ORIGINAL ARTICLE

OPTICAL COHERENCE TOMOGRAPHIC CHARACTERISTICS OF IDIOPATHIC CHOROIDAL NEOVASCULARISATION

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Background: Idiopathic choroidal neovascularisation (ICNV) is the development of choroidal neovascularisation (CNV) in young adults without any apparent manifestations of primary ocular or systemic diseases We aim to assess characteristics and pathological changes at various stages in ICNV by optical coherence tomography(OCT). **Methods:** We reviewed clinical charts of 40 ICNV eyes and classified them into three stages. Active stage <1 month, intermediate 1–3 months and cicatricial >3 months period after initiation of treatment in naïve ICNV eyes. OCT characteristics of these morphological changes were determined. Parameters such as mean volume (MV), central macular thickness (CMT) and neovessels size (thickness and diameter) were analyzed and compared using one -way ANOVA. **Results:** We have 12 males and 28 females with a mean age of 30.1±7.80 years. In active stage, heterogenous activity of CNV was observed, along with disrupted RPE layer, surrounded by subretinal fluids and loss of foveal depression. In intermediate stage, CNV reflection appears homogenous with smooth peripheral Retinal pigment epithelium (RPE) lesion and reduction in retinal thickness. In cicatricial stage, OCT presents dome shaped elevation, strong homogenous reflection, absence of subretinal fluids and reformation of foveal depression. We have found that difference in mean volume and choroidal neovessels thickness was statistically significant in the three stages. **Conclusions:** In our study we have concluded that OCT is useful tool for following the clinical course of ICNV and understanding the pathological changes in CNV regression.

Keywords: Idiopathic choroidal neovascularisation; Optical coherence tomography; Sub retinal fluid; Retinal pigment epithelium; Central macular thickness; Visual acuity, Reflectivity; Pathological stages; Pigment epithelial detachment

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INTRODUCTION

Idiopathic choroidal neovascularisation (ICNV) is development of choroidal neovascularisation (CNV) in young adults without any apparent manifestations of primary ocular or systemic diseases.[1–3] Exclusion of predisposing factors (primary ophthalmic diseases, such as the presumed ocular histoplasmosis syndrome, pathologic myopia, traumatic choroidal rupture or angioid streaks) for CNV together with an onset age of less than 50 years is a hallmark manifestation for ICNV.[4–7] Clinical outcomes of ICNV are favorable as compared to age related macular degeneration (AMD) with significant individual variations.[8] However ICNV has spontaneous regression, yet in some cases 20–30% of patients have poor visual outcomes and may not reverse with further treatment and effects the most productive years of patient's life.[9] Clinical presentation of choroidal neovascularisation is complex of subfoveal and juxtafoveal convex shape vascular protrusion arising from Retinal pigment epithelium (RPE), along with subretinal fluids leading to metamarphopsia and reduction in visual acuity. These pathological changes can be examined on fluorescein angiography or indocyanine green angiography and optical coherence tomography (OCT).[10] Hence we aim to observe detail hallmark structural changes in CNV at various pathological stages with OCT.

MATERIAL AND METHODS

This study was done by review of the records and was approved by the Institutional Review Board of Xi'an Jiaotong Medical University. We reviewed clinical charts of forty treatment naïve patients who received intravitreal bevacizumab (1.25 mg/0.05 mL Avastin; Genentech, Inc, San Francisco, CA) for idiopathic CNV between September 2013 and October 2014. All patients were younger than 50 years and showed active CNV with exudative fluids observed by ophthalmoscope, slit-lamp biomicroscope, fundus fluorescein angiography (FFA) and OCT at baseline. FFA showed well-defined classic CNV in all patients at initial visit. We have divided each patient images into three stages based on the OCT changes after initiating treatment. (1) Active stage <1 month (2) Intermediate stage 1–3 months (3) Cicatricial stage >3 month period. Eyes with retinal pigment epithelial detachment, loss of foveal depression, surrounded with subretinal fluids and classic CNV lesions with active leakage of

fluorescein in the late phase were classified as being in active stage. Eyes were placed in the intermediate stage when they had homogenous CNV reflection, decrease in retinal thickness and decrease in subretinal fluids level. Changes were marked as cicatricial stage if complete regression of CNV with homogenous reflection, loss of subretinal fluids, re-formation of foveal depression and no leakage of fluorescein in the late phase were observed.

