in Dec 2023.Kindly block your calendar for the same as it will be a treat to your eyes and mind both.

Regards

Dr Manisha Agarwal

Hon General Secretary VRSI

FROM THE CONVENER, SCIENTIFIC COMMITTEE'S DESK

Dear Friends,

Greetings!

This edition of the newsletter is the brainchild of Dr. Mahesh Gopalakrishnan, our deputy editor with Dr. Pradeep Sagar and Dr. Daraius Shroff working along tirelessly to bring out another great issue. This issue focusses on a common disease that is being redefined as a spectrum disorder – Central serous chorioretinopathy (CSC). Though a common entity, it can be a challenge to treat in the absence of photodynamic therapy (PDT) as a treatment option.

In this issue, Zarnegar et al describe the role of choroidal pathophysiology in CSC, enhancing our understanding of the role of underlying systemic conditions, scleral thickness, choroidal vasculature and other factors that play a role in this disease. Imaging plays a key role in CSC and Soman et al have elegantly detailed the same in their article, of course with beautiful images.

Day in and day out, we keep describing new findings in old diseases, thanks to optical coherence tomography. One such novel finding is detailed in the article by Manayath et al who show us that CSC can rarely mimic a choroidal mass lesion due to posterior choroidal fluid loculation. It is important to recognize this entity as this

may masquerade as more ominous choroidal diseases such as a melanoma. A retinal pigment epithelial tear associated with bullous CSC can also mimic a melanoma and one such case is detailed in this issue by Das et al.

On the treatment front, it is a challenge to treat subfoveal leaks of CSC, in the absence of PDT and subthreshold laser is one of the options as described by Upadhyaya et al. The guidelines to treatment, expected efficacy are detailed by them in their article and Joshi details a case wherein eplerenone was used in addition to micropulse. Venkatesh et al. also describe the role of topical and systemic pharmacotherapy in treating CSC, elegantly demonstrating the various pathways involved in the pathogenesis of CSC and the role of various pharmacological agents and their efficacy in disrupting these pathways to resolve CSC. Ultimately mind matters and Pradeep Venkatesh reviews the essential role of life style modification with meditation in treating CSC.

Lastly Dubey has summed up the management of CSC with a simple schematic, defining which treatment option to choose in a given case.

Since the release of the last newsletter, we have successfully published the VRSI study group's first study. We are working on other multicentric studies which will hopefully redefine the way we diagnose and manage vitreoretinal diseases.

Warm regards and happy knowledge sharing.

Thank you,

Dr. P. Mahesh Shanmugam

Convener, Scientific Committee, VRSI.

GUIDELINES:
MANUSCRIPT SUBMISSION FOR VRSI NEWSLETTER

Original Articles :

These include randomized controlled trials, interventional studies, studies of screening and diagnostic test, outcome studies, cost effectiveness analyses case-control series, and surveys with high response rate. The text of original articles amounting to up to 3000 works (excluding Abstract, References and Tables) should be divided into sections with the headings: Abstract, Key-words, Introduction, Material and Methods, Results, Discussion, References, Tables and Figure legends.

Case Reports / Challenging Case / Innovations / Instruments / Techniques:

New, interesting, challenging, rare cases, innovations, instruments and techniques can be reported. They should be unique and providing learning point for the readers. Manuscripts with clinical significance or implications will be given priority. These communications could be of up to 1000 words (excluding Abstract and References) and should have the following headings : Abstract (unstructured), Key-words, Introduction, Case, Discussion, Reference, Tables and Legends in that order. The manuscript could be supported with up to 10 references. Case Reports could be authored by up to four authors.

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INTRODUCTION TO THE ISSUE

Dear members

This edition of VRSI newsletter focusses on common but challenging Central serous chorioretinopathy. As we try to understand more it is becoming more elusive.

We have few articles by eminent persons in this topic. There will be some take home message in each. Hope it will be useful for everyone.

Happy reading

Dr Mahesh G

PRINCIPLES OF CHOROIDAL PATHOPHYSIOLOGY IN CENTRAL SEROUS CHORIORETINOPATHY

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Background

Central serous chorioretinopathy (CSCR) is a choroidal disease characterized by subretinal fluid (SRF) accumulation in the macula with or without pigment epithelial detachment (PED) [1]. Clinically, CSCR has presenting symptoms that may include metamorphopsia and blurred vision. CSCR is more common in men around 40 years of age [2]. Risk factors include but are not limited to [3] hypertension, [4] endogenous steroid production and exogenous systemic corticosteroid use, [5,6] and pregnancy [7]. Current treatments for CSCR include photodynamic therapy and anti-corticosteroids [8-11]. Although CSCR has been studied for over 150 years, the exact pathophysiological underpinnings are still being investigated. This article focuses on the role of the choroid in its pathogenesis and provides an overview of recent updates in our understanding of the choroidal involvement in CSCR.

CSCR is associated with systemic conditions such as autonomic imbalance and hemodynamic changes, which can alter choroidal blood flow. Increased sympathetic activity can lead to hypertension which is commonly seen in CSCR. Patients with CSCR exhibit elevated systolic and diastolic blood pressure on average compared to healthy patients, thus addressing hypertension may prove beneficial [12]. Fluctuations in blood pressure can damage endothelial cells lining choroidal vessels [13]. Erol et al., then later Latalska et al., employed nailfold videocapillaroscopy in patients with CSCR and identified more capillary abnormalities in the CSCR group compared to the control group. These results indicate CSCR may be a systemic microvasculopathy [14,15]. In the healthy eye, choroidal vasculature responds to systemic changes in blood pressure through autoregulatory mechanisms such as vasoconstriction of Sattler and Haller vessels [16]. These mechanisms may be negatively impacted in CSCR. Choriocapillaris

perfusion is increased in conditions of elevated cardiac output in eyes with CSCR compared to controls [12]. Vigorous physical exercise and greater blood volume during pregnancy may both be associated with a greater risk of CSCR [17] (Figure 1). Increased dysregulated choroidal blood flow during exercise or pregnancy may factor into vortex venous congestion and SRF accumulation [18].

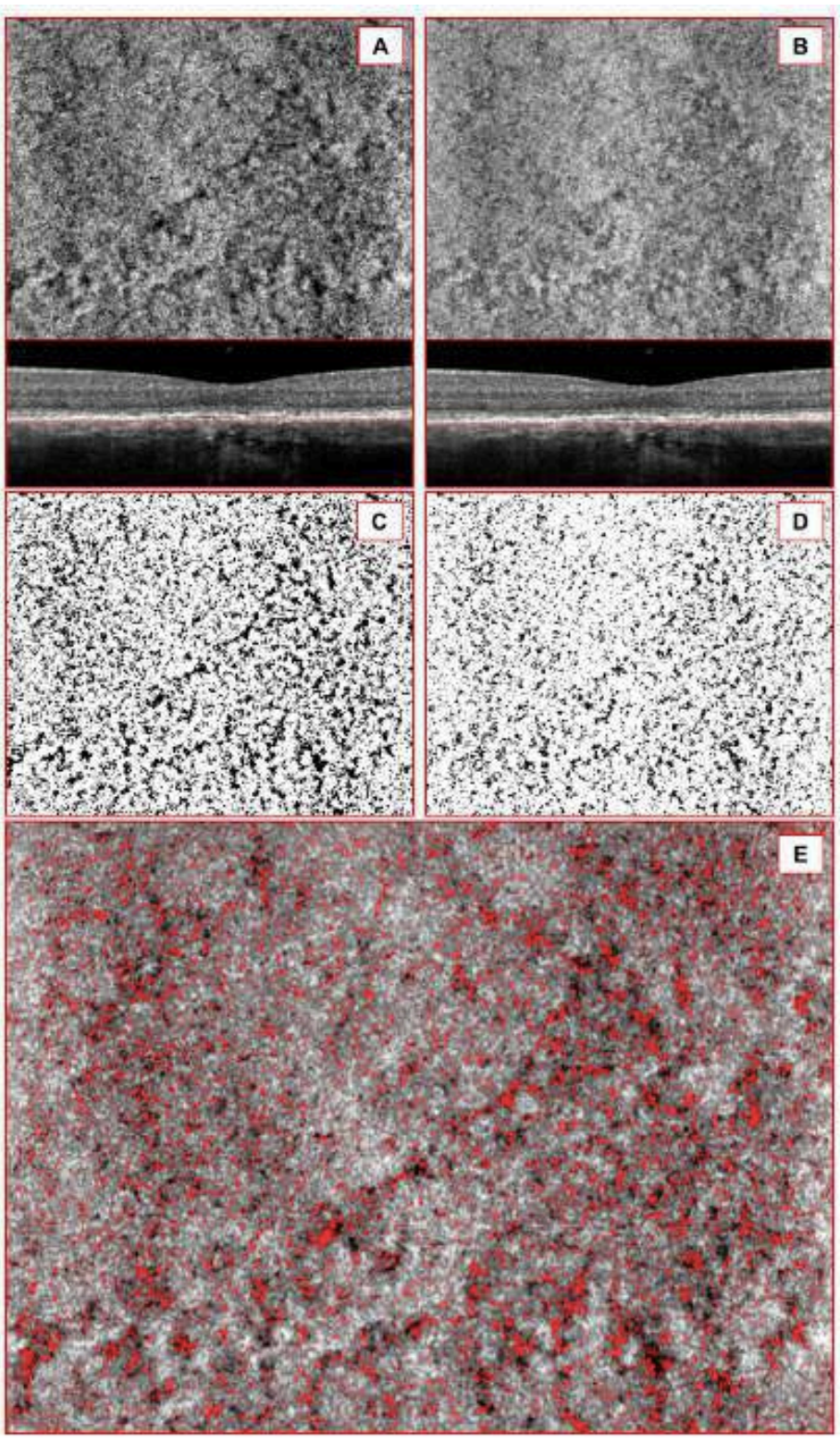

Figure 1. (A-E) OCT Angiography in a Patient with CSCR Undergoing the Handgrip Test.

Legend: An OCT angiography of the choriocapillaris was captured in a patient with CSCR at rest (A) and performing the handgrip test (B). Threshold images at rest (C) and during exertion (D) are demonstrated. A differential OCT angiogram (E) with red highlights show marked increases in blood flow under conditions of the handgrip test.

Patients with obstructive sleep apnea (OSA) are evidenced to have elevated sympathoadrenal activity and cortisol release, which may help to explain why OSA is associated with CSCR. Wu et al. employed enhanced depth imaging OCT to assess subfoveal choroidal thicknesses in patients with OSA and CSCR. Their study indicated that moderate to severe OSA may result in decreased subfoveal choroidal thickness [19]. Patients with Type A personality disorder exhibit higher catecholamine and cortisol levels, and an association between this disorder and CSCR has been suggested [20]. Recent studies have evaluated the relationship between narcissistic personality and the use of sympathomimetic drugs in CSCR [5].

Pharmacologic principles have played a role in further understanding CSCR. Phosphodiesterase inhibitors exhibit vasodilatory effects that result in pachychoroid formation [21]. Use of these drugs has been associated with CSCR in patients without other known risk factors [22,23]. Endogenous cortisol overproduction has been associated with CSCR [24,25]. Cushing syndrome is characterized by hypercortisolism, and studies in patients with this condition demonstrate a greater degree of pachyvessels and pachychoroid compared to normal patients [26,27].

A primary function of the choroid is to perfuse the outer and middle retina with vessels of the choriocapillaris, Sattler and Haller layers. Increased thickness of the choroid, dilated Haller vessels, and inner choroidal thinning are defining features of diseases of the pachychoroid spectrum [28], [29]. Choroidal vessel engorgement and hyperpermeability may result in ischemia of the choriocapillaris and result in SRF and PED. Venous congestion may cause pachyvessel and pachychoroid formation [30,31]. Blood arrives at the choroid from branches of the ophthalmic artery and venous drainage includes vortex veins that drain into the superior ophthalmic veins. Vortex vein

obstruction may contribute to the engorgement of Haller vessels [11]. Pang et al. observed vortex vein dilation in 83.3% of CSCR eyes imaged with ultra-widefield indocyanine green angiography [32].

Scleral thickness may also play a role in CSCR development, as well as serve as a helpful biomarker. As vortex veins exit the eye by way of the sclera, scleral thickening may impede venous outflow and contribute to venous overload, such as in eyes with hyperopia [33]. Spaide et al. [34] used contact B-scan ultrasonography probes to assess equatorial and posterior scleral thicknesses in 79 eyes with CSCR. Both parameters were elevated in the CSCR group compared to control. Swept source optical coherence tomography (OCT) of the anterior segment has been used to determine scleral thickness. Lee et al. [35] and Fernández-Vigo et al. [36] showed increased anterior scleral thickness in CSCR compared to control as measured under the lateral rectus and 0 mm and 2 mm from the scleral spur, respectively. Imanaga et al. [37] found increased anterior scleral thickness in eyes with CSCR compared to healthy controls.

Asymmetric venous outflow pathways have been proposed to predispose patients to diseases of the pachychoroid spectrum [38-40]. Hiroe and Kishi found that all 35 eyes with CSCR imaged with swept source OCT exhibited vortex venous asymmetry, whereas only 38% of healthy eyes did [40]. Bacci et al. [38] retrospectively analyzed ultra-widefield indocyanine green angiography in eyes with CSCR [11]. They found that nasal vortex veins, which drain the macular region, received greater outflow than other veins in eyes with CSCR. The macula may receive drainage primarily from a single vortex vein system, but this may differ across individuals [31] (Figure 2). Terao et al. [33] found shorter mean axial lengths with greater subfoveal choroidal thicknesses in eyes with CSCR and asymmetry.

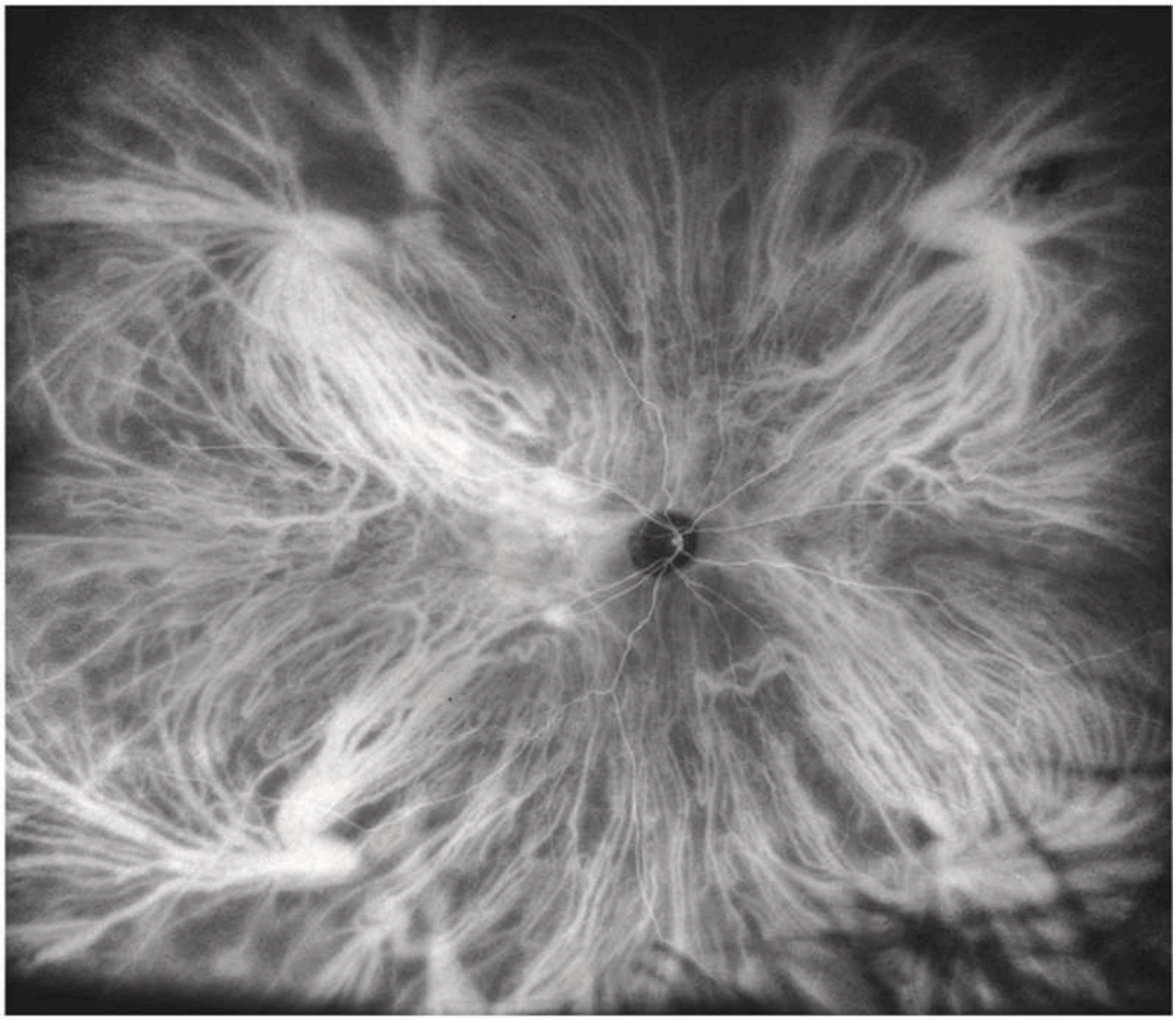

Figure 2. Asymmetric Vortex Venous Drainage of the Macula by the Superotemporal Vortex Venous System in an Eye with CSCR

Legend: The supertemporal vortex veins primarily drain the macula in this patient, demonstrating asymmetry which may be involved in CSCR pathogenesis.

Ultimately, there is a myriad of factors that may lead to the development of CSCR. Systemic conditions, pharmacologic agents, and venous overload are a few prominent processes implicated in CSCR. Hypertension, sympathetic overactivity, and states of increased cardiac output or blood volume, such as exercise and pregnancy, can cause endothelial damage and venous congestion. Type A personality disorder and OSA cause elevated catecholamines or cortisol levels and are associated with CSCR. Vortex veins are drainage pathways that are susceptible to dysfunction. Scleral thickening, asymmetric venous drainage, and anastomoses can precipitate venous overload and may cause SRF formation. CSCR remains a complex, multifactorial, vision-threatening disease, the pathomechanisms of which are not entirely understood. Thus, further research into the role of the choroid in CSCR pathogenesis may yield additional insights into treatment plans and visual outcomes

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ROLE OF MULTIMODAL IMAGING IN CENTRAL SEROUS CHORIORETINOPATHY

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Central serous chorioretinopathy (CSCR) is characterized by focal or multifocal areas of neurosensory retinal detachment and varying degrees of retinal pigment epithelium (RPE) cell loss and choroidal thickening or dysfunction [1, 2]. No consensus exists over the duration threshold that differentiates acute and chronic CSCR, which is arbitrarily set between 4 and 6 months in most published reports. The term “diffuse retinal pigment epitheliopathy” is characterized by widespread tracks of RPE atrophy and decreased fundus autofluorescence (FAF). Bullous detachments have also been described in CSCR patients. Thus the terms acute and chronic may not thoroughly describe or provide prognostic values for a disease with a wide spectrum of phenotypes. Multimodal imaging in CSCR includes fluorescein angiography, indocyanine green angiography, fundus autofluorescence, and optical coherence tomography. Newer imaging techniques

including optical coherence tomography angiography and wide-field angiography have also contributed to better understanding of the disease pathophysiology. The recently proposed classification of central serous chorioretinopathy using multimodal imaging has classified CSCR into simple, complex and atypical types based on the area of RPE involvement on FAF and OCT and other features [3].

<table>
<tr><td rowspan="3">Simple
Total area of RPE alteration ≤2 DA</td><td>Primary
First known episode of SRF</td><td rowspan="3">± Persistent
SRF >6months</td><td rowspan="3">± with outer retinal atrophy
ONL thinning and/or ELM disruption and/or EZ attenuation</td><td rowspan="5">± with CNV</td></tr>
<tr><td>Recurrent
Presence of SRF with history or signs of resolved episode(s)</td></tr>
<tr><td>Resolved
Absence of SRF</td></tr>
<tr><td rowspan="2">Complex
Total area of RPE alteration >2 DA or multifocal</td><td>Primary
First known episode of SRF</td><td rowspan="2">± Persistent
SRF >6months</td><td rowspan="2">± with outer retinal atrophy
ONL thinning and/or ELM disruption and/or EZ attenuation

± with intraretinal fluid</td></tr>
<tr><td>Resolved
Absence of subretinal fluid</td></tr>
<tr><td>Atypical</td><td>Bullous variant, RPE tear, association with other retinal diseases</td><td></td><td></td></tr>
</table>

Along with a good history, OCT evaluation and FAF forms the basic investigations in a case suspected to have CSCR. These investigations would help us to differentiate atypical CSCR from typical CSCR. Atypical CSCR includes bullous CSCR and those with RPE tears or associated with other retinal pathologies. Typical CSCR includes the simple and complex CSCR, which are better terms than acute and chronic CSCR.

