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Choroidal Neovascularization Characteristics and Its Size in Optical Coherence Tomography

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The classification, size and activity of choroidal neovascularization (CNV) by optical coherence tomography (OCT) were compared with those obtained by fluorescein angiography (FA) and Indocyanine green angiography (ICG). This study included 32 patients (32 eyes) diagnosed as having CNV. The etiology of CNV was found to be age-related macular degeneration (AMD) or non-AMD. Patients were studied retrospectively by FA, ICG, and OCT. Of the 13 eyes with AMD, the boundary of the lesion could not be defined using FA in 7 patients. Among the 7 poorly defined CNV cases by FA, the identification of the boundary was possible in one case by OCT. The mean diameter of the classic well-defined lesions was $3500 \pm 421\,\mu m$ by FA, $2624 \pm 1044\,\mu m$ by ICG, and $1927 \pm 1272\,\mu m$ by OCT. The size of the CNV by OCT was always smaller than by FA or ICG. Of the 19 eyes with Non-AMD, the boundary of the lesion could not be defined by FA in 5 patients. Among the 5 poorly defined cases by FA, the identification of the boundary was possible in 3 cases by OCT. The mean diameter of the well-defined CNV lesions was $2153 \pm 759\,\mu m$ by FA, $1929 \pm 673\,\mu m$ by ICG, and $1322 \pm 566\,\mu m$ by OCT. Retinal thickness, which represents retinal edema, was found to be proportional to lesion size, although the relationship was not statistically significant. Regardless of CNV type, FA, ICG and OCT used in combination increase the specificity of diagnosis if their findings are compared.

Key Words: Choroidal neovascularization, fluorescein angiography, indocyanine green angiography, optical coherence tomography

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INTRODUCTION

The growth of a choroidal neovascularization (CNV) is one of the most serious events that can be observed in the macula area. Determining the type and the boundary of a CNV is important when deciding on treatment in CNV cases. CNV is divided into two types, i.e., classic and occult CNV, on the basis of fluorescein angiography (FA) findings.[1] The majority of CNVs are not of the classic type, so it is not always easy to delineate the boundary of the lesion. Indocyanine green angiography (ICG) allows a classification to be made on a portion of an occult CNV as a well-demarcated CNV. Although hyperfluorescences observed by FA and ICG in patients with CNV indicate the extent of the CNV, it is unclear that they represent the total area of the lesion. Optical coherence tomography (OCT) is a new diagnostic imaging technique, which is based on the time delay created by light reflected from tissue microstructures as determined by interferometry. The use of optical rather than acoustic waves enables higher resolution in the posterior portion of eye using a non-contact noninvasive measurement.[2] Moreover, OCT may have potential for accurately quantifying the boundaries in a subset of angiographically occult CNV.

The purpose of this study was to evaluate the characteristics, sizes and activities of CNV by OCT, and thus, to compare the features and effectiveness of OCT in combination with FA and ICG in the clinical diagnosis of CNV.

MATERIALS AND METHODS

This study included 32 patients (32 eyes) diagnosed as having CNV. The mean age of the patients was 51.38 ± 20.68 years; 16 men and 16 women. The etiologies of CNV were age- related macular degeneration (AMD) in 13 eyes, pathologic myopia in 6 eyes, idiopathic in 10 eyes, angioid streak in 2 eyes, and choroidal rupture in 1 eye. All the lesions were classified as either AMD or non-AMD. Using OCT, the fundus was scanned on 5.65 mm horizontal and vertical planes through the CNV center and the position and the direction of the scanning beam were demonstrated on fundus photography. All CNV lesions were classified as either well defined lesions or poorly defined lesions on the basis of the angiographic features, and well defined lesions were further subdivided as classic type or occult type. Based on ICG, the CNVs were classified into well demarcated lesions or poorly demarcated lesions. On the basis of the classification of Hee, et al.,[2] we classified the lesions into five types by OCT: well defined lesions, poorly defined lesions, fibrovascular pigment epithelial detachment (PED), hemorrhagic PED and serous PED.

