Original Article

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Evaluation of Deep Choroidal Vascular Changes Using Enface Oct in Central Serous Choroidopathy

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Abstract

Background: To detect changes in deep choroidal vasculature following resolution of CSC using Enface SSOCT. **Subjects and Methods:** Nine eyes of patients with CSC were studied during the acute phase and following resolution. OCT-A scans were obtained and the deep choroidal layer was segmented between 150 to 300 microns below the RPE. The dilated deep choroidal vessels visible on EnFace OCT corresponding to the leak on FA were localized and the area and width of the vessel was compared using imageJ software. Other parameters like best corrected visual acuity and central choroidal thickness was also measured and compared before and after resolution of CSC. **Results:** Mean age of the patients was 41.22±7.45 years. There was a significant decrease in width (0.89±0.48mm vs 0.662±0.27mm, p=0.007) and area (0.81±0.61mm^2 vs 0.56±0.46mm^2,p=0.009) of the dilated vessel post resolution of CSC) however the overall decrease in choroidal thickness from 428.22±73.11 to 419±69.77 microns was not significant. (p=0.365). **Conclusion:** EnFace SSOCT scans can be used as a tool to identify anatomical changes in the deep choroidal vessels during the course of the disease and to help monitor the response of treatment in CSC.

Keywords: Central serous choroidopathy, Optical coherence tomography.

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Introduction

Central serous choroidopathy (CSC) is a disease which occurs in healthy middle-aged individuals, most commonly between the age group of 20 and 50 years.[1] It is more common in males with Type A personality, hypertension, steroid use and sleep disorders. The patients mostly present with a sudden deterioration of the quality of vision along with metamorphopsia or micropsia or central scotoma.[2] This disease was recognized by Von Graefe in 1866 and was termed as Relapsing Central Leutic Retinitis.[3] Later on Bennett coined the term Central Serous Retinopathy in 1955.[4] CSC has been classified according to duration as acute CSC, non-resolving CSC, recurrent CSC and chronic CSC. According to presence or absence of a pigment epithelial detachment it has been classified into three types by Spitznas; Type 1 includes presence of neurosensory detachment (NSD) alone, Type 2 includes pigment epithelial detachment (PED) alone and type 3 is the mixed type (both NSD and PED).[5]CSC usually resolves spontaneously in 90% of the patients in 3 months.[6]Thus observation is the main stay of management. Different modalities of treatment have been described in cases where spontaneous resolution does not occur. These can be broadly divided into laser and medical management. Photodynamic therapy,[7]laser photocoagulation and subthreshold laserhave been widely used in CSC with appreciable results. Medical management includes mineralocorticoid antagonists like eplerenoneand spironolactone, antibiotics like rifampicin and ketoconazole, mifepristone, betablockers, aspirin and anti H. pylori treatment.[8–16]

With the advent of enhanced depth imaging and newer choroidal imaging techniques, it was revealed that the major pathology was probably at the level of the choroid, especially the deeper Haller's layer (large choroidal vessels) and this disorder was later renamed as central serous choroidopathy (CSC) or central serous chorioretinopathy. Dilatation and hyperpermeability of the larger choroidal vessels causing compression of the medium sized vessels and the choriocapillaris along with reversal of retinal pigment epithelium (RPE) polarity and RPE microbreaks causing the fluid to collect in the subretinal space is regarded as the probable pathophysiology of CSC.[17] The imaging modalities available for in-vivo evaluation of choroid and

choriocapillaris are enhanced depth imaging optical coherence tomography (EDI-OCT), swept source optical coherence tomography (SS-OCT) and indocyanine green angiography (ICGA). Using EDI-OCT and SS-OCT authors have shown an increased choroidal thickness in cases of CSC whereas choroidal vascular dilatation and hyperpermeability has been appreciated on ICGA.[18]

Despite these new imaging techniques the response to specific treatment has not been anatomically correlated with changes in the choroidal vascularity. Resolution of neurosensory detachment (NSD) does not correspond to the reduction of subfoveal choroidal thickness (SFCT) in these patients.[19] Hence choroidal thickness alone cannot be used as a biomarker for response in CSC. Other choroidal biomarkers like choroidal vessel layer thickness analysis, choroidal vascularity index and enface OCT analysis of the choroid have been recently described but they have not been optimally standardized and manual manipulation of parameters like localization and segmentation have brought in more bias to the results.[20] We studied the deeper choroidal vessels seen on enface images obtained using swept source optical coherence tomography angiography (OCTA) and correlated these with the focal leak seen on fluorescein angiography. Additionally, we compared the choroidal vessel lumen width obtained from the en face scans before and after resolution of CSC.