OPTICAL COHERENCE TOMOGRAPHY (OCT):

OCT still remains the most popular primary imaging modality for evaluating and following up CSCR. In acute CSCR, even though there is subretinal fluid accumulation, retinal morphology usually remains unaltered. Enhanced depth imaging (EDI-OCT) or swept-source OCT (SS-OCT) clearly evaluates subfoveal choroidal thickness (SFCT) and identifies dilated Haller vessels and overlying choriocapillary compression. Elongations of

the photoreceptor outer segment may be seen in areas of serous retinal detachment, which is postulated to be due to the lack of phagocytosis by the RPE. RPE abnormalities include, serous PED which can occur within or outside the area of neurosensory retinal detachment, focal RPE thickening, RPE defects and flat irregular PED (FiPED). Findings associated with the site of leakage include serous PED, focal RPE thickening, fibrinous exudates in the subretinal space [4], sagging or dipping of the posterior layer of the neurosensory retina [6,7] and vacuole sign. Hyperreflective dots may be seen in neurosensory retina, subretinal space, at the site of leakage and even in the choroid. In chronic CSCR, OCT can demonstrate FiPED which is seen as double-layer sign and proposed to be harboring a neovascular network [8]. Morphological changes in the retina like thinning of the outer nuclear layer (ONL), cystoid macular degeneration, intraretinal and subretinal hyperreflective dots are seen in chronic CSCR. Choroidal vascularity index (CVI) defined as the area of the vessels divided by the total choroidal stromal area is an objective parameter of choroid evaluation for CSCR cases. (Figure 1)

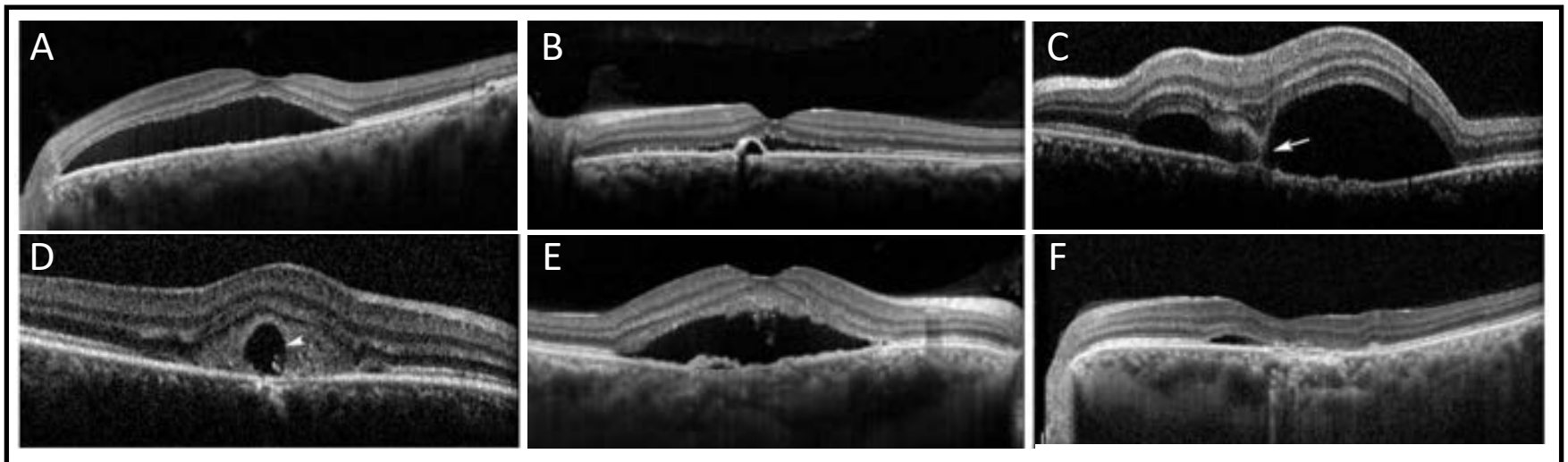

Figure 1: OCT findings in CSCR; Subretinal fluid with pachyvessels (A), SRF associated with serous PED (B), sagging or dipping of the posterior layer of the neurosensory retina (C), fibrin in the subretinal space with vacuole sign (D), Subretinal fluid with pachyvessels and Flat irregular PED (E), Hyperreflective foci in the choroid, subretinal fluid with pachyvessels (F).

FUNDUS AUTOFLUORESCENCE (FAF):

FAF is an in vivo marker of the photoreceptor and RPE function (Figure 2). In acute CSCR, areas of subretinal detachment are hypoautofluorescenct due to masking of the signals originating from the RPE by SRF or early elongation of photoreceptor outer segments[10]. Diffuse homogenous hyper-AF patterns both with and without the presence of hyper-AF punctate dots have also been reported [11]. In some cases, hypo-AF due to focal defects of the RPE or PED may correspond to the leakage point on FA [12]. The earliest change in chronic CSCR is usually diffuse hyper-AF due to the presence of SRF seen approximately 4 months after disease onset, while granular AF or diffuse hypo AF are observed with longer disease. Granular AF is due to partial loss of RPE cells and accumulation of lipofuscin while diffuse hypo AF represents diffuse RPE loss or

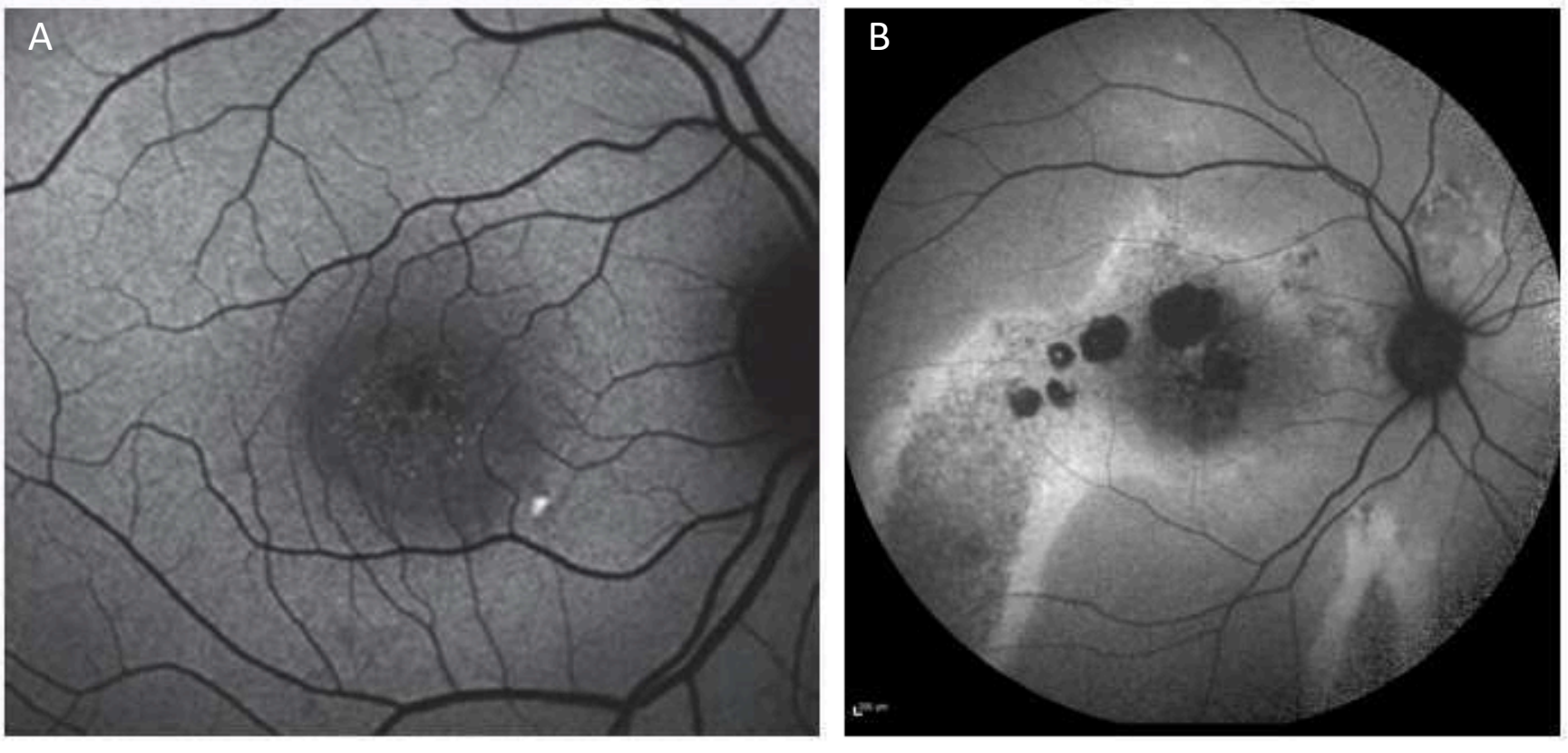

Figure 2: Blue peak FAF in a case of simple CSCR showing hypoautofluorescence corresponding to the area of subretinal detachment (A). Complex CSCR showing autofluorescenct gravitational tracks corresponding to sick RPE and patchy hypoautofluorescence areas due to loss of RPE (B).

thinning in chronic disease [14]. Confluent hypo-AF is a poor visual prognostic factor in CSCR [16, 17]. Autofluorescenct gravitational tracks are seen in some eyes and are pathognomic of chronic disease. The extent of autofluorescence abnormality (2 disc area) helps in classifying simple and complex CSCR.

FLUORESCEIN ANGIOGRAPHY (FFA):

Even though, CSCR can be diagnosed clinically or with noninvasive imaging such as OCT, FA and ICGA assist in treatment and provides insights into the choroidal vascular changes associated with CSCR. Three different patterns of leakage have been described- the smokestack pattern, the inkblot, and the minimally enlarging spot. The smokestack pattern is characterized by ascending hyperfluorescence followed by lateral diffusion, producing a mushroom-like image above the leaking point. The more common inkblot leakage pattern is characterized by a progressive and uniform expansion of a circular hyperfluorescence arising from a central pinpoint. In acute CSCR, one or multiple leakage site may be present [19]. (Figure 3)

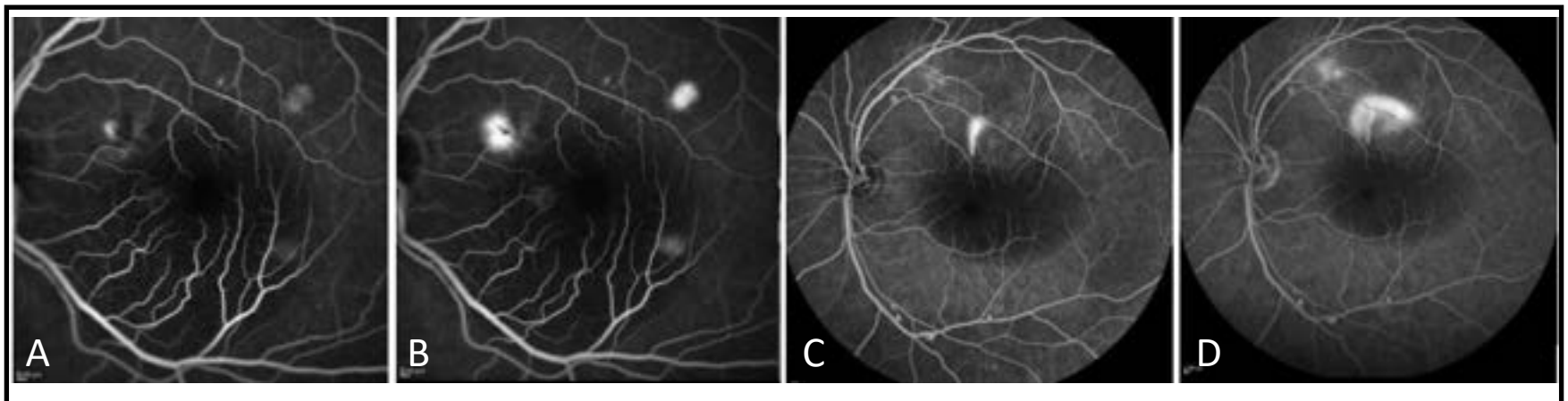

Figure 3: FFA in a simple CSCR showing a nasal inkblot leakage pattern characterized by a progressive and uniform expansion of hyperfluorescence arising from a central pinpoint foci (A,B). Two foci of PED pooling also can be seen temporally. FFA in a simple CSCR showing smokestack pattern characterized by ascending hyperfluorescence followed by lateral diffusion, producing a mushroom-like image above the leaking point (C,D).

In chronic CSCR, diffuse RPE damage with broad areas of retinal damage is often present. FA therefore shows multiple indistinct leakages or the diffuse oozing of dye, usually in the form of a descending tract, resulting in patches of granular or mottled hyperfluorescence in the mid and late phases [20]. In resolved CSCR or fellow eyes, areas of early hyperfluorescence are present due to increased transmission from window defects that are caused by localized RPE atrophy [21]. (Figure 4)

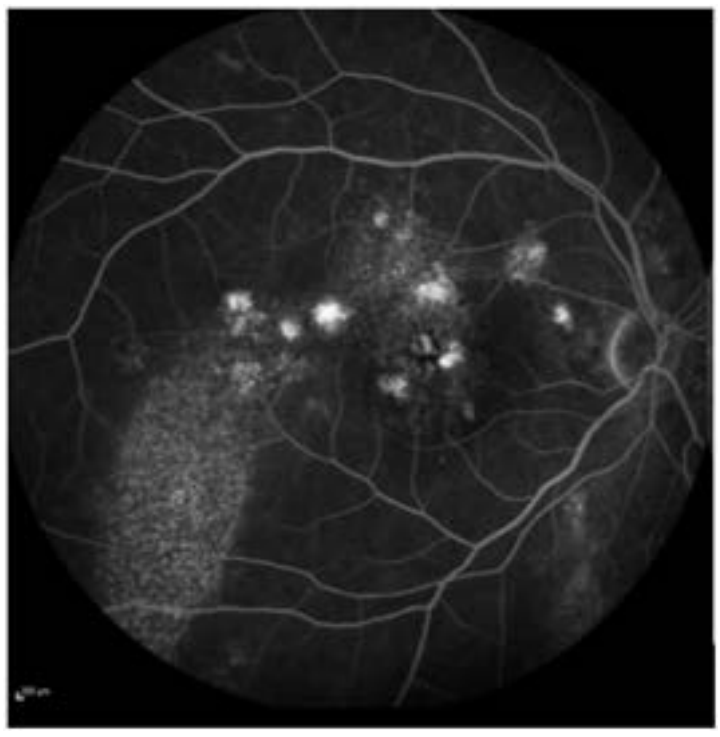

Figure 4: FFA showing multiple indistinct focal leakage points of the dye and a patchy area of granular or mottled hyperfluorescence in the form of a descending tract in the mid phase in a case of Complex CSCR

INDOCYANINE ANGIOGRAPHY (ICGA);

ICGA findings in CSCR can be categorized into early, mid, and late phase findings. In early phase, there is a delay in filling of choroidal arteries and choriocapillaris, resulting in areas of hypofluorescence that persists into the mid and late phases. In the mid-phase, focal choroidal hyperfluorescence surrounding the leakage point occurs due to choroidal vascular hyperpermeability. Dilated large choroidal veins are also seen in areas of atrophic or elevated RPE. These mid-phase hyperfluorescent areas develop into persistent, washout, or centrifugally displaced hyperfluorescence in the late phase. In addition, choroidal vessels exhibit transient hyperpermeability, seen as multiple

punctate hyperfluorescent spots, increasing in severity in the mid-phase and fading in the late phase. [22,23]. ICGA also helps to identify CNV that complicates CSCR. In these eyes, there is increasing hyperfluorescence from the mid to the late phase, showing an ill-defined, late-staining plaque that confirms the presence of occult CNV [24]. (Figure 5)

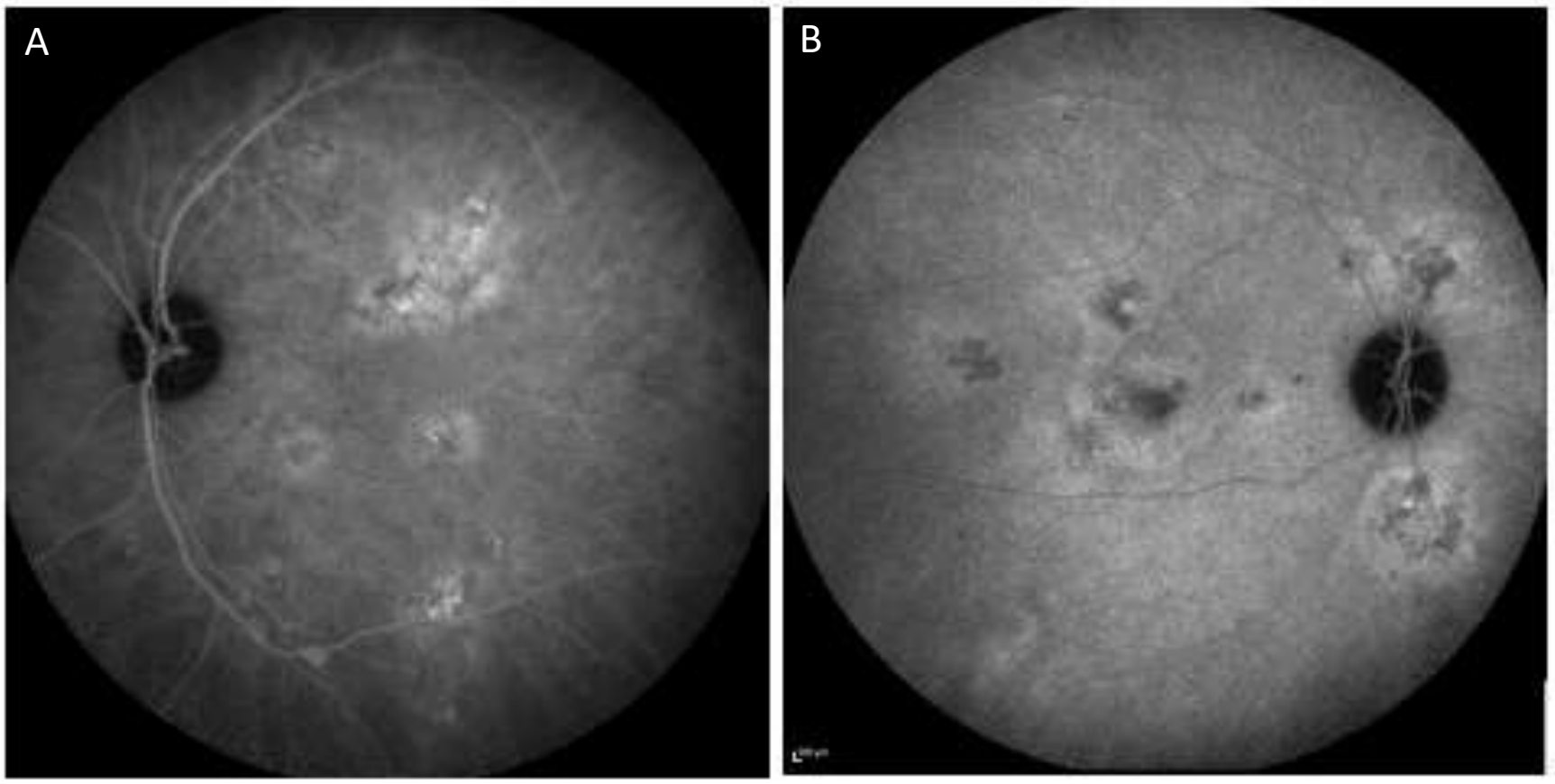

Figure 5: (A) ICGA mid-phase revealing, focal and patchy choroidal hyperfluorescence due to choroidal vascular hyperpermeability. (B) ICGA revealing areas of persistent, washout and centrifugally displaced hyperfluorescence in the late phase in a case of complex CSCR.

WIDE FIELD IMAGING IN CSCR:

Ultra-widefield (UWF) AF and ICG angiography in CSCR revealed more widespread disease in a single image than with standard field imaging and may be useful for identifying peripheral areas of previous or ongoing SRF and choroidal hyperpermeability that can assist in the diagnosis of CSC, surveillance of recurrent disease and treatment of

active disease. Dilated vessels were observed in association with 1 or more congested vortex veins ampullae, suggesting that outflow congestion may be a contributing factor to the pathogenesis of CSC. In areas with dilated vortex veins, the dominant side, choroidal thickening was significantly greater than that on the non-dominant side. CVI shows significant regional variation with macular segment showing the lowest CVI whereas nasal segments have highest CVI in both CSCR and their fellow eyes. (Figure 6)

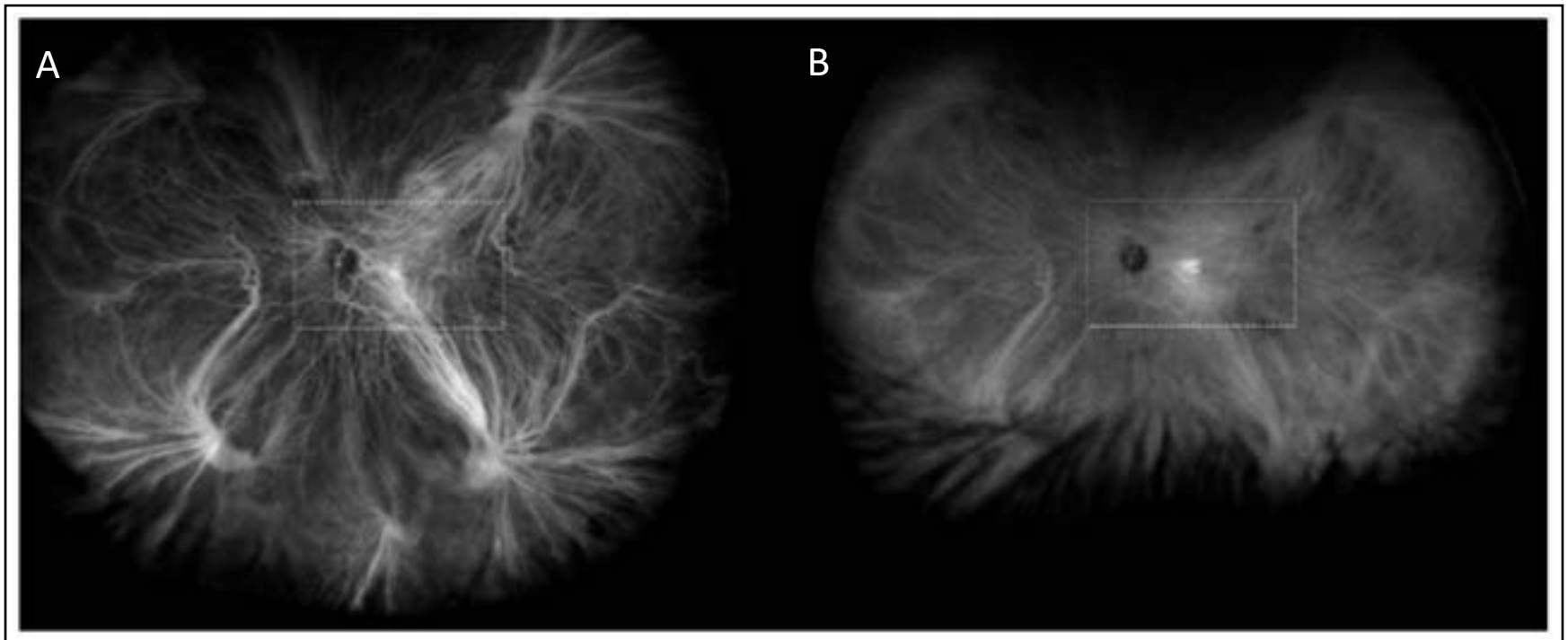

Figure 6: (A) Early-mid phase ultra-widefield indocyanine green angiography (UWF ICGA) image of the left eye of a 37-year-old man with simple central serous chorioretinopathy. The superonasal vortex vein system appears relatively hypoplastic. Consequently, the overall choroidal venous drainage appears imbalanced, with inferior vortex vein systems draining a greater proportion of the post-equatorial fundus compared to the superior ones. Their ampullae and major venous branches appear dilated, suggesting choroidal venous congestion mostly involving the inferior quadrants. Major venous branches of the inferotemporal vortex vein system surround the optic disc and drain a large portion of the parapapillary region, not respecting the physiologic geometry of choroidal venous watersheds that usually pass horizontally through the disc and fovea, and vertically through the papillomacular region. (B) Mid-late phase UWF ICGA image of the same eye, showing choroidal vascular hyperpermeability in the macular region.