We observed relevant OCT features at each stage (size, central macular thickness and mean volume). For this study we defined the diameter of CNV as the maximum horizontal margin that could be distinguished by OCT.[11] Thickness of CNV was defined as the maximum CNV thickness above the retinal pigment epithelial level that could be determined by hyper-reflectivity.[11–13] The above defined parameters were measured manually with the virtual caliper function included in the OCT software. Central macular thickness was defined as mean retinal thickness of 500 µm centre as described in the Early Treatment Diabetic Retinopathy Study and mean volume was measured by the OCT calibrated software.

Statistical analyses were performed using SPSS-20.0 and excel sheet was used for graphs presentation. The logarithm of minimal angle of resolution (logMAR) was calculated from decimal visual acuity for statistical analysis. Data were expressed as mean±SD. One way ANOVA was used to compare the difference between the three groups. For intergroup comparison Independent sample t-test was used to determine the significance. *p* values less than 0.05 were considered significant for the difference between the groups.

RESULTS

There were 12 men and 28 women with a mean age of 30.1±7.80 years. Clinical characteristics of the patients are shown in (Table-1). OCT changes in patients were observed as shown in (Table-2).

OCT features of idiopathic choroidal neovascularisation in three stages:

In active stage, heterogenous reflection of CNV was observed by OCT, surrounding by subretinal fluids, along with loss of foveal depression. (Figure-1) Among 40 eyes with ICNV, pseudo-cysts were detected by OCT in four eyes (Figure-2).

In intermediate stage, CNV reflection tended to be homogenous as compared with active stage, surrounded by low volume of subretinal fluid. Such CNV lesion was observed by OCT as comprising characteristics of active and cicatricial stages. CNV was covered by dome shaped RPE elevation continuous with normal RPE layer. (Figure-1)

In cicatricial stage, CNV reflection tended to be more homogenous than intermediate stage, covered with RPE layer, complete absorption of subretinal fluids and re-formation of foveal depression. These findings suggest regression of CNV activity (Figure-1).

Comparison of OCT characteristics between the groups

We compared OCT characteristics between the three groups. We found that difference in mean volume and choroidal neovessels thickness was statistically significant in the three stages (Figure 3–5). Using fundus fluorescein angiography (Left) and optical coherence tomography (Right). A subfoveal lesion with serous retinal detachment is seen in the macula. In the active stage, OCT revealed CNV as multi-layered area protruding into the subretinal space associated with subretinal fluids. In the intermediate stage, the margin in the subretinal space became smooth, with decrease in subretinal fluid volume. In the cicatricial stage, the ICNV is observed area covered by a dome-shaped highly reflective layer corresponding to the retinal pigment epithelium and loss of subretinal fluid.

Table -1: Characteristics of ICNV patients (n=40)

Characteristics	Numbers
Mean age±SD, years	30.1±7.80 (Range 17–48)
Male: Female	12:28
Eye (Right: Left)	19:21
Refractive error ±SD, D	–2.50±2.24 (range–4.50 to +0.30)
Number of Injections	2.28±1.69 (Range, 1–4)
Follow up period ±SD, months	3.60±1.20 (Range, 1–5)
Location of CNV	
Subfoveal	24 eyes (60%)
Juxtafoveal	16 eyes (40%)

CNV; choroidal neovascularisation, D; diopters

Table-2: Characteristics of idiopathic choroidal neovascularisation (ICNV) at various stages (n=40)