To determine the extent of lesion by FA, we measured the diameter of hyperfluorescent lesions and of CNV lesions along the same cross sectional planes of the OCT. A CNV lesion was defined as a hyperfluorescence with blocked fluorescent lesion by hemorrhage and/or elevated PED. A hyperfluorescent lesion by ICG was confined as the leaking on late phase, and measured relative to the diameter of the optic disc. Findings showing rupture or thickening of the RPE layer by OCT were considered to include CNV lesions, and irrespective of the size of RPE rupture or thickening, CNV lesion size was determined only on well defined CNV lesions. We estimated the activity of a CNV lesion by estimating the amount of intraretinal fluid, from the distance between the inner surface of the sensory retina and the RPE layer on a cross sectional OCT scan.

RESULTS

Of the 13 eyes with AMD, 3 eyes were determined as classic type and 10 eyes as occult type CNV by FA (Table 1A). Classic type CNVs were also identifiable by OCT and 1 eye among these was identified as fibrovascular PED. In 7 eyes among the 10 occult CNV, the boundary of the lesion could not be defined by FA. In the remaining 3 eyes, we were able to delineate the extent of the lesion as PED by OCT. Out of 7 eyes with a poorly defined lesion, the boundary of 1 eye was delineated only by OCT (Fig. 1). Two eyes originally considered as occult CNV by FA were confirmed as polypoidal choroidal vasculopathy (PCV) by OCT after re-investigating by ICG and FA (Fig. 2). Another 1 eye was diagnosed as occult CNV by FA but did not show a definite CNV lesion by OCT, but rather a large serous retinal detachment. Non-AMD showed morphologic characteristics somewhat different to AMD. Of the 19 non-AMD eyes, 13 eyes were defined as of the classic type and 6 eyes as occult type CNV by FA (Table 1B). One out of the 13 eyes with classic CNV was found to be fibrovascular PED by OCT (Fig. 3). All of the classic CNVs were defined by OCT. Among the 6 occult CNVs, 3 eyes were found to be fibrovascular PED.

Comparisons of lesion sizes, measured respectively by FA, ICG and OCT were performed in 6 AMD eyes, in which we could determine lesion diameter by OCT. The mean diameter of the 6 CNV lesions was 3500 ± 421 μm by FA, 2624 ± 1044 μm by ICG, and 1927 ± 1272 μm by OCT. None of the lesions measured using OCT exceeded that of those measured by FA in size. But with regard to hyperfluorescence, the lesion diameter in the OCT image was greater than the hyperfluorescent diameter in the FA image in 3 of 6 AMD eyes. That is, some of the CNV sizes by OCT were smaller than those determined by hyperfluorescence in FA, but these also included blocked fluorescent areas, in addition to the hyperfluorescent areas (Table 2A). Lesion size by OCT was larger than hyperfluorescence size by ICG in 3 eyes, the same size in 2 eyes, and smaller in 1 eye. Retinal thickness by OCT imaging was thicker than 700 μm in 5 eyes and in 8 eyes was between 400 and 700 μm. All were thicker than normal. Retinal thickness seemed to be proportional to lesion size, although the relationship was not statistically significant. However, no asso-

Table 1-A. Comparison of OCT and FA in AMD

FA	Well defined		Poorly defined
OCT	Classic	Occult	
Well defined	2	-	1
Poorly defined	-	-	3
Fibrovascular PED	1	3	2
Hemorrhagic PED	-	-	-
Serous PED	-	-	1

Table 1-B. Comparison of OCT and FA in non-AMD

FA	Well defined		Poorly defined
OCT	Classic	Occult	
Well defined	12	-	3
Poorly defined	-	-	-
Fibrovascular PED	1	1	2
Hemorrhagic PED	-	-	-
Serous PED	-	-	-

OCT, optical coherence tomography; FA, fluorescein angiography; AMD, age-related macular degeneration; PED, pigment epithelial detachment.

Table 2-A. Comparison of CNV Size by OCT and FA in Patients with AMD

	Hyperfluorescent lesion	Hyperfluorescent lesion + Blocked fluorescent lesion
OCT>FA	3	-
OCT=FA (FA size ± 10%)	-	1
OCT<FA	3	5

Table 2-B. Comparison of CNV Size by OCT and FA in Patients with non-AMD

	Hyperfluorescent lesion	Hyperfluorescent lesion + Blocked fluorescent lesion
OCT>FA	6	1
OCT=FA (FA size ± 10%)	1	3
OCT<FA	7	10

CNV, choroidal neovascularization; OCT, optical coherence tomography; FA, fluorescein angiography; AMD, age-related macula degeneration.

ciation was found between retinal thickness and size of leakage by FA.