OCT ANGIOGRAPHY (OCTA)

OCTA is a noninvasive imaging that allows qualitative and quantitative assessment of vascular structures in the retina and the choroid helpful in CSCR diagnosis and management (Figure 7). OCTA demonstrates larger vascular flow area in the choroid supporting the involvement of choroidal circulation in CSCR pathogenesis. OCTA also detects choriocapillary hypoperfusion as a subclinical change preceding CSCR. Studies have showed significant increase in vessel density at the deep capillary plexus and the choriocapillaris after treatment with low fluence PDT. Abnormal choriocapillary flow patterns can be associated with higher recurrence rates in resolved CSCR eyes. The CNVM network pattern in OCTA, was found to have either a loop-like or a tree-like structure. Choroidal island is a term defined on OCTA in CSCR as an island of detectable

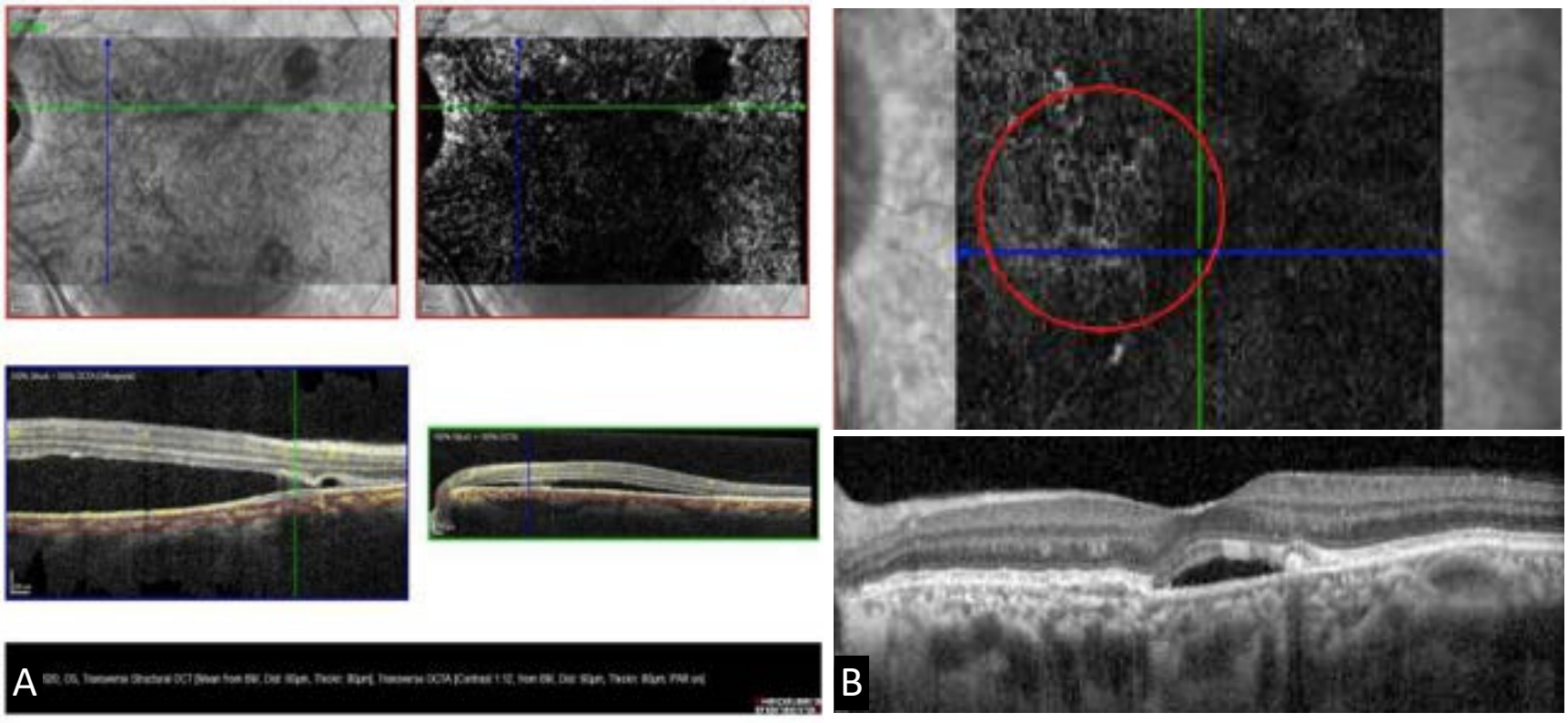

Fig 7; OCTA demonstrating decreased choriocapillary perfusion corresponding to the area of subretinal fluid and pachyvessels (A). OCTA demonstrating the presence of an abnormal neovascular network corresponding to the focal RPE thickening in an eye with chronic CSCR (B).

choriocapillaris flow surrounded by an area of undetectable or diminished flow underneath the area of neurosensory detachment. The longstanding anatomical and functional affection of the outer retinal layers at the CCI location, may render it most vulnerable to the development of CNV. OCTA thus provides an improved understanding of pathogenesis of the disease, to evaluate post treatment changes in retinal and choroidal vasculatures and also CNVM assessment. (Figure 7)

CONCLUSION:

Multimodal imaging has improved our clinical understanding of the pathophysiology of CSCR and has helped us improve on the terminology and classification of the disease and devise treatment protocols, prognosticate and predict treatment response.

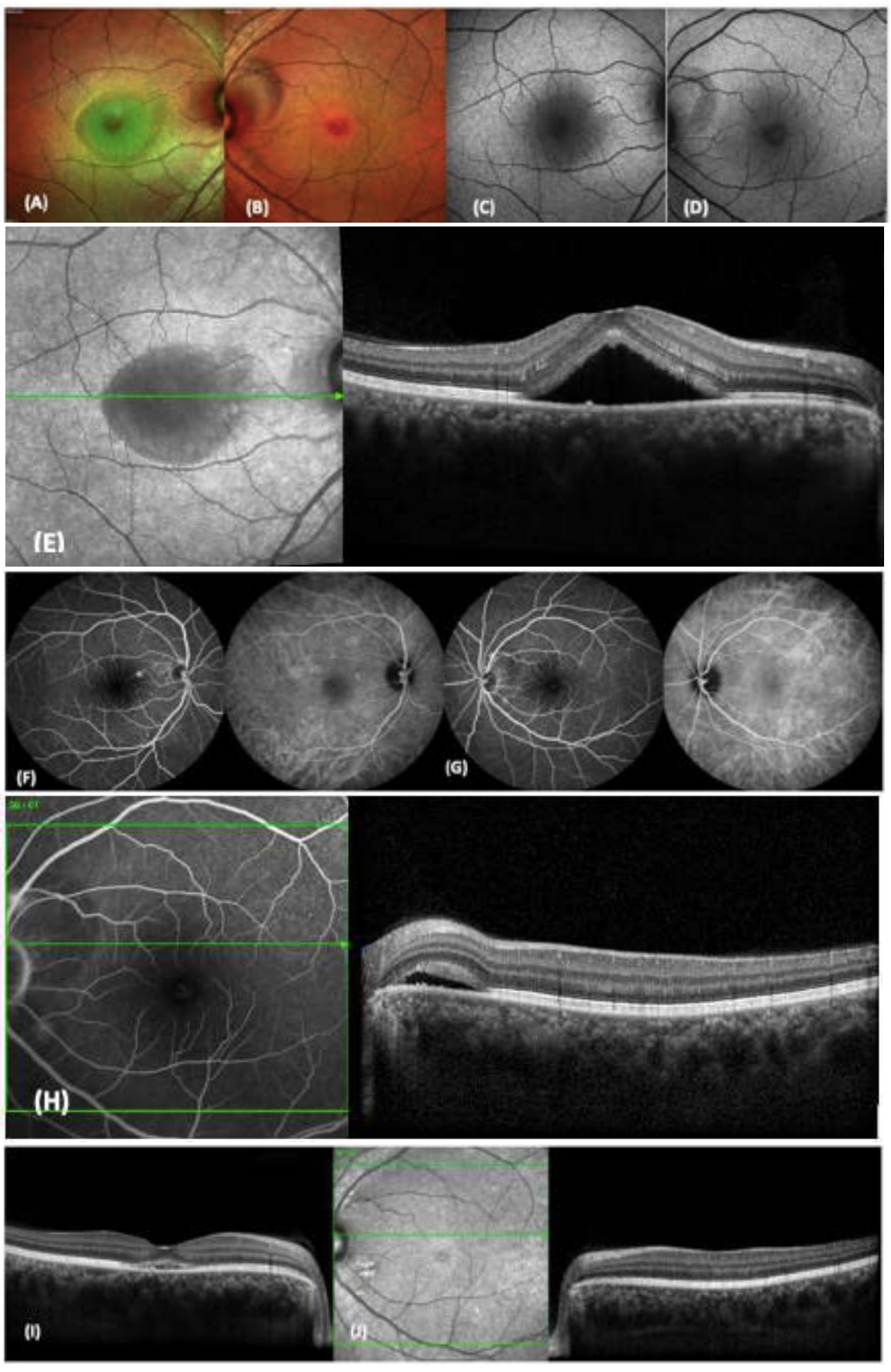

Fig 8: (A) Multicolour image of a 29 yr old male with right eye defective vision. The right eye shows the greenish hue of SRF at macula. (B) Multicolour image of left eye showing subretinal fluid temporal to disc. (C,D) FAF images of right and left eye showing hypo autofluorescence corresponding to SRF areas. Note that in the absence of RPE window defects or staining, the appearance corresponds to bilateral simple CSCR. (E) SD-OCT image showing SRF at macula with stretching of the EZ layer and underlying pachychoroid. (F)Right eye; FFA showing inkblot leak nasal to fovea with ICG showing hypercyanescence in the corresponding area and choroidal hyperpermeability. (G)Left eye; FFA did not reveal any leaks and ICG shows choroidal hyperpermeability. (H) SD OCT of left eye revealed SRF temporal to disc with elongated photoreceptors and pachychoroid. (I) Follow up OCT 2 months later revealing right eye spontaneous resolution with minimal SRF. (J) Follow up OCT 2 months of the left eye shows complete SRF resolution.

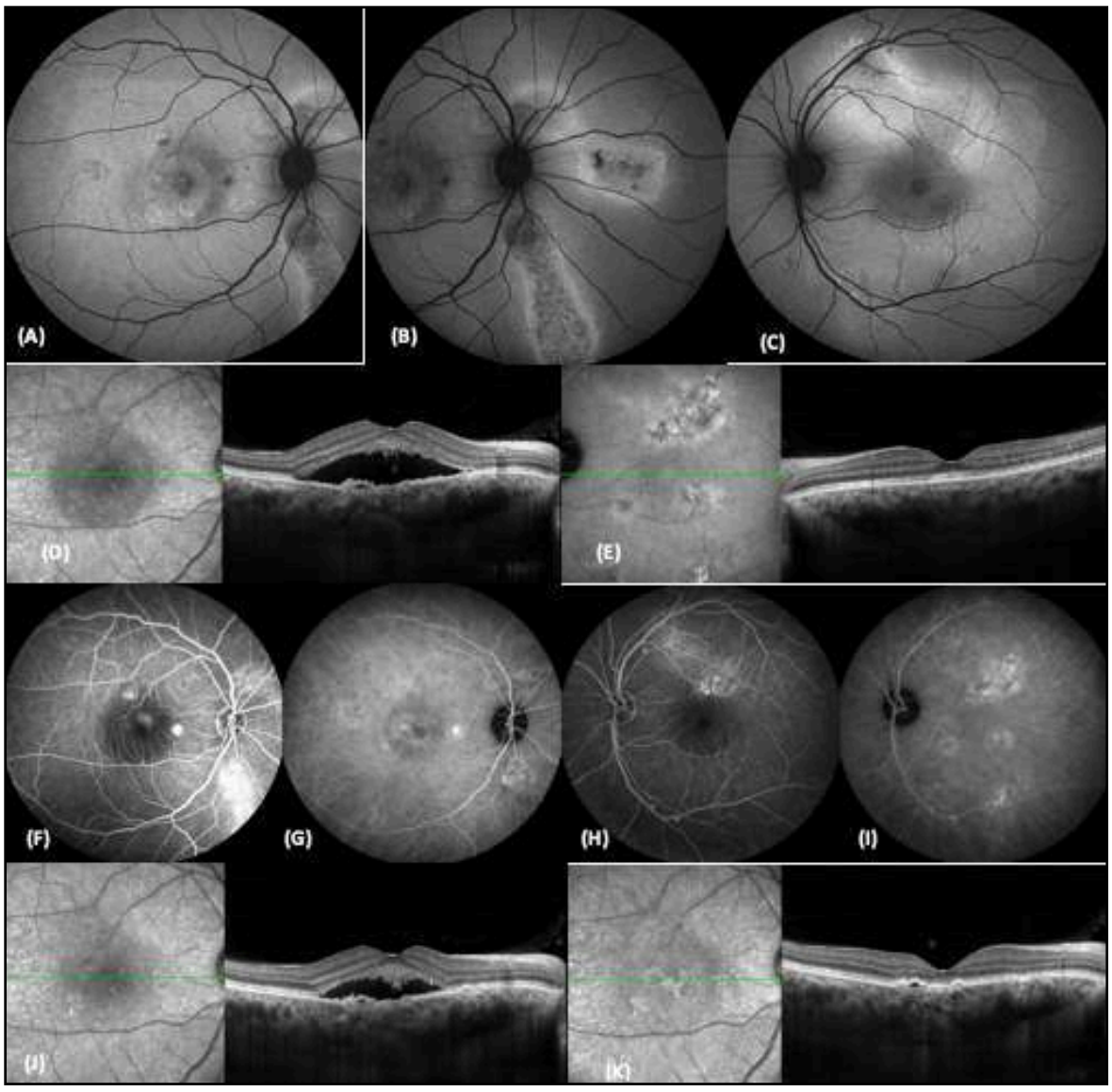

Fig 9: (A-C)- FAF images in a complex CSCR commonly referred to as chronic CSCR in a 35 yr old male who presented with right eye defective vision showing gravitational tracts corresponding to DRPE areas at macula and nasal retina in the right eye and large patchy abnormal FAF region in the left eye. The gravitational tracks in the right eye clearly show the hypoautofluorescence areas corresponding to the areas of RPE loss with hyperautofluorescent borders suggestive of sick RPE. (D) SD-OCT of right eye showing SRF, shaggy photoreceptors, subretinal fibrin, FiPED (Flat irregular PED) and underlying pachychoroid. (E) SD OCT of left eye shows absence of foveal SRF but reveals underlying pachychoroid features. (F) FFA of right eye showing abnormal fluorescence at the fovea and superior to fovea with inkblot leak nasal to fovea and staining of DRPE areas. (G) ICG of right eye reveals central hypocyanescence and no evidence of choroidal neovascularisation. However the nasal point of leakage was seen as a hypercyanescent spot on ICG also. (H) FFA of the left eye showing patchy fluorescence superior to fovea.(I) ICG of the left eye reveals the typical mutifocal patchy areas of hypercyanescence corresponding to the choroidal hyperpermeability. (J) 2 months after focal laser treatment the right eye revealed persistent SRF, elongated photoreceptor layer and persistent FIPED. (K) 4 months after laser treatment the right eye revealed complete SRF resolution even though the underlying pachychoroid showed no change and the FIPED persisted.

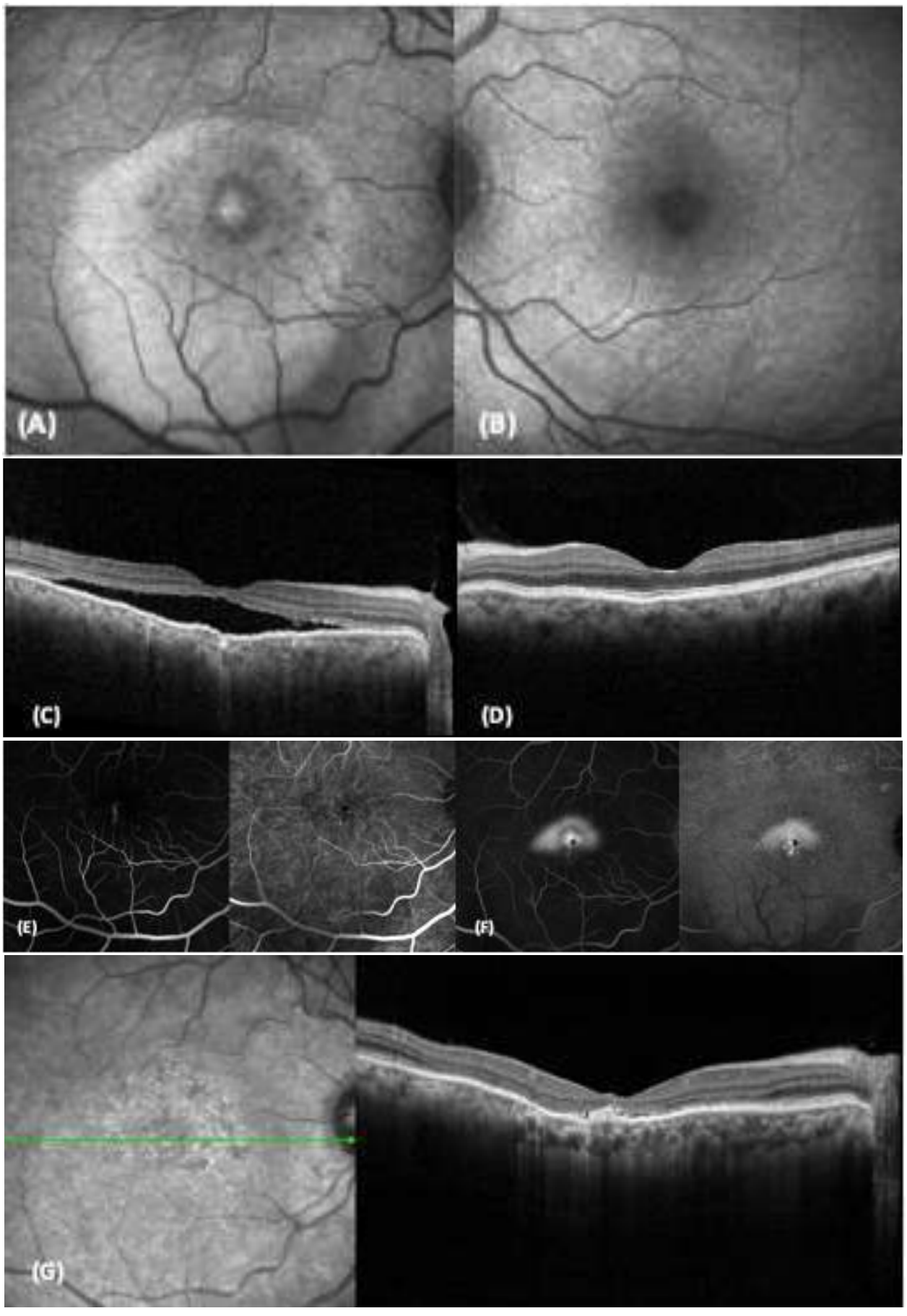

Fig 10: (A) FAF of right eye in a 30 yr old female who presented with right eye defective vision showing a large patch of hyper AF signals corresponding to CSCR suggestive of a complex CSCR. (B) FAF of left eye was normal. (C) SD OCT of right eye showing SRF, RPE thickening and no obvious pachyvessels. (D) SD OCT of left eye was normal. (E-F) FFA showing a subfoveal smokestack pattern of leak in right eye. ICG also reveals late hypercyanescence corresponding to the leakage on FFA. (G) Following treatment with low fluence PDT, OCT reveals good SRF resolution. Note the hyperreflective deposits at the fovea and streaks of choroidal hyper transmission showing poor RPE health.