Subjects and Methods

This is a prospective study which was performed according to tenets of Declaration of Helsinki. 9 patients in whom the CSC resolved were included in the study. Cases of CSC which were included were those which were classically type 1 according to Spitnaz[5] classification (only serous detachments). Patients with pigment epithelial detachment, double layer sign, suspicious choroidal neovascular membrane, other ocular or systemic co-morbidities and not compliant to regular follow ups were excluded.

For each patient we documented age, gender, best corrected visual acuity (BCVA), subretinal fluid height and central choroidal thickness at the fovea. Topcon DRI OCT was used to capture Swept source optical coherence tomography (SS-OCT) scans for choroidal thickness and presence of subretinal fluid. OCTA scan of the same machine was used to visualize the characteristics of deep choroidal vessels (primarily the Haller's layer). Image analysis was done using imageJ software (imajej.nih.gov) to measure the width and area of choroidal vessel lumen.

OCTA scan was captured for all eyes and the choroidal layer was manually segmented between 150 to 300 microns below the RPE level. 3x3 mm scans were taken and the density map image of enface OCT at this level of segmentation was used for analysis using imageJ software. At this depth the scans are basically en face topographical images as the decorrelation analysis is unable to detect any flow at this level. The density map image of the enface scan was pixelated using 8-bit to create a black and white image. The black tubular spaces were considered to be the lumen of choroidal vessels. The scale was calibrated according to 3x3 mm which was used to measure the exact width and area of vessels in mm and mm^2 form respectively rather than pixels.

Fluorescein angiography (FFA) was done in all patients with CSC and patients with extrafoveal leaks were excluded from the study as the corresponding point in 3x3 OCTA scan could not be accurately located. The x-y localisation (line) function of the OCTA software was used to mark the location of the leak on the superficial retinal vascular layer scan corresponding to the leak seen on fluorescein angiography. This point of leak was projected on the deep enface choroidal scan [Figure 1]. A choroidal vessel lumen either below or within 100 microns of this leak was identified. The largest width of this vessel was noted. This dilated vessel was delineated manually from adjacent connected branching vessels and the area of this luminal structure was calculated. A comparison between the width and area of lumen before and after resolution of CSC was made [Figure 2]. In the set of 9 patients, CSC resolved naturally in five patients, following half fluence photodynamic therapy in one, subthreshold laser in one and eplerenone therapy in two patients.

Data was analysed using IBM SPSS 23 software and the significance level was set at less than 0.05. Wilcoxon signed rank test and paired t-test was used to compare nonparametric and parametric tests respectively in the 9 patients who had complete resolution of subretinal fluid.

Results

Of the 9 patients, 7 were male and 2 were female. The mean age of the patients was 41.22±7.45 years. BCVA, central choroidal thickness, area and width of the vessel lumen were compared before and after complete resolution of subretinal fluid in 9 eyes. There was a significant gain in BCVA before and after complete resolution from 0.6±0.11 logMAR to 0.133±0.1 logMAR. (20 letters improvement on ETDRS chart) (p=0.0074) however the overall decrease in choroidal thickness from 428.22±73.11 to 419±69.77 microns was not significant. (p=0.365). On correlating the corresponding points of the leak on FA and the dilated vessel on OCT, 4 patients had the leak exactly above the dilated vessel whereas in the other 5 patients the leak was within 100 microns from the dilated vessel. On comparing the area and width of the vessel lumen corresponding to the leak, There was a significant decrease in both the area (0.81±0.61 to 0.56±0.46mm^2) and width (0.89±0.48 to 0.662±0.27mm) of the lumen. (p=0.007 and 0.009 respectively) following resolution of the CSC.

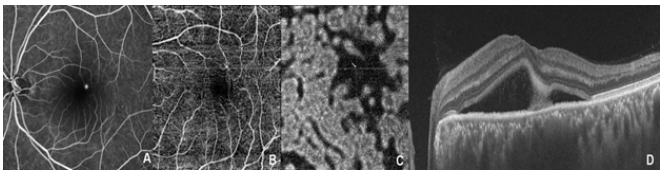

Figure 1: A) Fluorescein angiography showing afoveal ink-blot leak characteristic of CSC. B) Point of leak of FFA mapped on the OCTA (White arrow) segmented at the superficial vessel layer. C) OCTA segmentation at the deep choroidal layer (white arrow corresponds to the leak on FFA) shows a dilated vascular lumen. D)SSOCT of the same section shows subretinal fluid with choroidal thickening.

