Optical coherence tomography angiography findings in cystoid macular degeneration associated with central serous chorioretinopathy

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Abstract

Aim To describe the optical coherence tomography (OCT) characteristics and to identify and analyse the incidence of choroidal neovascular (CNV) network seen on optical coherence tomography angiography (OCTA) in eyes with cystoid macular degeneration (CMD) associated with central serous chorioretinopathy (CSCR).

Methods This was a retrospective, observational study of 29 eyes of 25 patients who were previously diagnosed as CSCR with CMD. Baseline patient characteristics, best-corrected visual acuity (BCVA), evidence of CNV network and its pattern on OCTA, distribution of CMD changes and OCT parameters, such as height of the neurosensory retinal detachment (NSD), presence of double layer sign, central macular thickness, were analysed. The eyes were classified into two groups depending on the presence or absence of CNV network on OCTA. BCVA, OCT parameters and CMD distribution were compared in the two groups at baseline using independent t-test.

Result A total of 13 (44.8 %) eyes had a CNV network, while only 9 out of the 13 eyes had pattern-I CNV. Among the eyes with CNV network (13 eyes), mean height of NSD was of 65.2±22.7 µ, whereas, among the eyes without CNV (16 eyes), it was 134.6±77.4 µ. The difference was statistically significant (p=0.013). There was no statistically significant difference between eye having a CNV and eyes without CNV in terms of other parameters.

Conclusion A CNV network is seen in a large subset of patients with CMD in CSCR. A shallower subretinal fluid may point towards the presence of an underlying CNV network.

Introduction

Central serous chorioretinopathy (CSCR) is primarily a disease of the choroid characterised by neurosensory detachment of the retina involving the posterior pole with or without the presence of a pigment epithelial detachment. It is usually a self-limiting condition with excellent visual outcome. However, in a major proportion of individuals, it persists as a chronic form which results in various forms of visual debility.

Cystoid macular degeneration (CMD) is a chronic manifestation of CSCR, characterised by intraretinal cystoid spaces with no evidence of fluorescein leakage. The condition has been described with various retinal conditions following cystoid macular oedema in the past.1-3 Iida et al described it as a manifestation of long-standing cases of CSCR.4 Be it due to the direct effect of the cystoid spaces itself or the result of retinal pigment epithelium (RPE) or foveal atrophy, visual prognosis is generally considered poor.5-10 In spite of multiple studies on the risk factors of these CMDs,7 8 the pathogenesis is still not clearly elucidated.

Multimodal imaging modalities including optical coherence tomography (OCT) have helped in the understanding of these cystoid changes and the changes in the outer retina associated with chronic CSCR. While the condition was suggested to have a poor functional outcome, studies have shown favourable structural outcomes following anti-VEGF (vascular endothelial growth factor) agents.11 Furthermore the coexistence of choroidal neovascularisation (CNV) in cases of long-standing CSCR points towards the possible role of CNV in the formation of these cysts.

The prevalence of CNV in cases of chronic CSCR has been reported to be around 2%–9%.12-14 However, these studies were mostly based on dye angiography. OCT angiography (OCTA) is a newer non-invasive modality for analysing the retinal and choroidal vasculature which uses decorrelation of signal amplitudes obtained from repeated B-scans from the same site to detect non-static structures such as blood in vessels against a static background.15 A recent study by Quaranta-El Maftouhi et al, with the help of OCTA, showed that 58% of eyes with chronic CSCR had CNV.16 Similarly, a higher sensitivity of OCTA has also been demonstrated in detecting polyps and branching vascular network in cases of polypoidal choroidal vasculopathy secondary to chronic CSCR.17

Considering the fact that a majority of chronic CSCR eyes present with cystoid changes in the inner and outer retina, it becomes imperative to analyse the proportion of CNV in these eyes with CMD in chronic CSCR. In this study, we tried to identify and analyse the characteristics of these CNVs seen in cases of CMD in CSCR using OCTA and OCT to evaluate its possible correlation with the formation of these cystoid spaces.