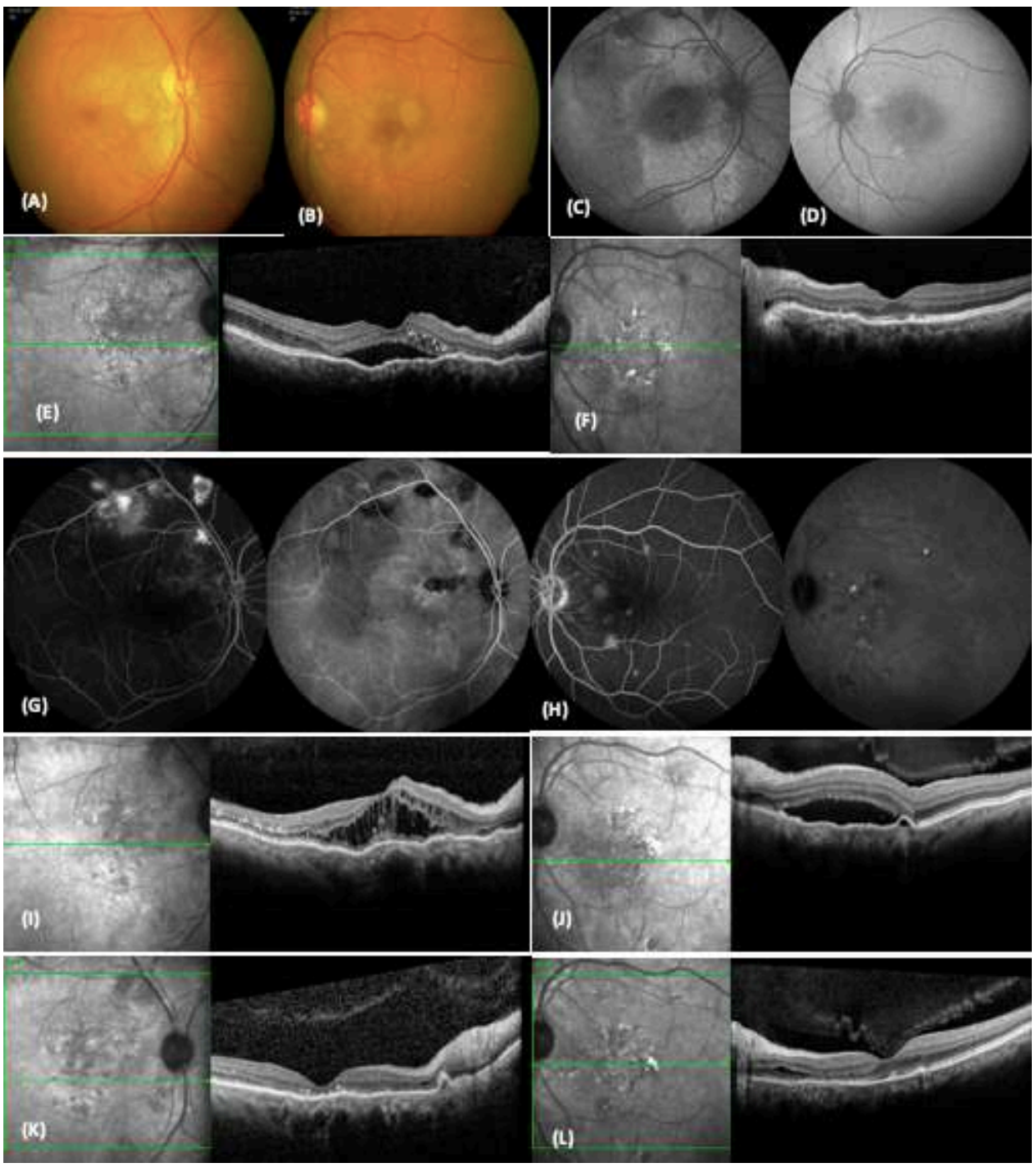

Fig 11: (A-B) Fundus photograph of a 45 year old lady showing SRF and multiple areas of RPE mottling in both eyes. (C) Right eye FAF showing a large area of hyperautofluorescene with patches of hypoautofluorescence corresponding to DRPE. (D) Left eye FAF showing patchy hyperautofluorescene areas in peripapillary area. (E) OCT of the right eye revealed SRF with intraretinal HRF nasally. (F) OCT of the left macula showed few focal EZ layer disruption. 4 months after initial presentation she came with bilateral defective vision. (G) FFA of the right eye revealed extrafoveal abnormal fluorescence with areas of focal intense staining. ICG angiography revealed multiple areas of focal hypocyanescence and an area of choroidal hypermeability. (H) FFA of the left eye revealed extrafoveal pooling of dye with pinpoint leak. Late ICG angiography revealed focal patchy choroidal cyanescence. (I) SD OCT of the right eye showing schitic edema with IRF, outer layer hyperreflective foci (HRF), RPE irregularity and pachyvessels. (J) SD OCT of left eye showing SRF, serous PED, outer layer HRF, along with pachyvessels. (K, L) Following 4 months of Eplerenone therapy, follow up OCT showing good resolution of fluid in both eyes. Note residual outer layer HRF and nasal residual outer layer IRF in the left eye.

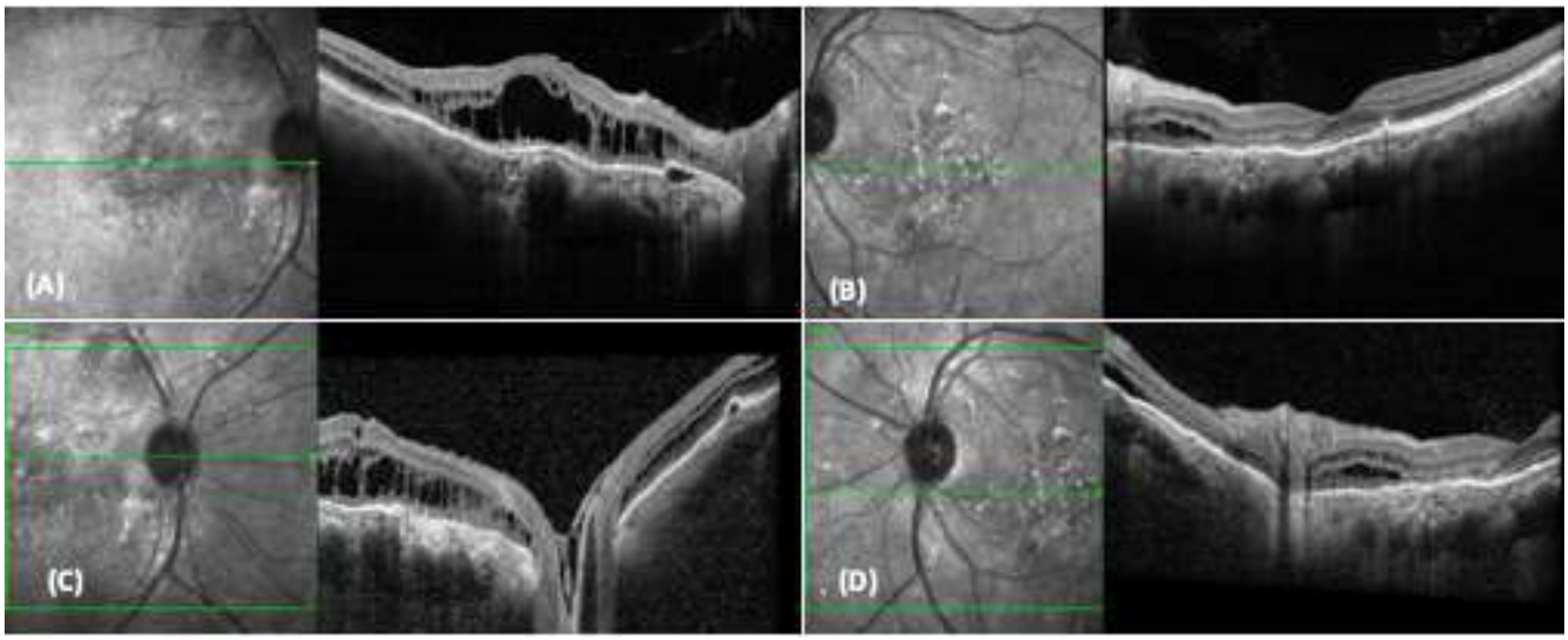

Fig 12: After cessation of eplerenone therapy in the above patient, (A) SD OCT of the right eye showing recurrence of schitic edema with IRF, choroidal HRF and large pachyvessels conspicuously seen nasally. (B) SD OCT of left eye showing nasal intraretinal fluid along with pachychoroid. (C,D) OCT of the nasal retina reveals outer layer schisis and small PED in the right eye and thin SRF in the left eye. Also the peripapillary pachyvessels are seen prominently in both eyes. A diagnosis of atypical CSCR with peripapillary pachychoroid disease was made and the patient was restarted on Eplerenone therapy.

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CHOROIDAL MASS LESION IN CSC- A RARE PACHYCHOROID PHENOTYPE !

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Central serous retinopathy (CSR) is now recognized as central serous chorio-retinopathy (CSC), a choroidal disease thanks to the progress in imaging technology such as Swept Source and enhanced depth imaging (EDI) optical coherence tomography (OCT), Ultra-widefield fundus fluorescien angiography (FFA) and indocyanine green angiography (ICGA), which has revolutionized the understanding of CSC pathophysiology. These advancements have brought about a plethora of knowledge regarding the pachychoroid disease, including the increase in choroidal thickness, dilated choroidal vessels, and other structural alterations in choroidal architecture. Recently, Spaide et al. have described a novel feature of posterior choroidal fluid loculation in the outer choroid in patients with CSC.[1] In CSC, leakage from choriocapillaries appears to be the primary pathology. This accumulation of fluid beyond a threshold of approximately 400µ saturates the choroidal stroma, leading to pooling of this additional fluid either under

the retinal pigment epithelium (RPE) presenting as pigment epithelial detachment (PED) or in the posterior suprachoroidal space. This collection can be differentiated from large choroidal vessels by its angulated inner border, homogeneous lack of reflectivity, lack of an observed bounding vascular wall, and the large size (>250µ) of the hypo-reflective lumina. This can either be 'interdigitated' or 'dissociated' forms - the former refers to fluid accumulation in the outer choroid with an extension in between the outer choroidal vessels, and the latter denotes isolated fluid collection posterior to the larger choroidal vessels.

In a recent report, we described an atypical variant of CSC presenting as a solitary choroidal elevation due to exaggerated form of posterior choroidal fluid accumulation, associated with sub retinal fluid (SRF) and which has a favorable outcome.[2] We described the multimodal imaging characteristics, clinical features and treatment outcomes of these cases presenting as solitary choroidal mass lesion with overlying SRF (two prototype cases depicted in Figure 1 and 2 below). This pachychoroid phenotype was identified more in 40-60 years age group and presented as solitary elevated lesion with overlying SRF, without signs of inflammation. All patients reported this as their first episode. OCT typically showed thickened choroid with characteristic fusiform hypo-reflective lumina in the outer choroid suggestive of posterior choroidal fluid loculation. RPE undulation with normal choriocapillary layer was observed in all cases. Angiographic studies showed presence of pachy-vessels on ICGA and focal as well as diffuse leaks on FFA.

Various pathologies are known to present with solitary choroidal elevation. Considering the above mentioned findings, our differential diagnoses included Choroidal hemangioma, Amelanotic choroidal melanoma, choroidal metastasis, choroidal

granuloma, nodular posterior scleritis and posterior uveal effusion syndrome. An extensive systemic evaluation is mandated to exclude the possibility of uveitic and metastatic components. This rare pachychoroid phenotype presenting as choroidal elevation was narrowed down by utilizing the combination of multimodal imaging features, detailed work-up including clinical examination and systemic investigations.

All cases were treated in the lines of pachychoroid disease with atypical CSC and posterior choroidal loculation of fluid, which included close observation, focal laser photocoagulation to the angiographic point leaks or oral eplerenone . All cases displayed marked resolution and no recurrence after one year of follow-up.

Posterior choroidal loculation of fluid due to excess choroidal hyperpermeability and leakage, is a less commonly described feature of CSC. This phenotype of CSC with solitary choroidal elevation due to exaggerated choroidal fluid loculation is rare and has not been previously reported. The exact pathophysiology behind the exacerbated fluid build-up in the posterior choroid remains unclear. This condition has a good prognosis when treated in the lines of CSC and a low recurrence rate. In patients presenting with solitary choroidal elevation, this pachychoroid variant should also be considered among the differentials, a systemic work-up to rule out inflammatory pathology and tumor is required. The diagnosis of exaggerated posterior choroidal loculation of fluid in pachychoroid disease may be narrowed down using the multimodal imaging features.

CHOROIDAL MASS LESION IN CSC- A RARE PACHYCHOROID PHENOTYPE !

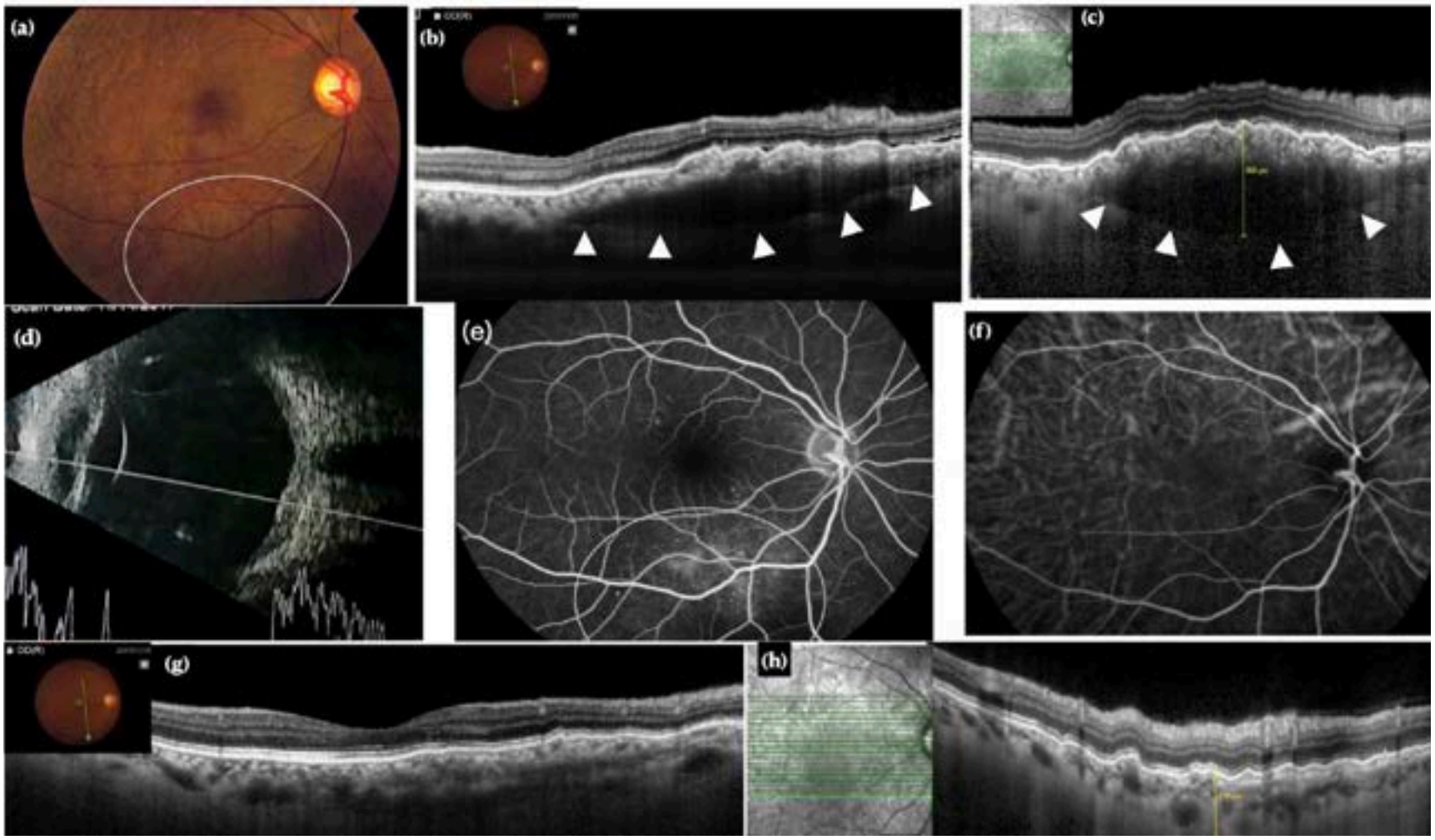

Figure 1. A 46-year-old-lady with right eye BCVA 20/40 presented with choroidal elevation inferior to macula with overlying SRF (a). At presentation, EDI-OCT image through the fovea and the lesion showing shallow subfoveal fluid, RPE undulations, choroidal elevation and fusiform hyporeflective lumina in the outer choroid (white arrowhead) (b), OCT through the inferior extension of the lesion showing RPE undulations and extension of hyporeflective lumina in the outer choroid (white arrowhead) with no choriocapillary compression (c), Ultrasonography showing localized RCS thickening (yellow arrowhead) (d), Fluorescein angiography showed multiple point leaks over the lesion in late phase (white circle) (e), Indocyanine-Green angiography showing few dilated choroidal vessels in superior half of choroid (f). EDI-OCT at 3 months following conservative management showing complete resolution of subfoveal fluid and considerable reduction in the size of hyporeflective lumina under the fovea (g), and through the inferior extension of the lesion (h)

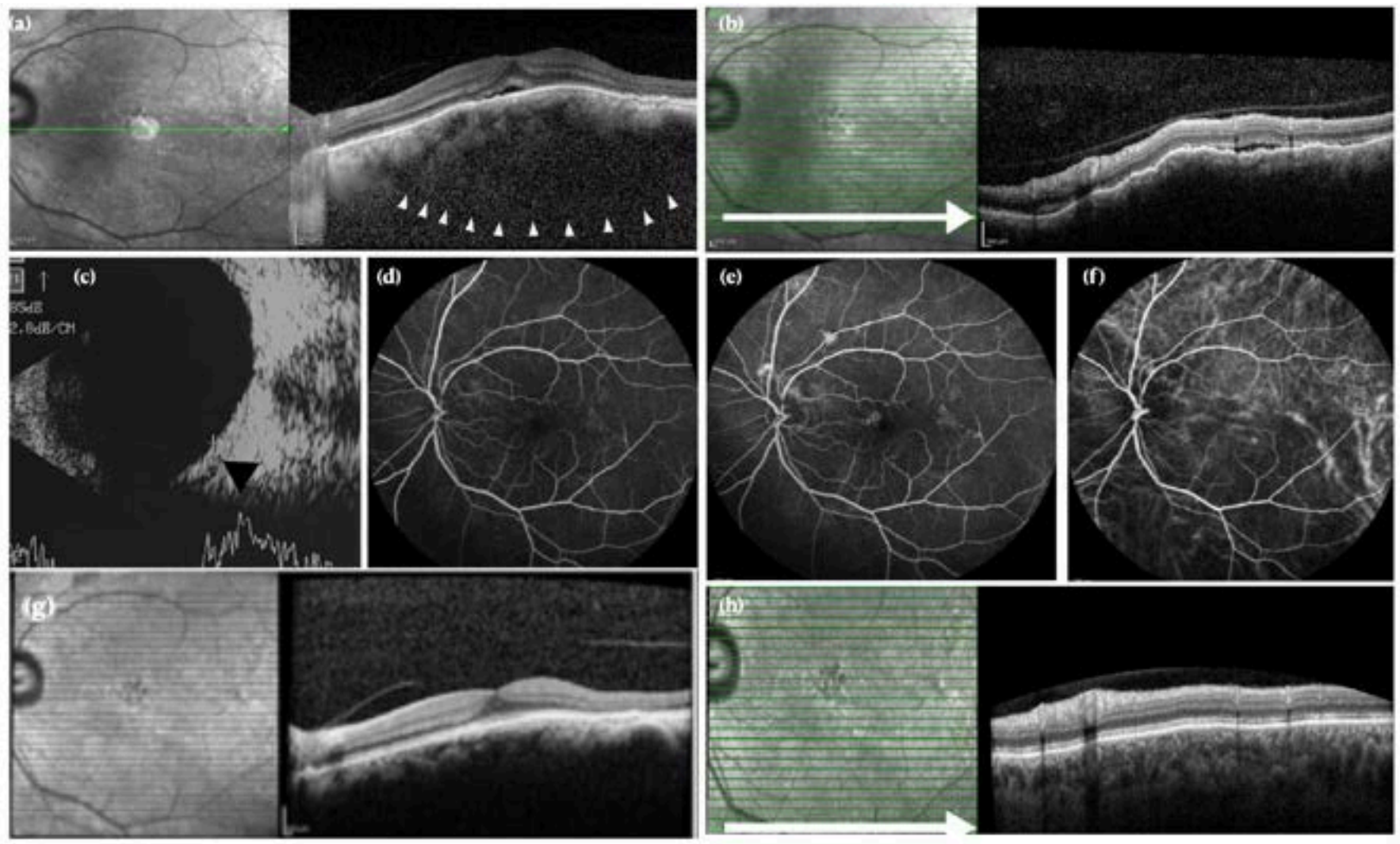

Figure 2. Left eye of a 65-year-old-male with BCVA 20/30 revealed smooth elevated mass lesion in the inferotemporal macula and inferotemporal vascular arcade – At presentation, EDI-OCT showing subfoveal fluid, choroidal elevation, a grossly thickened choroid and outer choroidal hyporeflective lumina without clear demarcation (interdigitated loculation) (white arrowhead) (a), OCT through the lesion (scan line highlighted as white arrow) showing subretinal fluid, RPE undulation with choroidal elevation (b), ultrasonography showing localized thickening of RCS complex (black arrowhead) (c), fluorescein angiography showing normal features with few points of RPE leakage in the mid and late phases (d and e), and, Indocyanine-green angiography showing dilated outer choroidal vessels (pachyvessels) (f). EDI-OCT through the line corresponding to A and B, at 8 weeks of follow-up after starting oral Eplerenone 50 mg OD, showing complete resolution of subretinal fluid and RPE undulations, flattening of choroidal elevation, and considerable reduction in the size of hyporeflective lumina in the outer choroid (g and h).