Comparison of CNV sizes among the different modalities was also performed for non-AMD eyes. Fourteen eyes were eligible for comparison. The mean diameters of the 14 CNV lesions were 2153 ± 759 μm by FA, 1929 ± 673 μm by ICG, and 1322 ± 566 μm by OCT. Thirteen of the 14 eyes showed the same or a smaller lesion size by OCT than by FA. However, lesion diameter in the OCT image was greater than hyperfluorescence in the FA image in 6 of the 14 eyes

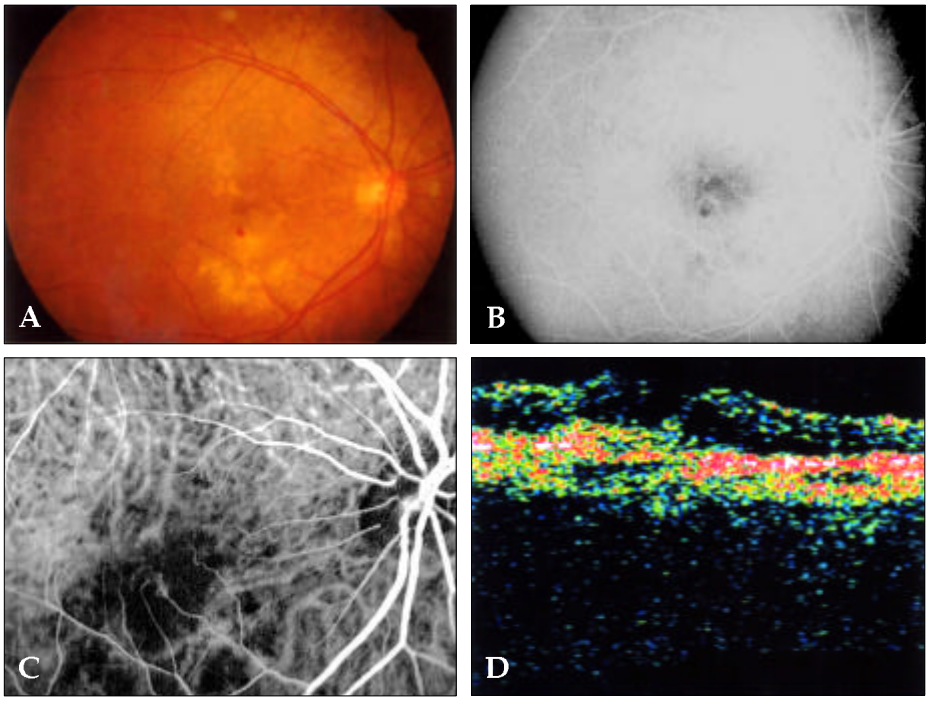

Fig. 1. A 78-year old female. Fundus photograph (A) shows exudative retinal detachment inferior to the fovea and multiple drusens. FA (B) shows a lesion that leaks 'F' dye from an undetermined source, and an obscure lesion boundary. ICG (C) exhibits mild leakage from choroidal vessel, without a distinctly observed lesion. OCT (D) shows localized disruption