Variable	Stage			*p*
	Active (SD)	Intermediate (SD)	Cicatricial (SD)	
Duration	**<1 Month**	**1–3 Months**	**>3 Months**	
BCVA¶	0.66 (0.24)	0.31 (0.18)	0.24 (0.17)	<0.01
IOP†	15.56 (1.46)	15.48 (1.52)	15.63 (1.44)	0.904
MV‡	9.20 (0.48)	9.92 (0.52)	9.73 (0.63)	<0.01
CMT*	347.26 (135.80)	337.48 (40.20)	251.29 (27.50)	<0.01
CNVT*	346.66 (132.78)	181.122 (51.46)	43.04 (24.12)	<0.01
CNVD*	461.44 (134.50)	194.34 (108.45)	212.05 (106.10)	<0.01

IOP, Intraocular pressure; BCVA, best corrected visual acuity; CMT, central macular thickness; CNVT, choroidal neovascularisation thickness; CNVD, choroidal neovascularisation diameter One-way ANOVA for all comparisons . *p* value significant at 0.01 level.
¶ logMAR, $\log_{10}$ of reciprocal of decimal visual acuity, † mmHg, ‡ mm^3, * µm

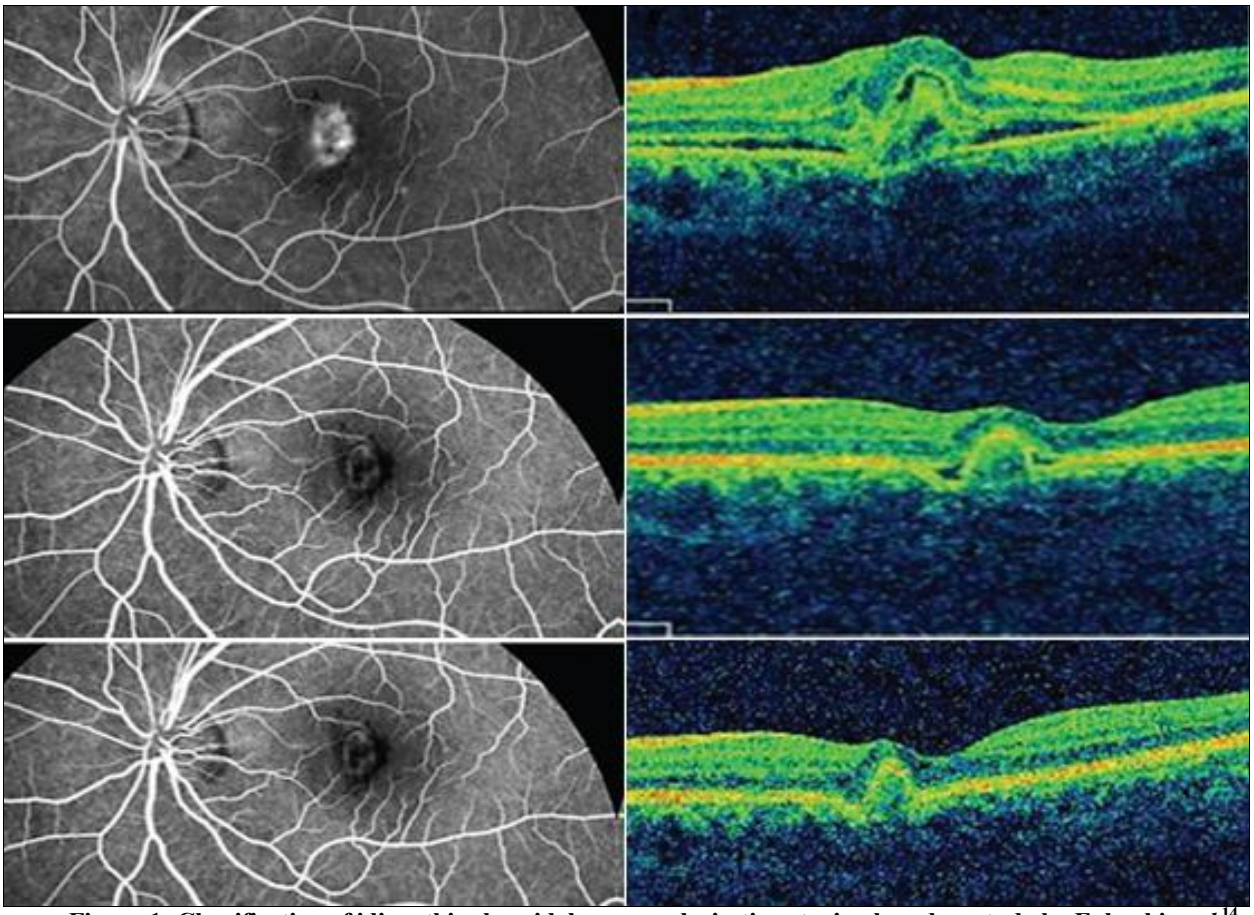