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CENTRAL SEROUS CHORIORETINOPATHY MIMICKING AS BULLOUS RETINAL DETACHMENT WITH RPE RIP: A CASE REPORT

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Introduction:

Central serous chorioretinopathy (CSCR) is characterized by serous detachment of the neurosensory retina, along with retinal pigment epithelium (RPE) detachments. Bullous retinal detachment is a rare and unusual presentation of chronic CSCR (1). Large, stressed RPE detachments in chronic CSCR can lead to “Blow out” resulting in RPE tears which remains the most common cause for exudative detachment (2). Due to its atypical presentation, it may pose diagnostic dilemma and often leads to inappropriate therapeutic procedures in many cases (3). We report a case of CSCR presenting as bullous exudative retinal detachment (RD) with RPE rip.

Case: A 60-year-old hypertensive lady presented with gradually progressive, painless diminution of vision in right eye (OD) since past 6 months. Her past history was not significant except for spondylitis, ulcerative colitis and history of retinal laser 3 months back. She was diagnosed to have OD rhegmatogenous RD and referred for further management. Best corrected visual acuity (BCVA) was 1/60, N 18 in OD and 6/5, N6 in left eye (OS). Anterior segment examination and intraocular pressure were within normal limits in both the eyes. There were no signs of inflammation. Fundus in OD showed inferior bullous RD with shifting fluid involving the macula which was confirmed on ultrasonography (USG). A large RPE tear was noted temporal to fovea at the superior margin of the detached retina with localised subretinal exudation inferotemporally. OS had few RPE alterations at macula. Fundus autofluorescence showed corresponding area of hypoautofluorescence with crumpled hyperautofluorescent RPE at the edge of the tear (Figure 1). Fundus Fluorescein angiography (FFA) in OD showed large area of window defect with pooling of dye in late phase suggestive of RPE rip with active leaking of dye from multiple points surrounding the area of rip in late phase (Figure 2). OCT showed sub-foveal sub retinal fluid (SRF) with loss of RPE in the area corresponding to RPE tear (Figure 3). On further questioning and detailed history evaluation, patient revealed use of corticosteroid inhaler on and off for breathing difficulties. Based on history, detailed clinical examination and multimodal imaging, she was diagnosed to have bullous variant of CSCR in association with large RPE tear. She was advised to stop all forms of steroids. At 6 week follow up, a fibrinous collection was noted at inferior margin of the RPE tear. FFA showed leakage of dye from the center of fibrin in ink blot pattern (dark spot sign) (4) suggestive of an active leak and was confirmed on OCT (Figure 4). FFA guided focal laser was done to the leak. No laser was done to RPE tear as

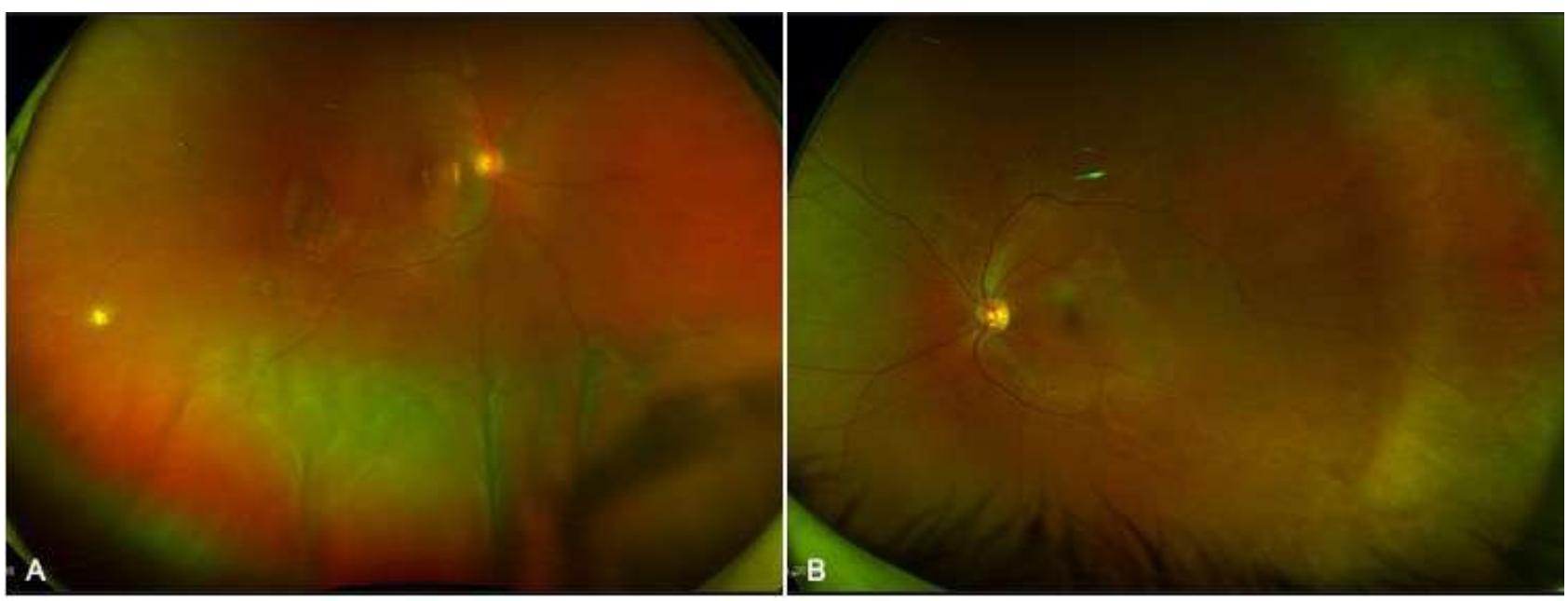

Figure 1 : Color fundus photo of (A) right eye showing bullous exudative retinal detachment with area of large RPE tear temporal to fovea. (B) left eye shows few RPE alterations at macula.

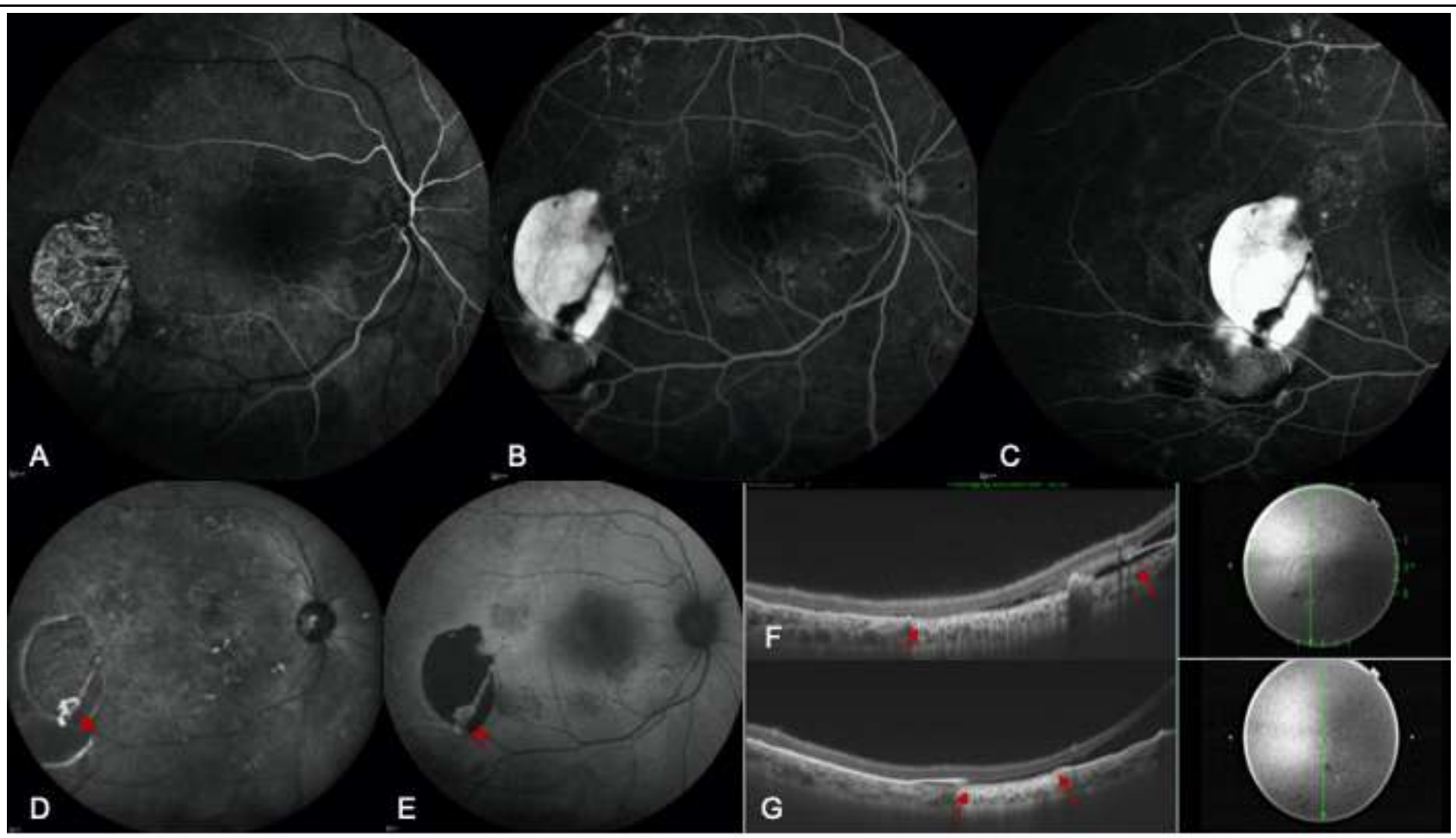

Figure 2 : FFA shows early window defect at the area of RPE tear (A), late pooling of dye (B) and multiple CSR point leaks around the tear (C). Scrolled RPE at the edge of the tear (asterix) are seen more clearly in infrared image (D). The RPE tear appears hypoautofluorescent due to absence of RPE (E). OCT line scans (F and G) shows loss of RPE and scrolled edges (arrows).

it appeared in healing stage. At 3 months follow up, her vision improved to 6/60, N10 with reattachment of retina and dry fovea (Figure 5). She maintained a BCVA of 6/18, N6 at 3 year follow up. She was off steroids with no recurrence of disease.

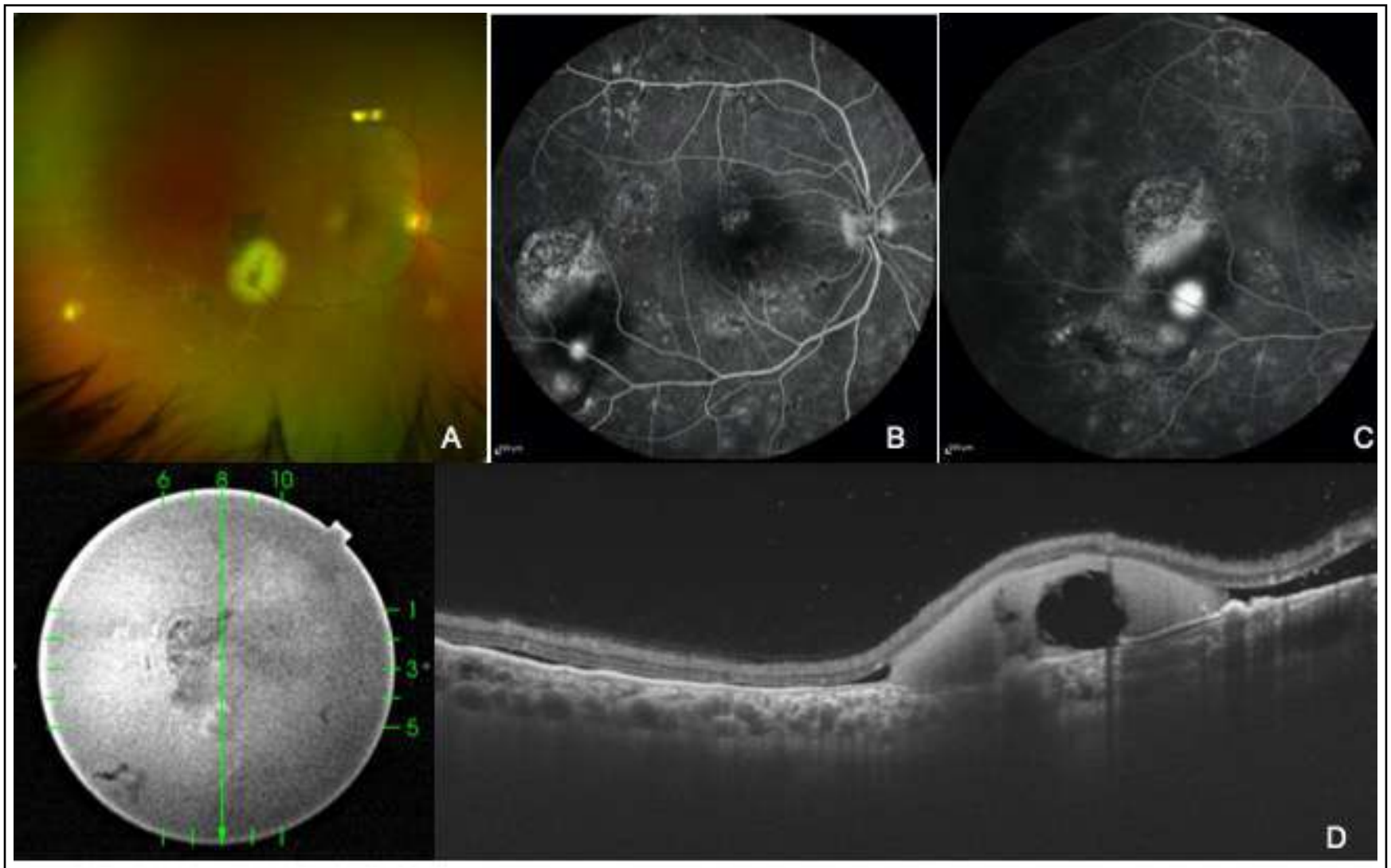

Figure 3: Color fundus at 6 weeks shows appearance of fibrin at the inferior edge of the tear with dark spot in the center of the fibrin. FFA showed leak corresponding to the area of dark spot in early phase (B) which intensifies in the late phase (C). OCT showed subretinal fibrin with clear space in the center at the edge of the RPE tear (D).

Discussion:

Acute RPE tear resulting in bullous retinal detachment in cases of CSCR can lead to sudden visual loss (1). Corticosteroid use may increase the risk of RPE tears in these cases by increasing the hydrostatic pressure within the pigment epithelium detachment (PED) and increasing fibrin exudation, which causes circumferential tractional vector to the RPE (5). Extensive RPE damage in chronic CSCR can also lead to concentric RPE

CENTRAL SEROUS CHORIORETINOPATHY MIMICKING AS BULLOUS RETINAL DETACHMENT WITH RPE RIP: A CASE REPORT

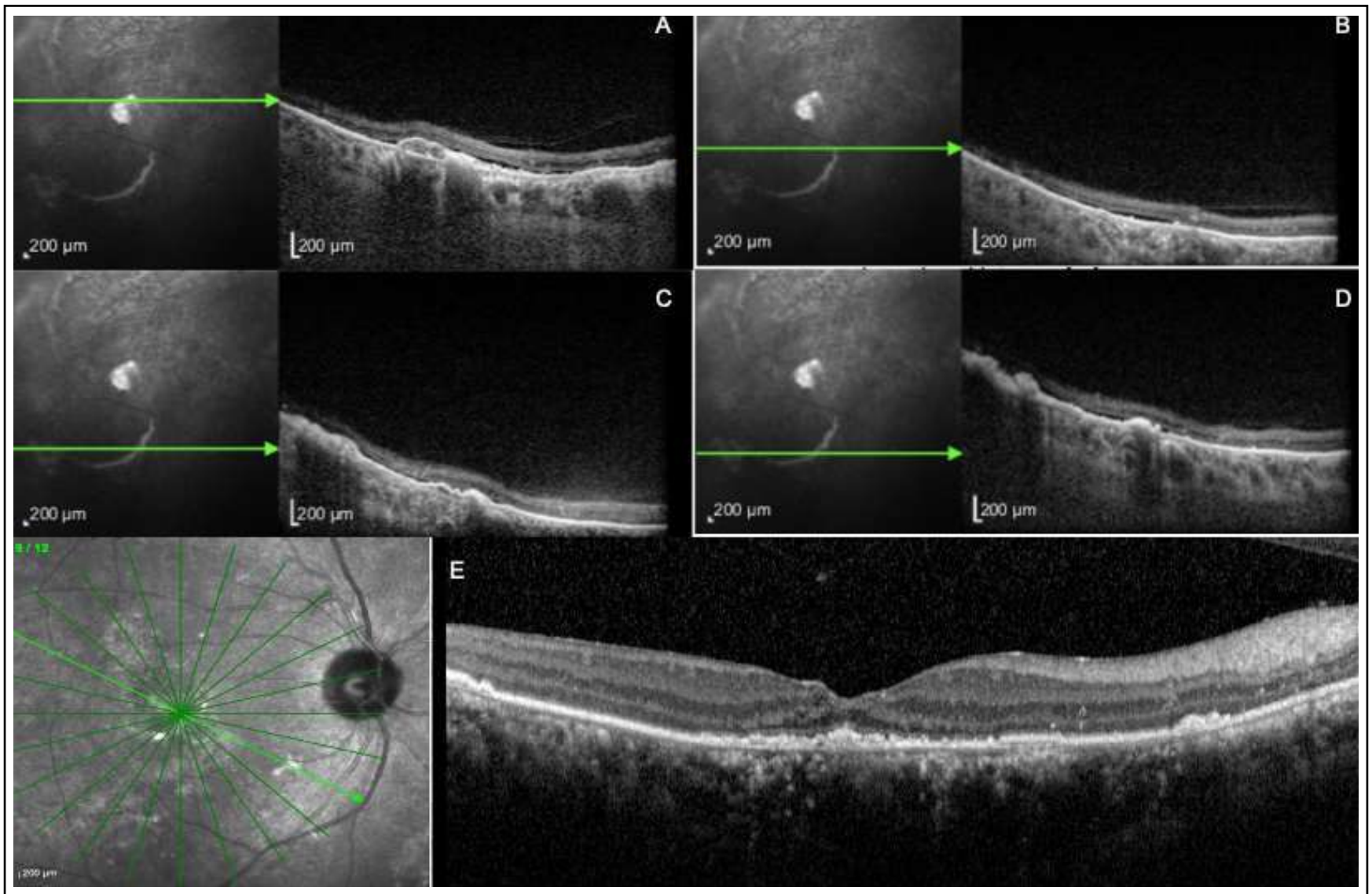

Figure 4 : At 3 months follow up, serial OCT line scans through the tear shows healing of the tear by scarring (A-D) and resolution of subretinal fluid (E).

tears. Bullous variety of CSCR can present as a diagnostic challenge and needs to be differentiated from other causes of inflammatory and non-inflammtory exudative detachments. Multimodal imaging comprising of color photography, FFA, ICG, fundus autofluorescence, near infrared imaging and high-resolution OCT can demonstrate underlying pathogenic mechanism of the tear formation and differentiate from other causes of RPE tears. Visual prognosis depends on location and extent of RPE tear. Rip involving fovea causes significant visual loss. However prognosis of CSCR related RPE rip is better than choroidal neovascularization related RPE rip. RPE tears usually heal by migration of RPE cells from the denuded edge to the center or by scarring. The underlying disease process should be treated for better visual and anatomical outcomes.

Early treatment by focal laser to the leak helps in early resolution of exudative detachment. Corticosteroids play a major role in pathogenesis of CSCR, hence should be avoided in any form to prevent recurrences of CSCR.

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SUBTHRESHOLD MICROPULSE LASER IN CENTRAL SEROUS CHORIORETINOPATHY

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Introduction

Central Serous Chorioretinopathy (CSCR) is one of the most common retinal condition which is predominantly seen in middle aged patients. It is characterised by the presence of a serous neurosensory detachment (NSD) with or without the presence of retinal pigment epithelial (RPE) detachment [1]. CSCR has been conventionally classified into acute or chronic form depending on the duration of serous NSD (4-6 months). No consensus exists over the duration threshold that differentiates acute and chronic CSCR, arbitrarily set between 4 and 6 months in most published reports [1]. Risk factors for CSCR includes Type-A personality, antipsychotic medications, stress, hypertension, obstructive sleep apnea and patients under systemic and local corticosteroid therapy [2-4].

The pathophysiology behind CSCR is still debated and this is because of our lack of understanding of the primary pathology. There have been several theories which point towards the clinical features seen in such patients – Choroidal vascular hyperpermeability with or without active pigment epithelial leaks or Pigment epithelial detachment (PED) [5], Dysfunction of RPE ion pumping [6] and Mineralocorticoid hypothesis which suggests choroidal vascular dilatation through upregulation of calcium dependent potassium channels [1,7]. Venous overload has also been proposed as a hypothesis behind subretinal fluid (SRF) accumulation. The dilated veins along with the dilated anastomoses will lead to increase in venous outflow pressure from the choriocapillaris, ultimately leading to leakage from the choriocapillaris. Thus, the intrinsic abnormalities of outflow, lead to a venous overload choroidopathy. The propensity for fluid to collect is dependent on leakage from vessels, potential absorbance by vessels and clearance through the sclera [8].