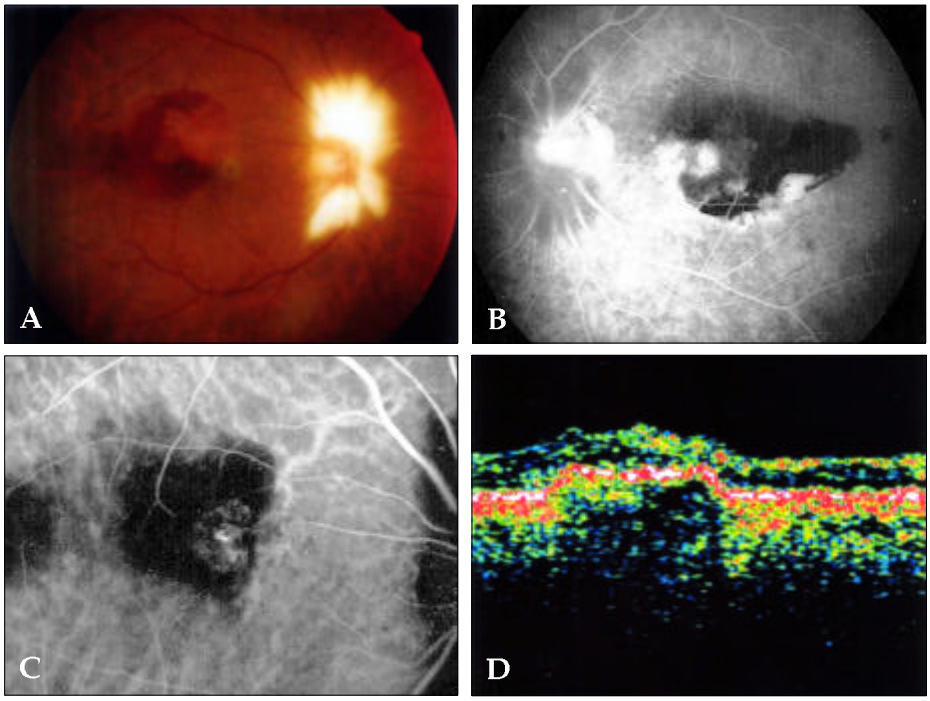

Fig. 2. A 78-year old male. Fundus photograph (A) shows a 2DD sized subretinal hemorrhage. FA (B) shows blocked fluorescence and multinodular hyperfluorescent lesions nasal to it. ICG (C) demonstrates the abnormal choroidal vascular channel and a pinhead sized multifocal hyperfluorescence. OCT (D) shows distinct PED and moderate reflectivity beneath the RPE layer, suggesting fibrovascular PED.

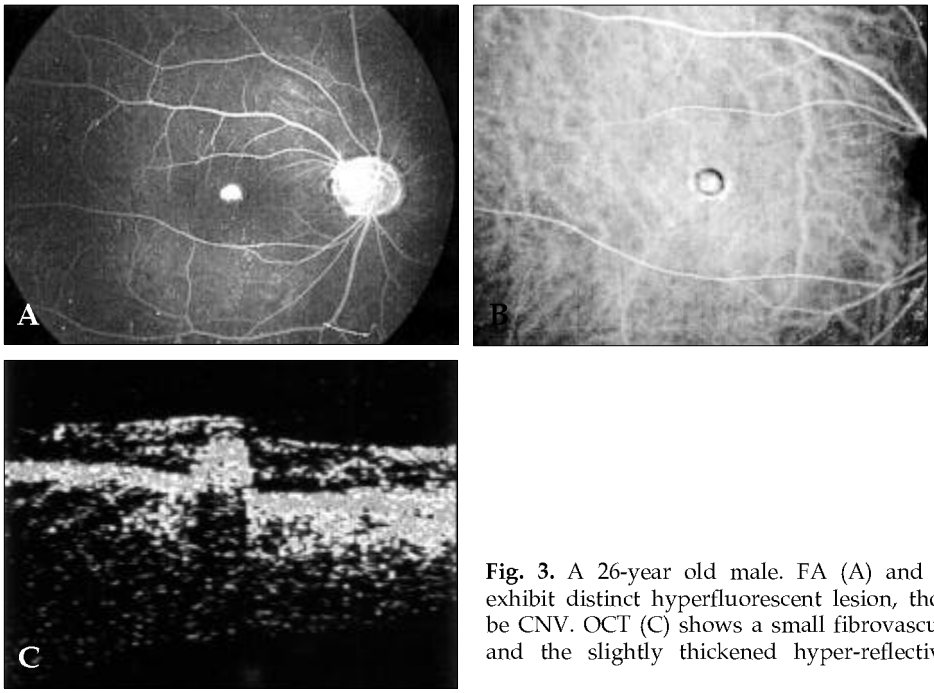

Fig. 3. A 26-year old male. FA (A) and ICG (B) exhibit distinct hyperfluorescent lesion, thought to be CNV. OCT (C) shows a small fibrovascular PED and the slightly thickened hyper-reflective layer

(Table 2B). None of the lesions sized by OCT exceeded the area of hyperfluorescence as determined by ICG. Retinal thicknesses on OCT images were between 400 to 700 μm in all 19 eyes and were greater than normal. Like AMD, retinal thickness showed a tendency to be proportional to lesion size, although the relationship was not statistically significant. No association was found between retinal thickness and the size of leakage by FA.