Figure-1: Classification of idiopathic choroidal neovascularisation staging based on study by Fukuchi *et al* [14]

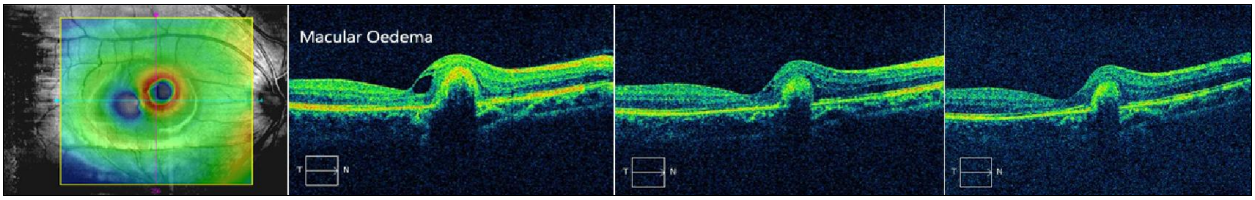

Figure-2: Macular oedema with clear contents and hyper-reflective elevated RPE. At cicatricial stage, oedema has been resolved.

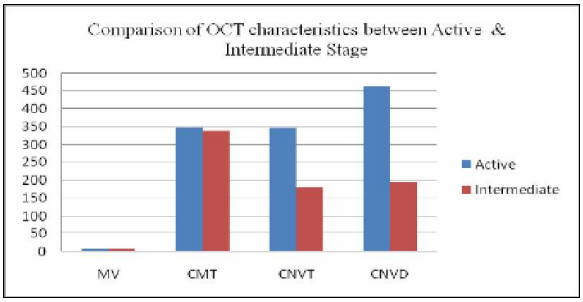

Figure-3: Comparison of active and intermediate stages. For central macular thickness (CMT) p=0.66, for mean volume (MV) p<0.01, choroidal neovascular thickness (CNVT) p<0.01, choroidal neovascular diameter (CNVD) p<0.01.

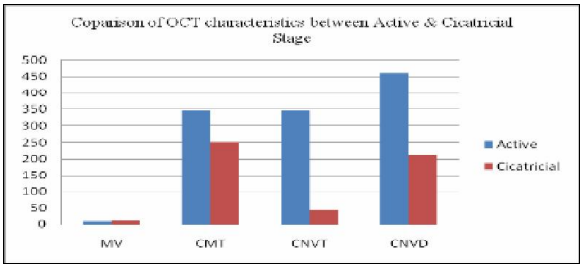

Figure-4: Comparison of active and cicatricial stages. For central macular thickness (CMT) p<0.01, for mean volume (MV) p<0.01, choroidal neovascular thickness (CNVT) p<0.01choroidal neovascular diameter (CNVD) p<0.01. p-value significant at 0.01 level