Patients with acute CSCR generally present with symptoms of decrease in vision, relative central scotoma, metamorphopsia, hypermetropisation, micropsia and decreased contrast sensitivity. Clinically the acute form is characterised by the presence of NSD. The fluid generally resolves within 3-4 months with a good prognosis apart from color discrimination defects in some patients [9]. Chronic CSCR is recognised by widespread RPE atrophy which can be seen as decreased fundus auto-fluorescence (FAF).[9]

The treatment of CSCR still remains a subject of controversy because of variety in clinical presentation, natural course as well as the incompletely understood pathophysiology of the disease [10]. In cases of acute CSCR, which has a relatively high rate of spontaneous resolution, an effective treatment should ideally prevent recurrences and subsequent disease progression. In chronic CSC, the primary aim of treatment is currently to achieve and maintain the complete resolution of SRF and intraretinal fluid (if present) [11]. The treatment options include laser therapy and medical therapy. Laser treatment options includes laser photocoagulation, Subthreshold Micropulse laser (SMPL), Photodynamic therapy (PDT), Transpupillary Thermotherapy. In this review, we will discuss regarding the role of Micropulse laser in CSCR.

Conventional laser to micropulse laser – where we stand now?

Conventional laser photocoagulation has been used since many years to treat retinal conditions. The laser passes through the retinal structures and is absorbed by melanin in RPE. This laser- tissue interaction is due to an increase in the retinal tissue temperature by tens of degrees celsius which results in the formation of a visible burn. An excessive increase in temperature at the level of RPE will result in conduction of heat to the surrounding tissues leading to damage and denaturation of proteins in the retina. The

laser intensity or duration is proportional to the damage to the RPE and the adjacent tissues. The focal laser used in treatment of CSCR targets the focal leakage points seen on fluorescein angiography (FA) and attempts to close the focal defect in the outer blood retinal barrier. Besides direct thermal sealing effect on the focal RPE defects, laser is thought to prompt fluid exit [12].

Subthreshold micropulse laser (SMPL)

One of the theories how the laser photocoagulation works is due to the metabolic stress induced by the laser. The laser tissue interaction also leads to the production of heat shock proteins (HSP) by the surrounding tissue [13]. The up regulation of Hsp70 in the culture of human epithelial ARPE-19 cells after the application of SMPL without inducing any thermal damage was noted in this experiment [14]. These proteins help in repairing damaged tissue and create ‘‘thermotolerance,’’ increasing the threshold at which cell damage and apoptosis occur from thermal, inflammatory, oxidative, or hypoxic injury [15, 16]. The increase in Hsp70 production was dependent on the number of impulses. In the study by Sramek et al, they have shown that significantly lower levels of laser energy was required to induce the production of HSP [16]. So basically an effective subthreshold laser relies on power modulation to a point where the laser energy is sufficient enough to induce stress in the RPE cells and not lead to scarring and damage to adjacent retinal tissues. This led to the introduction of Subthreshold laser. Unlike the conventional laser, this new modality was non-damaging to the retina. This could allow treatment of larger areas of retina involving the fovea and repetitive treatments without any structural and functional damage [17]. The neural retina can be spared from the damage by using a subthreshold laser just to raise the temperature at the level of RPE. However due to close proximity of the neural retina and the RPE, the laser energy has to

be in the microsecond range and not in the millisecond range as was used in the conventional laser. Delivering a single pulse laser energy in such short time may lead to micro explosions, gas bubbles formation and retinal hemorrhages [18]. These side effects can be avoided by using a repetitive series of very short pulses with low energy instead of a continuous-wave (CW) laser pulse [19-21]

In the paper by Dorin in 2003, the author described the operating mode and terminology related to micropulse laser (MPL). [22] In the conventional CW mode, a single laser pulse of 0.1–0.5 s delivers the preset laser energy. What is different in the micropulse (MP) mode is that the laser energy is in form of repetitive short laser pulses in typically 0.1-0.5s. The normal length of each pulse is around 100-300 µs. The wavelengths that have been used in MPL include 810nm, 532 and 577nm. The parameters which can be changed in MPL have been discussed below –

1. DUTY CYCLE (DC) - The duty cycle is defined as the ratio between the 'ON' time and the total ('ON' plus 'OFF') treatment time. The ON time denotes the time in which power was delivered to the tissue and OFF time denotes the time when no power was delivered allowing the retinal tissue to cool down. If the laser duration is set at 200 ms, 100 pulse cycles of 2 ms (2000 µS) duration each are delivered in a single delivery of laser. Simultaneously, if a 5% duty cycle has been selected, the energy is "ON" for 100 µs (5% of 2000 µS) and "OFF" for 1900 µs in each pulse (Figure 1)

2. POWER – Laser power is usually based on titration (described in detail below). The power setting of the MPL determines the intensity of the laser and ranges from 90 mW to 1800 mW in published studies.[23]

3. SPOT SIZE - The spot size refers to the size of each individual MPL treatment spot

which is usually kept at around 150–200 µm with no spacing.

4. PULSE DURATION- The array of repetitive short laser pulses is delivered within an "envelope" whose width typically varies between 100-500ms. It is recommended to keep it around 200ms

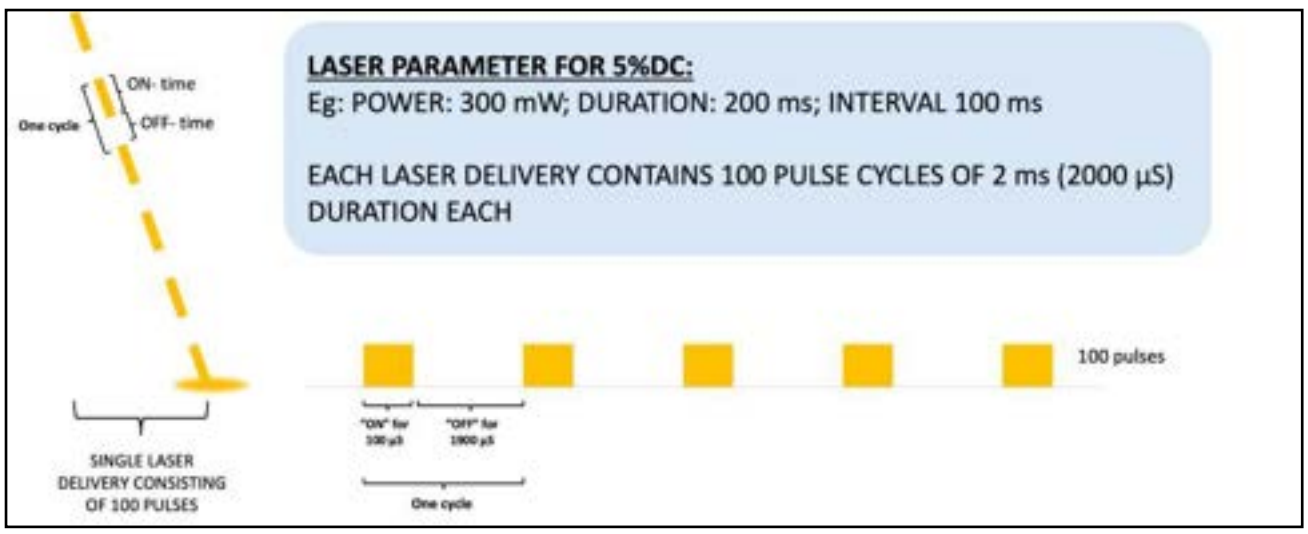


Figure 1: Schematic depicting the duty cycle and pulses

Laser power titration and area of treatment

Different laser power parameters have been used in different studies. There are two therapeutic approaches to set the laser power parameters to be used. One of them is power titration based on a test spot or use of fixed power (around 200-300mW for Yellow laser) [24].

Power titration based on test spot:

1. The titration method involves the use of micropulse laser mode to be performed at the border of healthy and edematous retina. The power should be gradually increased until threshold is reached at which a barely visible retinal whitening is seen. For SMPL, 30-50% of the threshold value should be used. In one of the report it was noted that SMPL was effective when performed at fixed low power levels in case of CSCR. [24] This could be explained due to the production of cytokines after SMPL

therapy. However, the therapeutic effect is achieved after reaching a certain threshold irradiance and increasing the laser parameters does not increase the biological effects but increases the risk of damaging the retina [25].

2. The laser power can also be titrated based on a test spot in CW mode to create a barely visible or threshold burn, and then switched over to MP mode with a short duty cycle (5–15%) and increased power (100–400%), with the endpoint being an ophthalmoscopically invisible ‘‘burn.’’ [22]

In multispot laser, the laser spots are delivered to the area to be treated without any spacing (confluent laser burns). This dense treatment is essential for the therapeutic effect of the SMPL as undertreatment leads to suboptimal results.[26] In MPL, the low temperature gradient re-equilibrates to baseline temperature within a short spreading distance, thus preventing collateral damage to adjacent tissues and limiting the therapeutic effect to the targeted area. For this reason, in MPL, the laser burns are kept confluent to address the treatment area.

The area to be treated is generally determined as active leakage on mid-phase FA or hyperfluorescent areas on mid-phase Indocyanine Angiography (ICGA) images. Optical coherence tomography (OCT) can also be used for SMPL guidance and cover all of the areas of subretinal fluid with the confluent laser foci. Although there is controversy on whether to avoid treating the very central part of the retina, usually the fovea is treated but foveola is spared [27]. In a recent paper by the Subthreshold Ophthalmic Laser (SOL) Society, the recommended settings for Subthreshold laser in CSCR includes the use of 5% duty cycle, 200 ms pulse duration and 100–200 µm spot size with 50% power titration and no spacing in between.[28] The society also recommends treatment of focal leak and adjacent area, for acute CSCR, and areas of focal as well as diffuse

hyperfluorescence on fluorescein angiography in chronic CSCR. The recommended follow up for such patients can be at 6-8 weeks. In case of suboptimal response or persistence of SRF, repeat laser can be done with the same settings along with any adjuvant treatment as per physician's discretion [28].

The safety of SMPL has also been analyzed according to the duty cycle. A study by Lutrull reported a reliable safety of 5% DC as compared to 10% DC in which the risk of biological damage to the retina increases 10-fold [29]. Lutrull also recommended using a small spot size to minimise heat accumulation and maximise efficiency of heat dissipation [30]. The SOL society also recommends the use of 5% DC for SMPL in cases of CSCR. [28]

Efficacy

Although the pathology of CSCR lies in the choroid, it is the RPE cells that transfer SRF to choroidal vessels. The micropulse laser improves the cell function and thus improves the pumping efficacy of RPE. The micropulse laser stimulates the cells which results in production of cytokine and probably reduces inflammatory processes accompanying the disease [27].

The first pilot study investigating the use of Micropulse diode laser (810nm) was in 2003. In this study, the author reported complete resorption of SRF in all eyes within 1 month of treatment and no recurrence of SRF during follow up of 2-6 months. No evidence of RPE or retinal changes were discernible at FA or fundus biomicroscopy after laser treatment [31]. In one of the prospective randomised controlled trial evaluating the efficacy of SMPL vs observation in acute CSCR cases, it was seen that the group which underwent laser therapy had better visual acuity at 2,4,6,16 weeks follow up. The laser parameters used for the study included a spot size of 125µm with 200ms

duration exposure and a duty cycle of 15%. No laser induced iatrogenic damage was noted in the group at the final follow up (on FAF and OCT). SMPL reduced the chances of CSCR going into chronicity and recurrence compared to the current standard of care (observation) [32]. Another study by Long et al, published similar results regarding the use of SMPL in acute CSC cases [33].The use of SMPL in acute scenario can shorten the course of disease, improve visual acuity and reduce the risk of chronic transformation without adverse events.

The PLACE trial is one of the largest prospective randomised controlled trial (RCT) to be conducted which evaluated the efficacy of SMP diode laser in chronic CSC cases. However in this study, the rate of SRF resolution has been reported to be 14% at 2 months and 29% at 7-8 months [34]. Better rate of resolution was seen with half dose PDT. The rate of SRF resolution reported in this study are lower than those reported in other studies. This difference can be attributed to the retrospective nature and relatively small sample sizes of the previous studies, as well as possible differences in inclusion and/or exclusion criteria. Another prospective RCT compared SMPL with conventional laser photocoagulation in patients with CSC of <6months duration. There was no significant difference in both the groups in terms of improvement in visual acuity as well as rates of SRF resolution at 12 week follow up [35].

In the PACORES study group, which compared yellow SMPL (577nm) with half dose PDT in chronic CSCR, a significant improvement was noted in best corrected visual acuity (BCVA) in SMPL group at 12 months of follow up. Around 17% of eyes required re-treatment in the SMPL group as compared to 9% in the half dose PDT group. The trial suggested that SMPL is effective in restoring the macular anatomy in chronic CSCR cases. In places where verteporfin dye is not available, yellow SMPL can be a viable

alternative [36]

Verteporfin PDT therapy includes the cost of the drug and infusion which can cause financial strain on the patient. The therapy requires additional manpower and longer time to perform as compared to SMPL. Adverse events associated with verteporfin PDT include a transient reduction in macular function, choroidal non-perfusion, RPE atrophy and choroidal neovascular membrane formation [37, 38]. SMPL treatment may be more effective in those cases in which focal leak is present as compared to diffuse leak [39]. In a subgroup analysis from PLACE trial, 38% of patients who had focal leak had complete resolution of SRF as compared to 21% of patients with diffuse leak at 7-8 months of follow up. However, in this analysis better rates of SRF resolution were noted with Half dose PDT in both focal and diffuse leak cases [40].

One study has addressed the OCT biomarkers related to SMPL use in CSCR cases [41]. Thicker baseline subfoveal choroidal thickness (SFCT) in the affected eye and the presence of RPE/ inner choroidal alterations predicted unsatisfactory outcomes post SMPL. In this study, it was noted that a failure in SFCT reduction after SML indicates the likelihood of SRF persistence.

Navilas® system (OD-OS GmbH, Teltow, Germany) laser is a slit lamp based laser machine which is coupled with multimodal imaging and retinal tracking system thus allowing targeted laser spots with high accuracy. Multimodal images including FA and ICGA can be imported into the machine and can be integrated into the management. Thus, reliable confluency over large areas and accurate documentation of the treatment are provided. In one of the studies that evaluated the safety of NAVILAS laser using different laser parameters, it was noted that none of the cases had any adverse event related from the laser at final follow up. During the follow up, around 68%

patients showed decrease in the SRF and 88% cases had stable or an improvement in the BCVA [42].

The SOL society guidelines support the use of SMPL in both acute and chronic cases of CSCR. The society recommends the use of SMPL in acute cases at 1 month of non-resolution of SRF considering the safety of the treatment. The laser therapy can be considered as the first line therapy with adjuvant therapy in cases of chronic CSCR [28].

Treatment outcomes with SMPL have been encouraging, but long term outcomes, including side effects, require further evaluation. Various studies have used different laser sources, different laser protocol, and standardisation of laser treatment is required. The location of laser treatment, in particular the number and distribution of laser spots applied, varies between trials, whereas there is still controversy over the requirement to treat the area of NSD alone, fovea or surrounding normal retina. The lack of treatment endpoint in the form of visible retinal burn has been suggested as reason for under treatment and non-response to treatment modality [43]. Very few studies have reported complications from subthreshold laser. While mild asymptomatic RPE pigmentary changes have been noted, neither the development of scars nor choroidal neovascularisation has been reported [40].

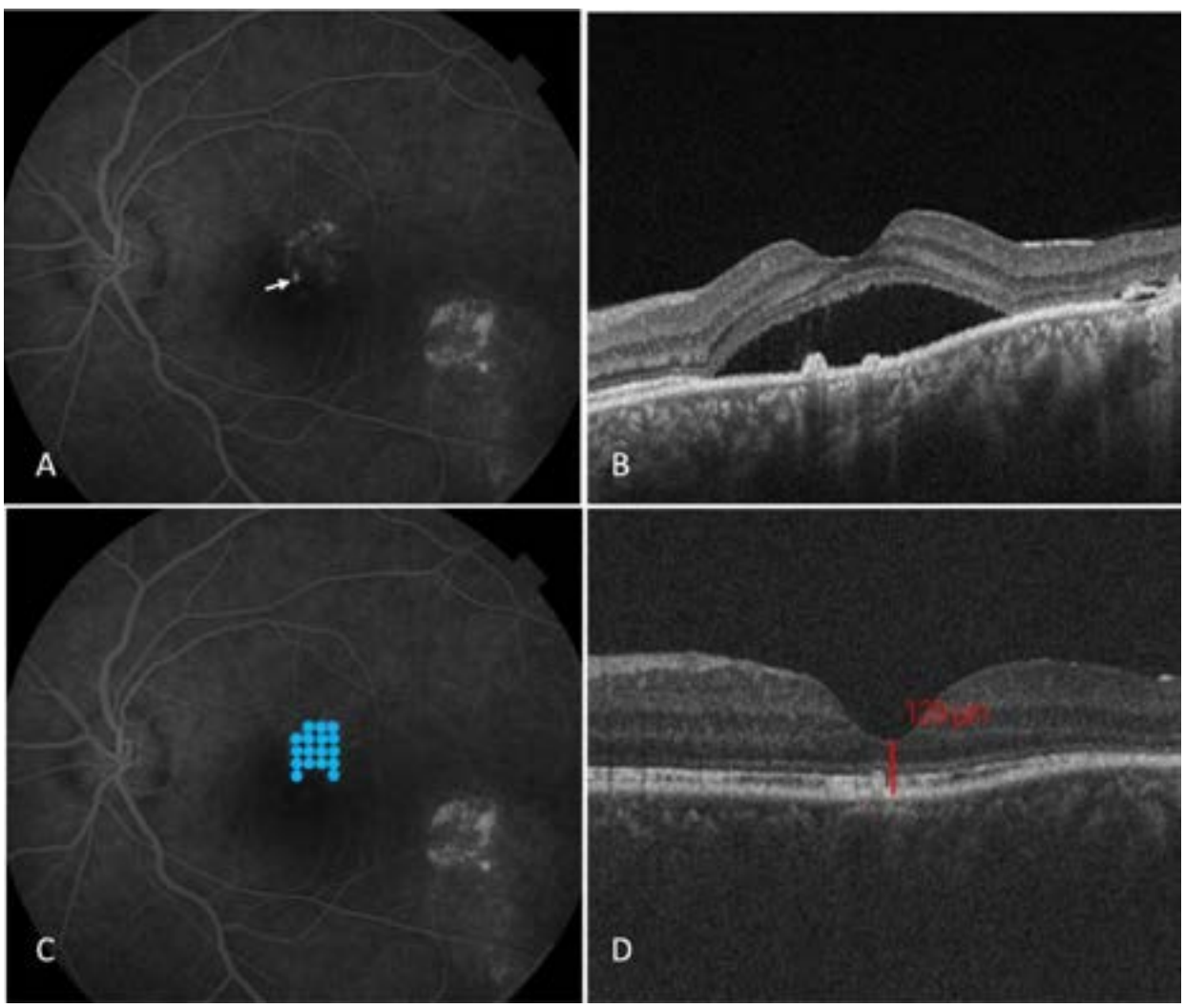
Conclusion

SMPL has been used in both acute and chronic cases of CSCR and can be used as a promising modality of treatment in both with the unavailability of verteporfin dye. With the proven efficacy in many of the studies along with its safety profile, SMPL is one of major treatment options that we have in our armamentarium for treating cases of CSCR. The non-visible retinal laser burn can be a reason for undertreatment or poor response in many patients. More studies will be required to prove the superiority of

SMPL in cases of acute CSCR. However in chronic cases, it still remains as a viable modality of treatment.

Case example

A 46-year-old gentleman presented with complaints of painless decrease in vision in left eye since 1 month. The patient gave history of having similar complaints 2 years back in the same eye which resolved after focal laser. FFA depicted small leak on the superior aspect of fovea along with retinal pigment epithelial alterations (Figure 2A) (*white arrow*). OCT depicted subretinal fluid (SRF) in the foveal area with two small PEDs (Figure 2B). The patient was planned for MPL to the leakage area (*blue circles*) (Figure 2C). The laser parameters used for this particular patient was – 300mW, 5% DC, 100µm spot size, to the leaking and adjacent area using 577nm laser. Three months after laser, the SRF had completely resolved and the vision had returned to 20/20. (Figure 2D)



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CENTRAL SEROUS CHORIORETINOPATHY: SUBTHRESHOLD MICROPULSE LASER AND EPLERENONE AS TREATMENT MODALITIES- A CASE REPORT

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Introduction: First recognized by Albrecht von Graefe in 1866, central serous chorioretinopathy (CSCR) usually causes unilateral diminution of vision due to the development of a serous neurosensory macular detachment. The exact pathophysiology behind CSCR is unknown, but endogenous and exogenous hypercortisolism has the strongest association with its development. Increased choroidal vascular permeability combined with retinal pigment epithelium (RPE) barrier dysfunction has been postulated to be the reason for subretinal fluid (SRF) accumulation. It is generally a self-limiting condition but persistent, recurrent and bilateral CSCR are some complications that are known to occur. CSCR tends to affect males more than females (6:1) and recurrence of the disease has been noted in almost 50% cases within one year.

Case report: A 53 year old lady presented with subacute, painless diminution of vision in her left eye since 1 month. She did not have any remarkable past ocular history or systemic history. Her best corrected visual acuity (BCVA) at the time of presentation

was 6/6 in the right eye and 6/12P in the left eye. Ocular movements, ocular adnexal examination and anterior segment examination in both the eyes were within normal limits. Intraocular pressure in the right eye was 14 mmHg and that in the left eye was 16 mmHg, assessed on Goldmann applanation tonometer. Fundus examination in the right eye showed no abnormalities. Left eye fundus evaluation showed a normal optic disc with a round serous macular detachment around 2 disc diameter in size with small yellow sub-retinal deposits in the centre of detached area (Figure 1). A provisional diagnosis of left eye CSCR was made.