Methods

We performed a multicentric, prospective, observational study of 29 eyes of 25 patients who were previously diagnosed as CSCR with cystoid changes in the posterior retina. Local ethics committee approved the study at each centre, and informed consent was obtained from each subject. CMD was
defined as the presence of optically empty spaces in the retina that were separated by reflective tissue from the RPE, detected on OCT cross-sectional scans. The time of the first detection of CMD was taken as the baseline. Patients with evidence of intraretinal fluorescein leak on fundus fluorescein angiography (FFA) (suggestive of cystoid macular oedema) due to different retinal vascular diseases were excluded from the study. Baseline patient characteristics, best-corrected visual acuity (BCVA), OCT parameters and any evidence of CNV network on OCT angiography (OCTA), were recorded. The eyes were either managed by observation or received some form of treatment. OCT and FFA were performed using swept source DRI OCT-plus (Triton, Topcon, Tokyo, Japan), Swept source (SS) OCT PLEX Elite 9000 (Carl Zeiss Meditec, Dublin, California, USA) or Angiovue (Optovue, Fremont, California, USA). FFA and Indocyanine green angiography (ICGA) were performed using Heidelberg Spectralis HRA+OCT (Heidelberg Engineering, Vista, California, USA).

OCT parameters

The distribution of CMD (involvement of papillomacular bundle or the fovea) changes and various other OCT parameters were assessed such as height of the neurosensory retinal detachment (NSD), presence of double layer sign [defined as irregular shallow pigment epithelium detachments (PEDs) with hyper-reflective content inner to an intact hyper-reflective Bruch membrane], central macular thickness (CMT). CMT was manually measured by using an in-built calliper tool by drawing a perpendicular vector from the outer edge of the hyper-reflective RPE to the inner retinal boundary at the fovea.

OCTA parameters

The eyes were analysed using OCTA to look for the presence of any CNV network in the outer retina or inner choroid.

Definitions

The CNV lesions were classified into pattern-I and pattern-II on the basis of OCTA characteristics as described by Darwish A., has been summarised in table 1.

A scar on OCT was defined as a hyper-reflective tissue accompanied by retinal atrophy. Double layer sign was defined as irregular shallow PEDs with hyper-reflective or hypo-reflective content inner to an intact hyper-reflective Bruch membrane. All the images collected in four centres (Germany, Switzerland, Italy and India) were interpreted by a single observer.

| Table 1 Classification of choroidal neovascular lesion on OCTA |
|---------------------------------------------------------------|
| **Pattern-I** | **Pattern-II** |
| A CNV lesion was considered as Pattern I, requiring treatment, if it showed all or at least three of the following five features | A CNV lesion was considered as Pattern II, not requiring treatment, if it showed less than three of the OCTA features |
| ▶ A well-defined (lacy-wheel or sea-fan shaped) lesion | |
| ▶ Branching, numerous tiny capillaries | |
| ▶ The presence of anastomoses and loops | |
| ▶ Morphology of the vessel termini, assessing the presence of a peripheral arcade | |
| ▶ Presence of a perilisional hypointense halo | |

CNV, choroidal neovascularisation; OCTA, optical coherence tomography angiography.

Group characteristics

The eyes were classified into two groups depending on the presence or absence of CNV network on OCTA. BCVA, OCT parameters and CMD distribution were compared in the two groups at baseline.

Statistical analysis

Data was analysed using SSPS V.20.0 software for Windows (SPSS, Chicago, Illinois, USA). The baseline characteristics between the two groups were compared using independent t-test. BCVA was measured in Snellen’s chart and was converted to LogMAR (Log of Minimum Angle of Resolution) for statistical analysis. A p value of less than 0.05 was considered significant.