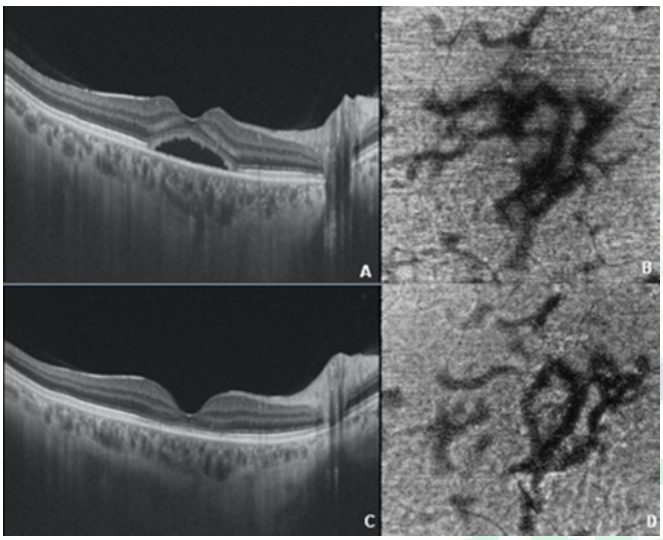

Figure 2: A) SSOCT during acute stage of CSC shows-subretinal fluid with choroidal thickening. B) Enface OCT at the deep choroidal layer of the same section shows dilated vascular lumen. C) SSOCT of the same patient at 2 months post spontaneous resolution of CSC shows disappearance of subretinal fluid. D) Enface OCT at the deep choroidal layer following resolution shows reduction in width and area of the previously dilated lumen.

Discussion

The exact pathogenesis of central serous chorioretinopathy is still not fully known. Initially this disease was referred to as central serous retinopathy in view of the subretinal fluid and focal leaks identified at the posterior pole. Thereafter studies revealed a thicker choroid and Indocyanine green angiography revealed multiple areas of increased cyanescence from the choroidin central serous retinopathy and the terminology was changed to central serous choroidopathy (CSC).[21,22] Further studies using enhanced depth imaging optical coherence tomography revealed that the thickness of Haller's layer was increased in cases of CSC. Role on nonvascular smooth muscles of the choroid in CSC has also been suggested.[23] This was done using axial OCT scans in the z axis. Branchini and coworkersmeasured the thickness of the large vessels by taking the largest vessel from OCT B-scans near the choroidoscleral interface and used the inner edge of this vessel as the demarcation line between the large and middle-sized choroidal vessels.[24] Enface SS-OCT imaging has been recently described in CSC,[25] in which the pathologically dilated choroidal vessels was shown to have an abrupt termination, in contrast to the normal vessels which gradually taper. Focal and diffuse pattern of vascular dilation have also been described using SS-OCT in all three layers individually.

We were able to examine the lumen of the larger choroidal vessels (between 150-300 microns below retinal pigment epithelium) better in two dimensions (x-y plane) using the en face images generated by Optical coherence tomography angiography (OCT-A) software. The enface images and the density maps clearly show the luminal structures as hypo reflective channels as opposed to the adjacent stroma. We correlated the vascular lumen with the focal leak seen on fluorescein angiography and found found that a dilated choroidal vessel lumen was present underlying the leak or in its vicinity (within 100 microns of the leak). We also compared the width of the same vessel post resolution of CSC and found it to reduce significantly in caliber. An approximate area of the dilated vessel was also calculated and compared pre and post resolution and this was also found to be significantly reduced following resolution of CSC.

All the factors regulating the choroidal blood are not well understood. Various hormonal, neural, paracrine and autoregulatory mechanisms may be involved in regulation of choroidal blood flow.[26] Unregulated increased flow through the larger choroidal vessels may enhance outflow from the fenestrated choriocapillaris. A microripin the retinal pigment epithelium might eventually cause this fluid to seep into the subretinal space causing CSC.[27] Abnormal autoregulation of choroidal blood flow after exercise[4] and an increased sympathetic activity in individuals with CSC has already been demonstrated.[28]

Our study confirms the presence of dilated choroidal vessel lumen in the vicinity of the fluorescein leak and that resolution of CSC is associated with reduction in width of this dilated vessel. Analysing the enface images reaffirms the hypothesis of CSC being a disorder of choroidal circulation. Resolution occurs when physiological compensatory mechanisms or therapeutic measures are able to reduce the flow through the focally dilated choroidal vessels. En face imaging enables

characterization of this change. The overall choroidal thickness in our study did not show a significant reduction despite reduction in the width and area of the dilated choroidal vessel lumen under the leak. This re-establishes that choroidal thickness alone may not be a good marker of disease activity.

Future research in CSC should be aimed at developing therapeutic measures which enhance reduction in the caliber of focal dilated choroidal vessels without leading to choroidal ischemia. EnFace OCT-A based analysis of deeper choroidal vessels can serve as a good tool to monitor such therapies.

Conclusion

Enface OCT enables us to visualize change in choroidal vascular thickness in cases of CSC and following resolution. This could be used as a tool to determine response following a treatment modality or help us in the search for therapeutic medications targeting the deep choroidal vessels. A larger study is required to determine the accuracy of this investigative modality, whereas a control group is required to compare the choroidal vascularity between age matched normal individuals and cases of CSC.

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