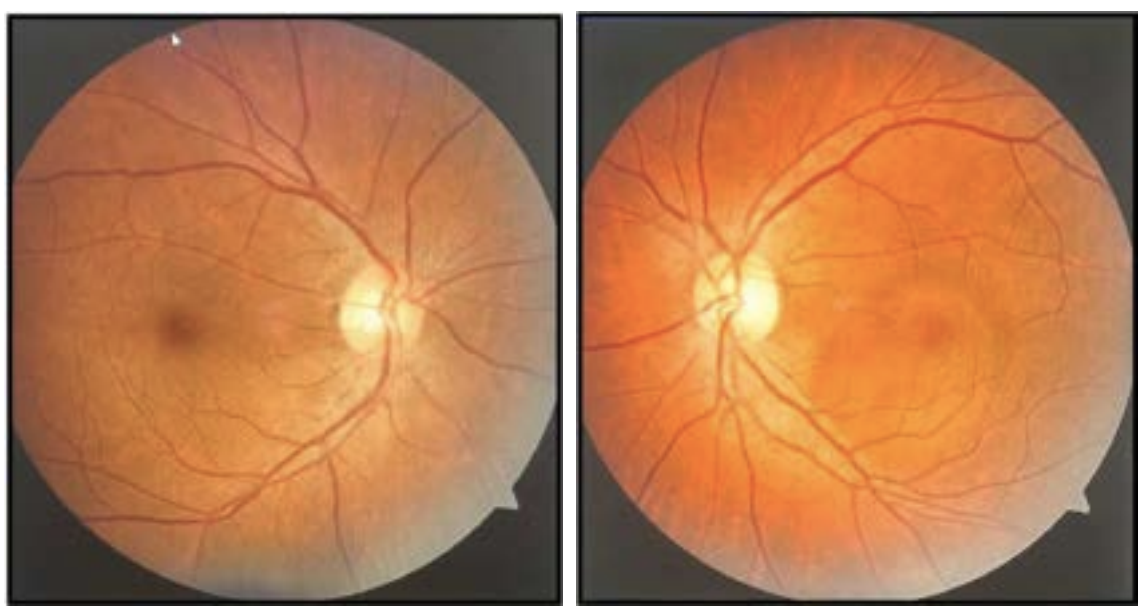

Figure 1: Color fundus photograph showing normal posterior pole in the right eye and serous macular detachment in left eye

Optical coherence tomography scan was done in the left eye which confirmed the presence of a neurosensory detachment with an associated pigment epithelial detachment (Figure 2). Fundus fluorescein angiography (FFA) was performed which showed multiple ink-blot leaks in the macular area (Figure 3). Based on the FFA findings, the leaky areas were treated with subthreshold micropulse yellow laser. At one month follow-up, subretinal fluid was reduced with an improvement in the visual acuity to 6/9P. She was started on Tab Eplerenone 25 mg OD for 1 month.

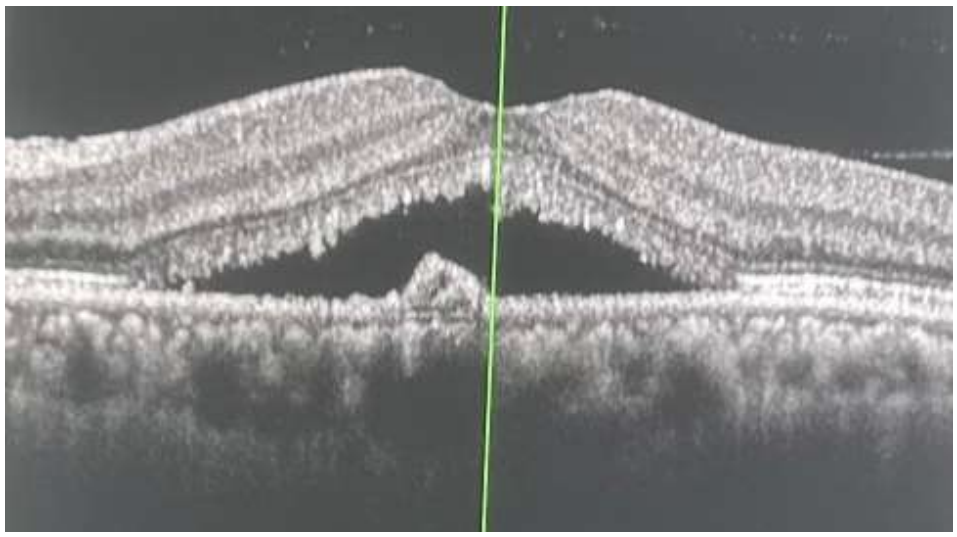

Figure 2: Optical coherence tomography of the left eye showing the presence of a neurosensory detachment with an associated pigment epithelial detachment

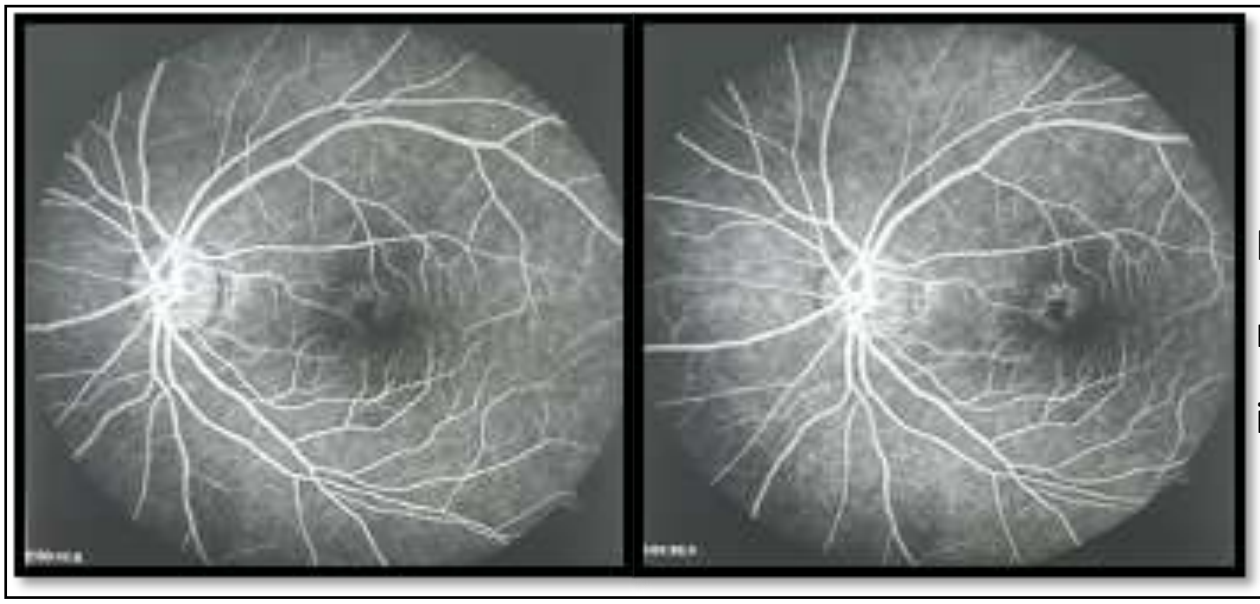

Figure 3: FFA showing multiple ink-blot leaks in the macular area

At two month follow up, subretinal fluid was reduced as evidenced on OCT scan (Figure 4). Her visual acuity had improved to 6/6P in the left eye at three month follow-up. She had minimal SRF on OCT (Figure 5). Eplerenone therapy was further stopped. The visual acuity was stable at her 1 year follow up with no recurrence of CSCR.

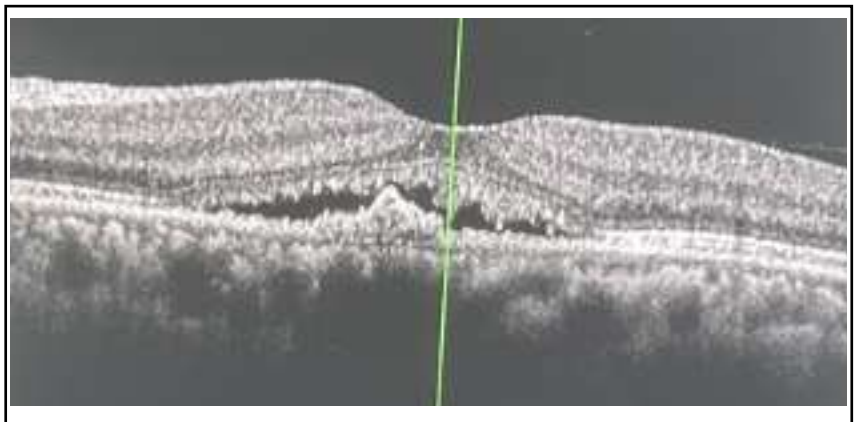

Figure 4: OCT at two month follow up showing reduction in SRF

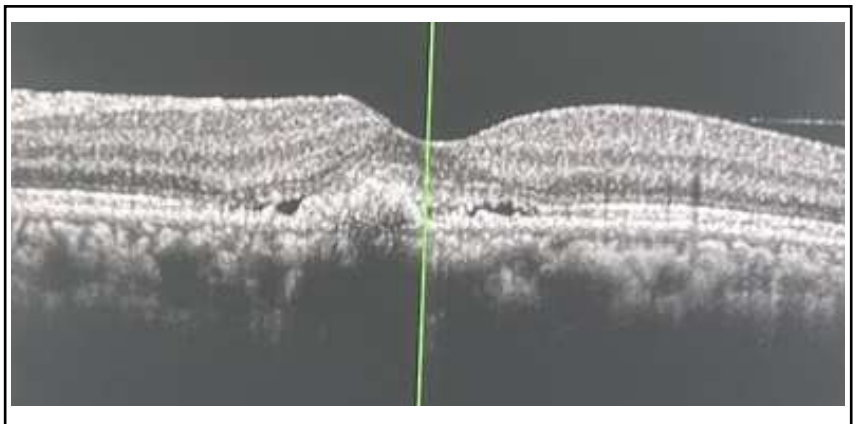

Figure 5: OCT at three month follow up showing minimal SRF

Discussion: An alteration in choroidal circulation has been suggested to be the main causative factor behind CSCR. An upregulation of sympathetic system leading to vasospasm and choroidal ischemia causing choroidal vascular hyperpermeability has been postulated to be the mechanism behind the accumulation of SRF.[3] Steroids potentiate the action of epinephrine which results in an increase in choroidal capillary permeability and dysfunction of the ionic pump in the RPE.[4] Eplerenone, a mineralocorticoid receptor antagonist, has been shown to promote rapid resolution of subretinal fluid in CSCR with its action lasting for up to five months after treatment. Spironolactone is another mineralocorticoid antagonist that has been tried with similar results.[1] Subthreshold diode laser photocoagulation (810nm) has been shown to be effective in treating juxtafoveal leaks in CSCR.[5] Laser therapy using subthreshold micropulse laser is another excellent choice when the area to be treated is close to the fovea. Micropulse laser uses repetitive short pulses at low temperatures and the yellow light has excellent absorption rate in oxyhemoglobin without much absorption by foveal lutein and zeaxanthin. These factors allow treatment of the central macular area without foveal damage.[1] In our case, we made use of combined micropulse yellow laser (577nm) and eplerenone therapy which led to a rapid resolution of the patient's symptoms and no recurrence at one year follow-up. Eplerenone therapy has shown variable results in different randomized control trials, with some advocating its use in CSCR while others equating it to a placebo. It is known that spontaneous resolution is a part of the natural history of the disease. At the time of presentation, patient had distressing visual symptoms (diminution of vision, central scotoma) for a little more than a month. Hence, we chose to intervene early. The absence of recurrence at one year follow up suggests that the treatment with micropulse laser is at least, in part, beneficial in this regard.

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IS THERE A ROLE OF TOPICAL AND SYSTEMIC PHARMACOTHERAPY IN CSCR?

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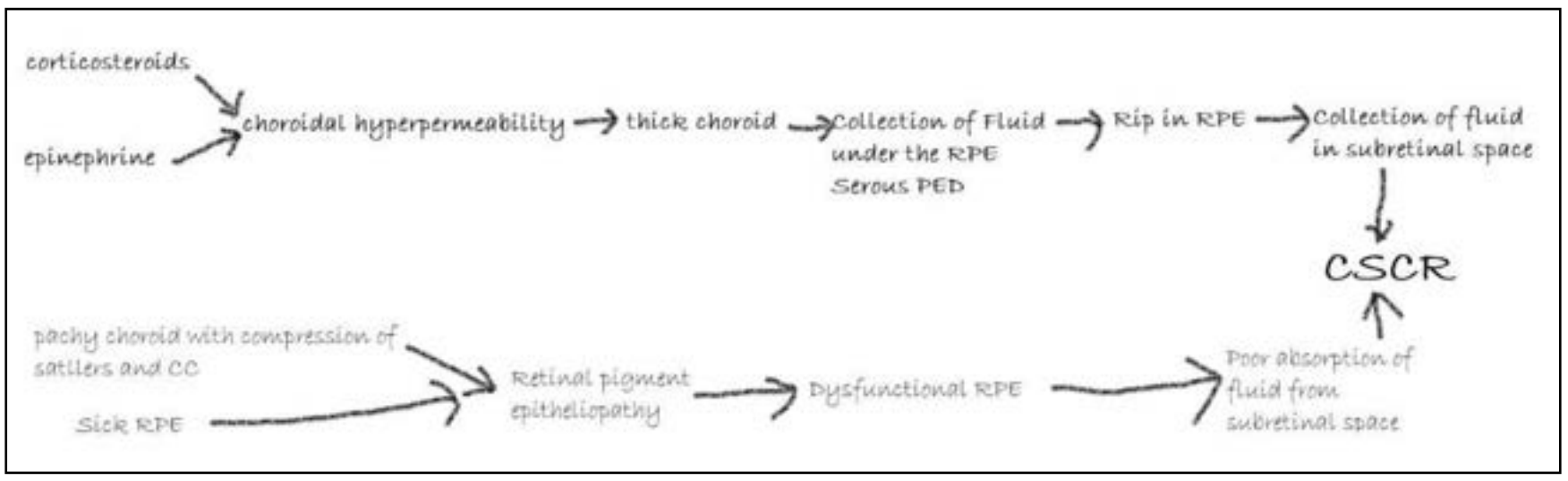
Introduction:

Central serous chorioretinopathy (CSCR) is a condition characterised by subretinal fluid (SRF) accumulation, most commonly at the macula, caused by a mismatch between increased choroidal vascular permeability and retinal pigment epithelium detachment (RPED), resulting in increased SRF accumulation (inflow mechanism) and/or decreased SRF absorption by the dysfunctional retinal pigment epithelium [DRPE] (outflow mechanism).[1] Increased cortisol and adrenaline levels in the body cause increased choroidal vascular permeability. The presence of long-term turbid subretinal fluid or the compressive effects of the dilated Haller's choroidal vessel (pachy vessel) on the overlying Sattler's layer, choriocapillaris layer, Bruch membrane, and RPE causes DRPE (Figure 1).

Figure 1: Pathogenesis of CSCR:

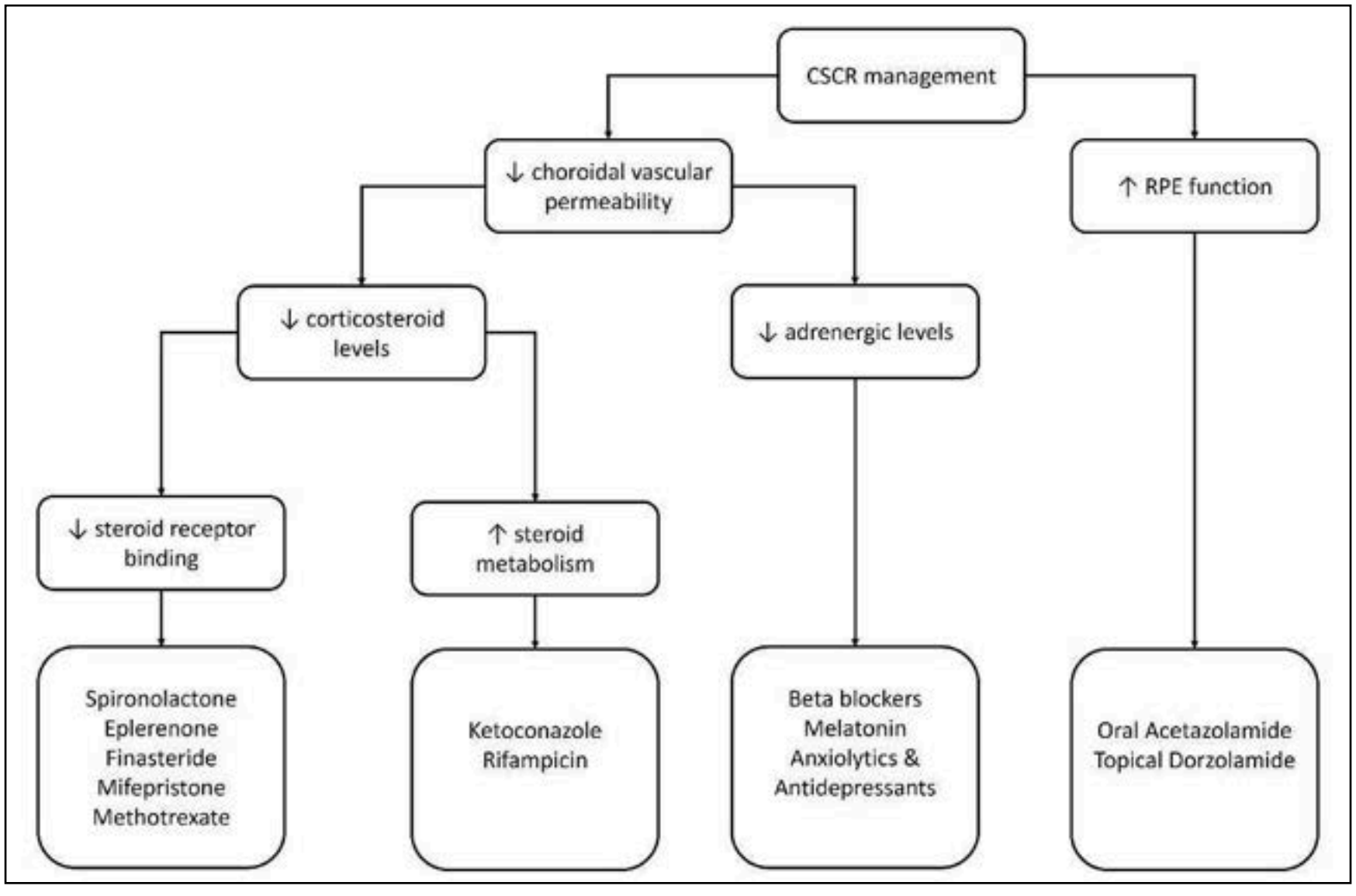


The primary goal of CSCR treatment is to achieve faster SRF resolution in order to avoid irreversible RPE damage and permanent visual impairment. In the treatment of CSCR, both acute and chronic forms, various therapeutic options are available, including observation with lifestyle modifications, pharmacotherapeutic agents, focal thermal laser photocoagulation to the leak, subthreshold micro pulse laser to the region of

dysfunctional RPE, and photodynamic therapy or transpupillary thermotherapy to the hyperpermeable choroidal vessels and leaking RPE.

The role of pharmacotherapeutic agents in the management of CSCR is primarily A) to reduce corticosteroid levels in the body, either by lowering steroid receptor levels or by increasing the metabolism of endogenous corticosteroid levels, and B) to improve RPE function in order to achieve faster SRF absorption. Figure 2 depicts the various mechanisms targeted by different therapeutic agents in the treatment of CSCR.

Figure 2: Flow chart depicting the mechanisms targeted by various pharmacotherapeutic agents in the treatment of CSCR:



1. Pharmacotherapeutic agents having corticosteroid antagonistic action:

A. Spironolactone:

Spironolactone is a potassium-sparing diuretic that acts as an aldosterone binding competitor and is approved for the treatment of congestive heart failure and primary hyperaldosteronism.[2] Due to its aldosterone antagonistic action, there is reduction in corticosteroid levels which helps in faster resolution of SRF and reduction in central macular thickness and improvement in visual acuity. Several studies have reported that spironolactone may be beneficial in acute and/or non-resolving CSCR patients.[3–6] Prolonged usage of spironolactone can cause sexual side effects like gynecomastia, decreased libido, menstrual irregularities and erectile dysfunction.

B. Eplerenone:

Eplerenone is a mineralocorticoid receptor (MR) antagonist that was initially approved for the treatment of heart failure. Eplerenone use is associated with a lower incidence of hormone-associated spironolactone adverse events due to its selective MR antagonistic action. Long-term eplerenone use has been linked to electrolyte imbalances and renal impairment. The use of eplerenone in CSCR management has yielded mixed results. While eplerenone treatment in acute CSCR cases resulted in faster SRF resolution, rapid improvement in visual acuity, fewer recurrences, and fewer side effects, treatment in chronic CSCR cases did not outperform placebo.[7,8] A large, multicentre, randomised, double-blind, parallel-group, placebo-controlled VICI trial that randomised 114 patients with chronic CSC to either eplerenone (n = 57) or placebo (n = 57) was recently completed.[8] After 12 months, the mean BCVA in the placebo group was 79.5 letters and 80.4 letters in the eplerenone group, indicating a mean difference of 1.73 letters

(95% CI 1.12 to 4.57; p = 0.24). According to the findings of this large-scale, randomised trial, eplerenone clinical efficacy in patients with chronic CSCR was not superior to placebo. The absence of corticosteroids in the pathogenesis of chronic CSCR can explain no superior beneficial response to observation in chronic CSCR cases.[8] Most clinicians use eplerenone at a dose of 25-50 mg/day, with some cases requiring a dose of 100mg/day.

C. Mifepristone:

Mifepristone (RU-486) is a high-affinity glucocorticoid receptor (GR) and progesterone receptor antagonist that is commonly used in gynaecological clinical practise to induce medical abortion. Mifepristone has been shown in a few studies to be effective in the treatment of CSCR without much side effects.[9,10] More evidence is needed to establish the efficacy of mifepristone in the treatment of CSCR.