RESULTS

A total of 29 eyes of 25 (24 males and one female) patients that fulfilled the inclusion and exclusion criteria were included. The age of the patients ranged from 37 to 78 years (mean age of 54.5±9.7 years). The eyes had a mean baseline BCVA of 0.71±0.39 LogMAR (Snellen’s equivalent 20/100). The average duration of symptoms was 52.8±41.6 months. A total of 22 eyes had a double layer sign seen on OCT. In 24 eyes (82.8 %), the cystoid spaces involved the papillomacular bundle while it involved the fovea in 17 eyes (58.6 %). The mean CMT of the eyes was 294.9±173.2 µ. Subretinal fluid (SRF) was present in 18 eyes with a mean NSD height of 114.2±72.9 µ. Seven eyes had received anti-VEGF injections out of which, two eyes had SRF. Four out of the seven eyes had a CNV network; however, these four eyes had no SRF on OCT.

Group characteristics

The eyes were analysed for the presence of CNV network using OCTA. A total of 13 (44.8 %) eyes had a CNV network seen in outer retinal and choriocapillary layer. The remaining 16 eyes (55.2 %) did not show any CNV network. However, only 9 out of 13 eyes had pattern-I CNV. The remaining four eyes pattern-II CNV.

Among the eyes with network, double layer sign was seen in 11 (84.6 %) eyes and scar in 4 (30.8 %) eyes (both scar and double layer sign were seen in two eyes). Among the eyes without the CNV network, 11 eyes (68.8%) had a double layer sign and 2 (12.5%) eyes had a scar. The cystoid spaces were present over the areas of double layer sign in all patients.

Among the eyes with CNV network (13 eyes), subretinal fluid was seen in 5 (38.5%) eyes (mean height of 65.2±22.7 µ), whereas, among the eyes without CNV (16 eyes), a total of 12 (75%) eyes (mean of 134.6±77.4 µ) had a NSD. There was statistically significant (p=0.013) difference between the height of SRF in the eyes with and without CNV. The baseline BCVA was numerically better in the CNV group (0.61±0.24 logMAR (Snellen equivalent 20/80) compared with the non CNV group (0.80±0.46 logMAR, Snellen equivalent 20/125), although this finding was not statistically significant (p=0.2). There was no statistically significant difference between eye having a CNV and eyes without CNV in terms of CMT.

DISCUSSION

CNV in the setting of chronic CSCR is relatively uncommon, with an incidence of around 2%-9%. It is often difficult to clearly demarcate the presence of a CNV in the setting of chronic CSCR, due to overlap of FFA findings or the coexistence of certain findings typical of CNV. With the advent of OCTA, an increased incidence of these CNV has been reported in chronic
et al reported the presence of CNV in flat irregular PEDs in 35.6% of cases. This finding supports the higher prevalence of a double layer sign seen in eyes with CNV in our study. In all the cases, the double layer sign was seen immediately below the cystoid spaces.

CSCR often manifests with varying degrees of SRF, which is an indirect indicator of disease severity. However, we found a significantly shallower (p=0.009) SRF in patients with CNV on OCTA than the patients with no CNV. Although it is alluring to think that the presence of a CNV may predispose to a higher SRF, the lower height of SRF in our patients could be due to low activity of CNV lesion formed as a result of increased chronicity of CSCR. This is in contrast to large SRF seen in classical CSCR cases which respond to treatment, probably due to higher disease activity.

Other than the study being retrospective in nature, there were several limitations of the study. First, the sample size was too small to associate the presence CNVs to the disease pathogenesis. Second, whether CNV is the cause of the cystoid spaces in these eyes or it develops following development of the cystoid spaces could not be verified due to the cross-sectional nature of the disease. Third, the eyes in the study could have been in different stages of progression of the disease and thus could have underestimated the prevalence value of CNV.

A CNV was found in a majority of patients with CMD in CSCR. A shallower SRF may point towards the presence of an underlying CNV. OCTA appears to be a faster, non-invasive alternative to conventional dye angiography, which demonstrates high level of sensitivity in detecting CNV lesions. Further studies are required to evaluate the follow-up and prognosis of these patients in order to better understand the pathogenesis.

Contributors MRM, EP and JC: design. SBM and NKS: conduct of the study. SBM: collection. NKS: management. NKS, SBM, CI and SRS: analysis. NKS and CI: interpretation of the data. NKS, SBM, CI and SRS: preparation. MRM, LB, EP and JC: review. MRM, LB, EP and JC: approval of the manuscript.

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