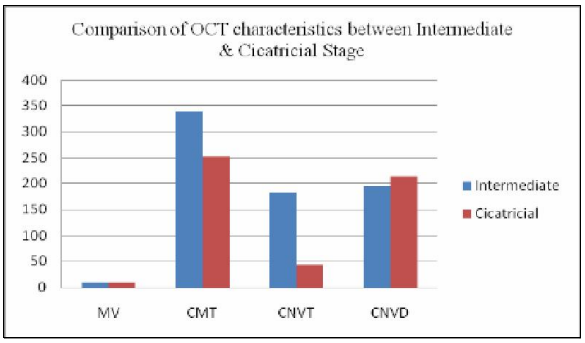

Figure-5: Comparison of intermediate and cicatricial stages. For central macular thickness (CMT) p=0.143, for mean volume (MV) p<0.01, choroidal neovascular thickness (CNVT) p<0.01, choroidal neovascular diameter (CNVD) p=0.457. p-value significant at 0.01 levels.

DISCUSSION

Optical coherence tomography was initially reported by Huang *et al*[15]and gain wide application in clinical practice due to its non-invasive method and high resolution.[16] We analyse CNV stages and OCT characteristics in 40 eyes and elucidate hallmark changes during CNV regression.

In this study we observed reflectivity of CNV changed from heterogenous reflection to homogenous reflection at intermediate stage. We suspect change in level of CNV reflection is due to increase in neovessels fibrosis which cause significant reduction in CNV thickness (346.66±132.78:181.12 51.46) p<0.01 and diameter (461.44±134.50: 194.34±108.45) p<0.01 between the two stages. Increase in CNV reflection was observed at cicatrizing stage which support our view that high level of vascular fibrosis leads to hyper-reflectivity and homogenous appearance of fusiform neovessels. Fukuchi *et al*[14] have observed highest reflections in CNV fusiform lesions and suggested fibrotic changes in CNV membrane after prolong disease duration. Iida *et al*[10] have reported transformation of protruding CNV to fusiform tissue with increase in reflectivity during regression. In an experimental model of CNV in monkeys and rats[14–20] observed with OCT, the authors reported mixture of reflections of various densities at initial stage and highly reflective area at cicatrizing stage as the CNV regress.

In intermediate stage we have observed envelopment of peripheral CNV with highly reflective layer continuous with normal RPE. In cicatrizing stage, RPE colour density gradually change from periphery of the lesion towards central part which suggests complete RPE envelopment as the disease progress. Development in RPE cell proliferation can be observed as hyperfluorescent rim surrounding neovascular membranes in the late phase of ICG angiography. Ryoko *et al*[21] have observed 12 eyes of ICNV patients with ICGA and near- Infrared Autofluorescence (IR-AF). They arrive at conclusion that dark ring-shape hyperautofluorescence indicates involutional process of CNV enveloped by the RPE which corresponds to dark rim on ICGA.

In this clinical investigation BCVA logMAR, CMT, CNVT and CNVD have statistically significant changes among the three groups (p<0.01). Increase in visual acuity was associated with decrease in subretinal fluid level and changes in OCT parameters. Punjabi *et al*[22] have demonstrated that decrease in subretinal fluid and inner retinal fluid have association with increase in BCVA in a retrospective chart review of 72 eyes of 64 patients with pigment epithelial detachment. In another study the author[23,24] has concluded increase in BCVA logMAR has positive correlation with CNV thickness in ICNV patients.

OCT is a useful tool and provides sufficient information to characterize CNV stages which can be helpful in selecting appropriate therapy in clinical practice. Shortcomings of this study need to be highlighted. We have relatively small number of patients and several study parameters, including size of choroidal neovessels thickness and diameter were measured manually due to absence of automated software. BCVA was measured by the standard decimal visual acuity chart rather than the Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity chart. A clear understanding of the pathological changes will require further studies with larger sample size and OCT modalities with higher resolution.

CONCLUSION

Our study suggests that OCT provide significant information in CNV diagnosis and regression progress. Combination of OCT with other imaging modalities may allow detail information in selecting appropriate therapy and ICNV staging.

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AUTHORS CONTRIBUTION

SNAS: Conceived the study design, supervised the study, write up and proof reading, QYK, BM, SG, UF: Literature review Data collection, Statistical analysis.

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