D. Finasteride:

Finasteride, a 5-alpha-reductase inhibitor that works by inhibiting dihydrotestosterone, is commonly used to treat benign prostatic hypertrophy and androgenic alopecia. In a prospective pilot study of five patients with CSCR, the finasteride-treated group experienced complete SRF resolution, while four patients (n = 4/5) experienced an increase in SRF after treatment discontinuation.[11] Another study found that 76% of 23 patients with chronic CSCR treated with finasteride had complete SRF resolution after a 15-month follow-up period.[12] However, due to the possibility of relatively common side effects (such as loss of libido) and the lack of evidence, finasteride should not be considered a viable treatment option for CSCR at this time.

E. Methotrexate:

Methotrexate is an antimetabolic and immunosuppressive agent commonly used for treating inflammatory diseases, such as rheumatoid arthritis. Considering its interaction with steroid receptors, this drug was postulated to be effective for CSC treatment.[13]

F. Ketoconazole and Rifampicin:

Ketoconazole is a cytochrome P450 enzyme inhibitor and Rifampicin is a cytochrome 3A4 enzyme inducer. Both of these drugs help in the reduction of endogenous corticosteroids. Thus, the use of ketoconazole (600mg/day) and rifampicin (600mg/day) in the treatment of non-resolving chronic CSCR has shown to be beneficial.[14,15] However, due to the severe risks associated with rifampicin, as well as the risk of developing rifampicin resistance, rifampicin should not be used as the first-line treatment option in the management of CSCR.

2. Pharmacotherapeutic agents that enhance the RPE function:

Carbonic anhydrase inhibitors:

Acetazolamide is an oral carbonic anhydrase inhibitor that works by inhibiting carbonic anhydrase IV in the RPE, causing SRF resorption and restoring RPE cell physiological polarisation. In a retrospective study, 15 patients were given oral acetazolamide and showed a shorter time to complete resolution of SRF than the control group (3 weeks versus 8 weeks, respectively); however, no differences in BCVA or recurrence rates were found between the two groups.[16] Another retrospective study divided 45 patients with acute CSCR into two groups: acetazolamide (group 1, n = 20/45) and control (group 2, n = 25/45). In both groups, there was no significant improvement in BCVA (p = 0.083 and 0.183). Furthermore, after 3 months, SRF height and choroidal vascularity decreased

significantly in both groups (all p 0.05). Although acetazolamide had no effect on functional or anatomical status in CSC patients, it did shorten the time for SRF absorption.[17] Dorzolamide, a topical carbonic anhydrase inhibitor, has been used to treat CSCR. Dorzolamide acts on the RPE, causing SRF resorption to be faster than in the control group.[18] Larger-scale, well-designed clinical trials are needed in this regard to better define the role of carbonic anhydrase inhibitors in the treatment of CSCR.

3. Pharmacotherapeutic agents having antiadrenergic action:

A. Melatonin:

Melatonin is involved in the physiological regulation of circadian rhythm, and it has been proposed that it may have a beneficial effect on CSCR. In a prospective case series, 13 patients with chronic CSCR were treated for one month with 3 mg of melatonin orally and 5 mg of placebo. They reported an improvement in BCVA in 87.5% of the melatonin group (7 of 8 patients, $p<0.05$) and a reduction in CMT in all patients ($p<0.01$).[19] Because no other studies have been conducted to investigate the role of melatonin in CSCR treatment, more research is required to demonstrate its potential clinical efficacy.

B. Beta-blockers:

Beta-blockers are commonly used for systemic hypertension and anxiety disorders. The already mentioned association between stress, type-A personality and CSCR onset has suggested that beta-adrenergic blocking agents may represent as a possible therapeutic option for CSCR. In a study by Chen et al, CSCR patients revealed an excellent prognosis and success rate of 95.0% after taking propranolol.[20] The treatment was able to enhance subretinal fluid (SRF) absorption, shorten the time to total complete remission, and significantly decrease CSCR recurrence.

C. Anxiolytics & antidepressants:

Patients suffering from severe anxiety or depression are more likely to develop CSCR.[21] As a corollary to that, subset of CSCR patients with Type A personality are treated with anxiolytic (acting on GABA pathway) and anti-depressant (serotonin pathway action) drugs. The usual medications used are tab etizolam (0.5 mg) or tab clonazepam (0.5 mg) once a day in the mild group and adding tab escitalopram (10 mg) or sertraline tablet (25 mg) in the cases which appear depressed on clinical assessment for a duration for 1–3 months depending on the stressors.[22] The rationale in CSCR is that anxiety precipitates autonomic vasomotor instability, leading to elevation of circulating cortisol and epinephrine which can cause choroidal vascular leakage and CSCR. The anxiolytic and anti-depressant drugs break the vicious cycle by reducing the psychic influence on the release of these stress hormones and block the neurotransmitters downstream leading to rapid resolution of the SRF and improvement in vision.

4. Other pharmacotherapeutic agents rarely used in the treatment of CSCR:

Drugs like aspirin, antioxidants, antiVEGF agents and H.pylori eradication therapies have been tried in the treatment of CSCR with limited success.

Conclusion:

CSCR is a disease of the young population caused by increased choroidal vascular permeability as a result of increased cortisol or adrenaline hormones, or by increased RPE dysfunction, or by both. Pharmacotherapeutic agents that lower cortisol or adrenaline levels have resulted in faster SRF resolution in patients with acute or acute-on-chronic CSCR, whereas drugs that improve RPE function have resulted in faster SRF

resolution in chronic CSCR. Anti-VEGF agents used in CSCR cases have shown promising results only in the subgroup of patients with CSCR-related neovascularisation.

Finally, larger-scale, well-structured clinical trials would provide more evidence about the clinical efficacy of oral and topical medications in the treatment of CSCR.

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THE POTENTIAL YET INSCRUTABLE ROLE OF MEDITATION TRAINING IN CENTRAL SEROUS CHORIORETINOPATHY

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Central serous chorioretinopathy (CSCR) is a long recognised but poorly understood, idiopathic, non-inflammatory, primary or secondary [to choroidal vasculature changes] disruption of the outer blood retinal barrier, and characterised clinically by localized serous detachment of the neurosensory retina and retinal pigment epithelium, and angiographically by a more widespread affliction involving both eyes. CSCR is among the most common vision-threatening diseases of the retina after age related macular degeneration (AMD), diabetic retinopathy, and branch retinal vein occlusion.[1] CSCR is usually a self-limiting disease, with 85% of the patients showing spontaneous recovery within a few months.[2] Some patients may develop chronic or recurrent disease that leads to areas of RPE atrophy or hypertrophy with visual loss (RPE decompensation). There is 50% chance of recurrence, with about half of these occurring within the first year.[3]

CSCR is typically classified into two clinically distinct entities, the acute and chronic forms. The distinction is made based on the duration of the serous retinal detachment and on the presence of extended retinal pigment epithelium (RPE) changes. The acute form is typically characterized by the presence of sub-retinal fluid, clinically seen on fundus examination and also on OCT, with limited focal or multifocal RPE alterations

that may be limited to small pigment epithelial detachments (PEDS), and leakage through the RPE on fluorescein angiography (FA). The term “classic” CSCR is also used to describe these patients, with the typical fundus finding of well circumscribed area of sub-retinal fluid in the posterior pole, associated with one or a few leaks seen on FA. On the other hand, “chronic” CSCR was described as a variant of CSCR and historically, it was initially termed “diffuse retinal epitheliopathy”. It is characterised by wide spread tracks of RPE atrophy. Chronic, severe, or recurrent variants of the disease also co-exist and are usually associated with persistent sub-retinal fluid (SRF), yellow sub-retinal precipitates, central RPE atrophy, atrophic RPE tracts inferior to the macula, cystoid macula edema and choroidal neovascularisation (CNV).

Acute CSCR is usually a self-limited disease with reattachment of the detached neurosensory retina occurring within 3-4 months in the majority of cases. So, periodic follow up and observation is sufficient in most cases. In selected cases however, treatment with focal laser, indirect laser, subthreshold laser, and low fluence photodynamic therapy are reported as useful interventions to assist disease resolution. More recently, disease resolution with intravitreal anti-VEGF therapy and systemic anti-corticosteroid treatment have been reported. However, there is yet no consensus or proper guidelines on how to choose any of these modalities when the leakage involves or lies close to the foveal centre. In addition, it is important to note that none of the interventions have been noted to impact the recurrence rate.

Since the disease has a high recurrence rate it is imperative to look for plausible risk factors. Of these, there are numerous and include male gender, mid age range, type A personality, systemic hypertension, use of glucocorticoids, and psychological stress.[4] Type A personality is characterised by a competitive nature, a sense of urgency, an

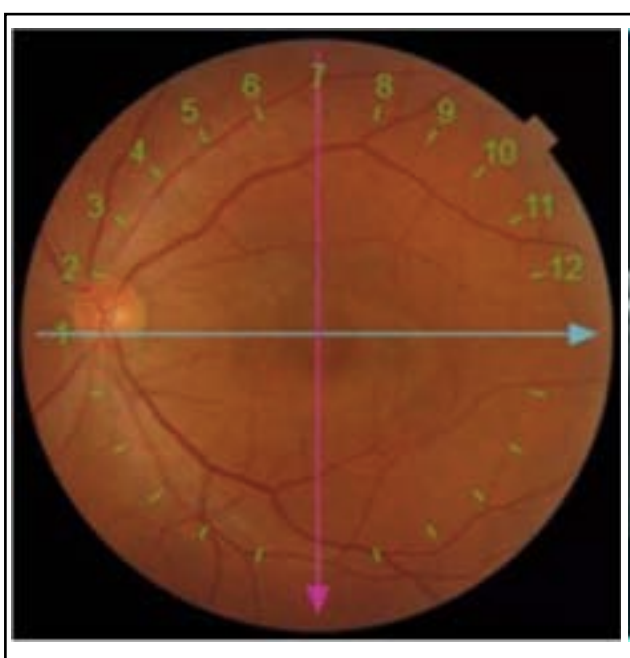
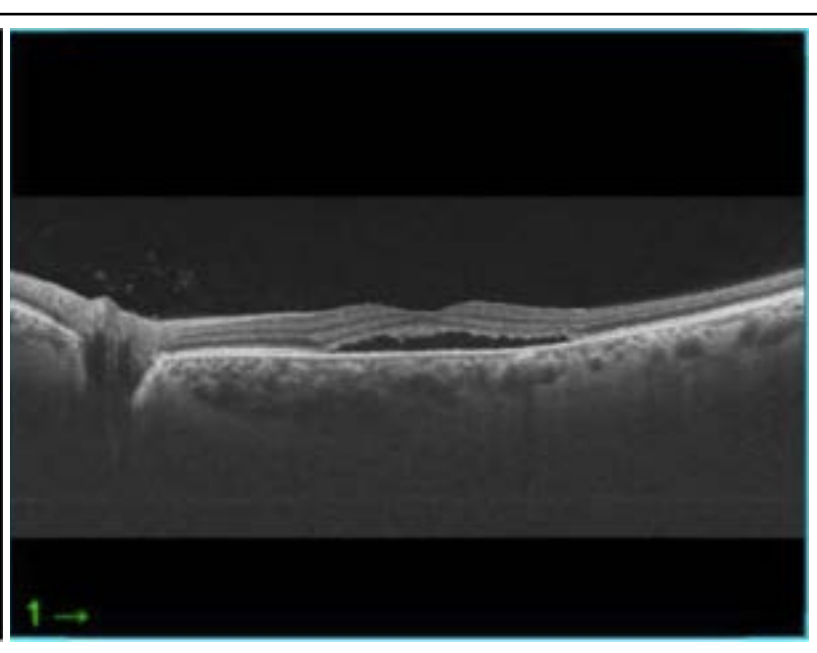
aggressive character and a hostile temperament. A history of psychiatric illness is associated with a higher rate of recurrence. Systemic corticosteroids have been associated with causation, prolongation, exacerbation and recurrences of CSCR. Steroid induced CSCR comparatively has less male predilection than idiopathic CSCR, and frequently has a bilateral and atypical presentation. CSCR is also associated with elevated levels of endogenous corticosteroids as seen in patients with Cushing's syndrome, and also shown in some controlled studies.[5, 6] Gastroesophageal reflux and CSCR is another association that share stress and adaptive response to stress as risk factors, and CSCR patients are said to have a higher risk of gastroesophageal reflux disease.[7] Drug induced CSCR (other than steroids) have been linked to sympathomimetic drugs such as pseudoephedrine and oxymetazoline (component in nasal sprays), MMDA (an illicit amphetamine), and ephedra (component in body building dietary products). CSCR has also been described after the use of phosphodiesterase-5 inhibitors (sildenafil, tadalafil, and vardenafil) and in patients receiving oral MEK- inhibitors (binimetinib) for metastatic cancer.

In 1987, the association of CSCR with "type A" personality was hypothesised by Yannuzzi in conjunction with experimental evidence linking catecholamines with CSCR.[8] A report based on patient self-reporting, by Tittl et al in 1999, identified psychopharmacologic medication use, corticosteroid use, and hypertension as risk factors associated with CSCR.[9] Haimovici et al conducted a similar study in 2003.[10] Furthermore, studies conducted decades ago at our centre suggested that patients with CSCR may have deranged autonomic nervous system responses [both sympathetic and parasympathetic axis] and a statistically significant higher prevalence of prehypertension.[11, 12]

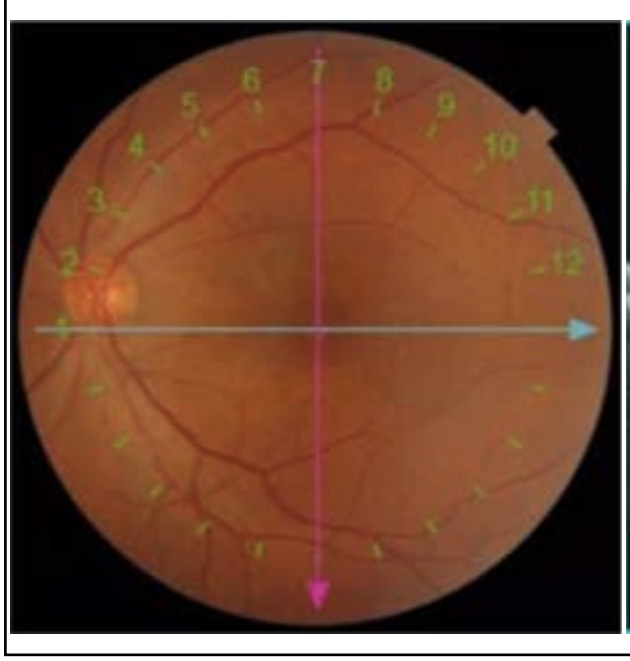
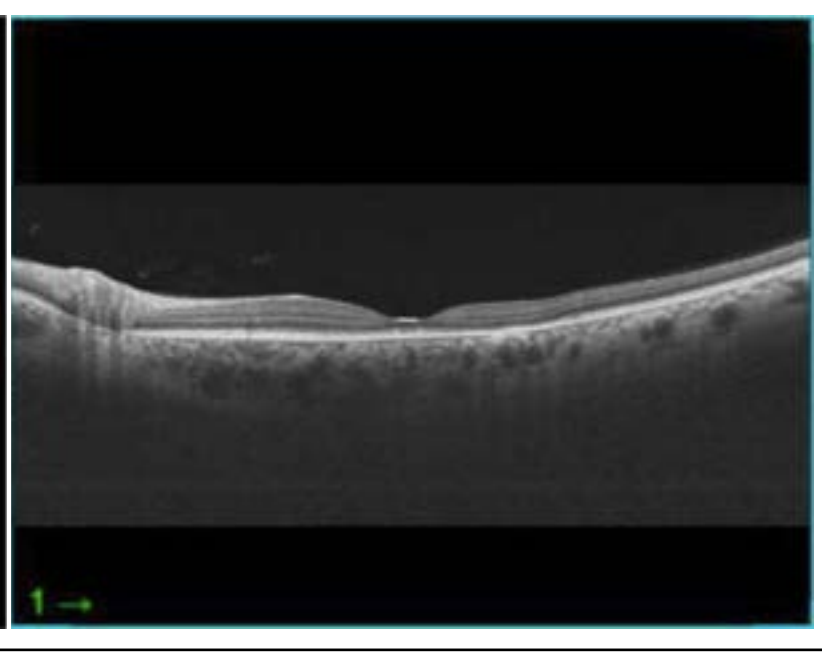
Meditation is now one of the most widespread and researched of all psychotherapeutic methods according to Walsh and Shapiro.[13] There are many definitions of meditation. According to western definitions, meditation is a self regulation strategy with a particular focus on training attention. According to Walsh and Shapiro, the term meditation refers to "a family of self-regulation practices that focus on training and awareness in order to bring mental processes under greater voluntary control and thereby foster general mental well-being and development and/or specific capacities such as calm, clarity and concentration". Likewise, the definition distinguishes related practices such as yoga, Tai Chi, and Chi Gong, that incorporate meditation. Meta-analysis of results from 55 studies have indicated that some meditation practices produced significant changes in healthy participants. It has been however reported that the physiological and neuropsychological effects of meditation practices have been evaluated in poor quality studies, rendering that most of these studies have low methodological quality.[14] Regardless, meditation has also been found to significantly reduce stress, anxiety, and blood pressure in other studies.[15]

With this background we recently conducted a pilot study to assess the possible effect of short term meditation training in patients with CSCR. The total duration of meditation practice was 4 weeks, of which 2 weeks were done under supervision, and another 2 weeks by the patients themselves. Meditation training was provided by trainers at the Integral Health Clinic, Department of Physiology, at the institute. The total duration was 1 hour of training every day and the meditation protocol included breathing exercises (pranayamas) for 20 minutes, sukshma vyayama for 15-20 minutes, and meditation (shavasana) for another 15-20 minutes. In addition, patients' anxiety level was also measured before and after 4 weeks of meditation (in consultation with clinical

psychiatrist) by using STAI Y1 and Y2 anxiety scoring system. The State Trait Anxiety Inventory (STAI) is a commonly used measure of trait and state anxiety. It can be used in clinical setting to diagnose anxiety and to distinguish it from depressive syndromes. Form Y has 20 items for assessing trait anxiety and 20 for state anxiety. The primary outcome measure in this study was the time to resolution of CSCR. Secondary outcome measures included changes in EDI-OCT, changes in OCT-Angiography and changes in blood pressure. Detailed reports from our study has been published recently,[16] and pre and post meditation resolution of the neurosensory detachment is shown in the figure, in one of the enrolled patients.

Pre treatment OCT showing subretinal fluid

Post treatment OCT showing resolution of subretinal fluid

Though we observed significant difference in the time to resolution along with blood pressure, choroidal thickness [on EDI-OCT] and anxiety scores, the study was fraught with a high drop-out rate and non-compliance [to continuing meditation]. These drawbacks, in addition to the pilot nature of the study, makes it difficult to offer strong recommendations for its routine implementation.

The management of CSCR remains haphazard with lack of strong and unequivocal results and recommendations [except with laser for leaks away from the fovea], with most therapies. This is largely because of the high unpredictability in its natural history and the high rates of spontaneous resolution. With a high spontaneous resolution rate of about 85%, the sample size needed for any study to reveal a significant difference [superiority] would be humongous. In the absence of such studies, it is the author's belief that therapies [including meditation] should be initiated only when a patient develops a 2nd relapse or presents with features of chronicity. In this situation, it may be useful to initiate a multimodal approach [e.g., topical carbonic anhydrase inhibitors plus subthreshold laser plus oral Eplerenone plus meditation training] rather than experimenting with only a solitary approach, or a sequential approach. Combined approaches versus sequential and solitary intervention interventions needs to be evaluated in an unbiased manner using randomized controlled trials (RCTs). Meditation training may not only have a positive effect on the ocular pathology but may also likely prevent progression from prehypertension [seen in a significant number of CSCR patients] to higher grades of hypertension. So, the author provides all patients with CSCR the option of considering meditation training as a potentially useful measure in their disease management. The effectiveness of meditation would be most rewarding if it were to reduce the relapse rates, and studying this aspect remains under consideration, but unexplored, as yet.

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MANAGEMENT OF CSC IN A SCHEMATIC

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CSC

Presence of Subretinal fluid (confirmed on OCT)

Acute CSC

First CSC related symptom within past 3 months
One or more focal leakage points on FFA
No signs of CNV or macular disease clinically or on imaging

Look for history of local/ systemic/ inhalation steroid: Stop steroid if possible

Recurrent episode
Bilateral disease
Patients requirement for early recovery

- Yes → FFA guided laser photocoagulation on focal leakage points (for leaks >400 microns away from fovea)

  ICGA & FFA guided half dose (or half fluence) PDT (subfoveal leak)
  -Subthreshold micropulse laser

  → No SRF → Observe
- No → Observe for 3 months
  - No SRF → Observe
  - Persistent SRF → FFA guided laser photocoagulation on focal leakage points (for leaks >400 microns away from fovea)

    ICGA & FFA guided half dose (or half fluence) PDT (subfoveal leak)
    -Subthreshold micropulse laser

    → No SRF → Observe

Eplerenone is used by many physicians, but is not proven to be effective conclusively

Chronic CSC

Persistence of SRF on OCT for > 4-6 months, &
>1-2 disc areas of atrophic RPE changes
One or more focal leakage points on FFA
Hyperfluorescent choroidal abnormalities on ICGA
No signs of CNV or other macular diseases clinically or on imaging

- FFA guided laser photocoagulation of extra-foveal (>400 microns away) leaks → No SRF → Observe
- ICGA guided half dose (or half fluence) PDT in case of no definite leak or subfoveal leak
  - No SRF → Observe
  - Persistent SRF → Repeat FFA & ICGA
    - Presence of CNV at re-evaluation → Intravitreal anti-VEGF treatment
    - Persistent focal or diffuse leakage on FFA/ICGA without evidence of other diagnosis → Repeat half fluence/dose PDT Or High density micropulse laser