DISCUSSION

OCT is a method that allows the high resolution, cross sectional visualization of tissue.[3,4] OCT was initially reported by Huang, et al.[3] in 1991, and since it has been widely used in clinical practice as a noninvasive method to study the fine features of the posterior pole of the eye.[2,5-7] The physical basis of imaging depends on the different optical reflectivities of different tissue microstructures. OCT is an analogue of conventional clinical ultrasound, except that the optical rather than the acoustic properties of tissues are measured. Like ultrasound, cross-sectional images of reflectivity in tissue are obtained to differentiate internal tissue structure.[8] Differentiating the relative reflectivity of different tissue layers and morphological changes in tissue structures on OCT are mainly depended on the ability of the viewer.[7] Angiographically, in general, classic CNV usually presents a well-defined CNV on OCT, and occult CNV is divided into fibrovascular PED and poorly defined CNV.[2] The reason why classic CNV produces a well defined lesion is thought to be due to penetration of new vessel being localized through RPE breaks, but in one case, classic CNV showed fibrovascular PED on OCT.

The exudative change around a CNV makes it difficult to determine the presence of the CNV by fluorescein angiography, especially at the boundary of the lesion. Also, hemorrhage typically obscures the boundaries of a CNV on FA. However, the near infrared wavelength of the OCT probe light allows enhanced penetration and imaging capability through blood and exudates, facilitating the identification of the boundaries of some lesions obscured in FA. Identification of the boundary in occult CNV was possible in one case by OCT. But, even in the case of OCT, the presence of a severe hemorrhagic or exudative RPE detachment decreased the penetration of light abruptly and blocks reflection of the choroid. So, there are limitations to the imaging of lesion

components lying below the RPE, and not all of the entire CNV lesion may be elucidated by OCT. Furthermore, because current OCT shows only two-dimensional boundaries of CNV, the presentation of three-dimensional images of entire lesions is impossible.

It is important to demarcate the size of a CNV lesion for therapeutic planning. Like FA, a hyperfluorescent lesion in ICG doesn't confine a CNV lesion. Only reduced exudative manifestations after laser treatment of a hyperfluorescent lesion prove that the lesion has been active. Several authors have reported that the actual membrane size was found to be uniformly larger than expected by FA.[9] By using ICG or OCT it is an effort to demarcate and localize the CNV lesion. But, it is based on the fact that a hyperfluorescent lesion by ICG or a CNV lesion by OCT reflect only the true lesion. In fact, on comparing a well demarcated lesion by ICG with the lesion by OCT, it was found that the lesion size by OCT is never larger than the hyperfluorescent lesion by ICG, making it clear that the CNV lesion is no larger than the hyperfluorescent lesion on ICG. So, it is believed that laser treatment based on ICG is a reasonable choice, but the evaluation of only the hot spot as the active lesion is controversial. Slakter, et al.[10] performed indocyanine green- guided laser photocoagulation, and reported 2 lines or more improvement of V/A in 13%, and stabilized V/A in 53%.

The TAP study advised using a spot size with a diameter 1000 μm larger than the greatest linear dimension of the CNV lesion when deciding upon the lesion size for treatment, and it has been reported that this method is beneficial if the classic component is more than 50% by FA.[11] But, CNV size on OCT is always smaller than the CNV size on FA, so that adding 1000 μm to lesion size as determined by OCT make it indifference to the treatment result. Also, even if the effect of photodynamic therapy (PDT) is temporary, the accompanying nonperfusion of choriocapillaries means that a large spot size is not necessary. In our experiences, PDT on a small hemorrhage or PED is thought to be effective, and an OCT classification may be used to evaluate the result of a modality; however, these issues remain for further investigation.

CNV progress shows fluid accumulation in the retina, and retinal edema is manifested as an increased retinal thickness.[12,13] We believe that measuring retinal thickness reflects the activity of the CNV indirectly. In AMD, 5 cases of over 700 μm in height by OCT, and 8 cases of 400 - 700 μm were found, and all were thicker than normal. In non-AMD, all 19 cases had between 400 - 700 μm in height by OCT, and all were thicker than normal. Giovannini, et al.[14] reported a mean 411.7 μm as the neuroretinal thickness of 9 CNV cases, which required operation regardless of size and location; moreover, retinal thickness was found to increase as the size of the CNV lesion increased in all CNV cases, but no statistical relationship was found between retinal thickness in OCT and the severity or size of leakage by FA.

In this report, we previously mentioned that the presence of severe hemorrhagic or exudative RPE detachment reduces light penetration abruptly and blocks the reflective line from the choroid even in OCT. Moreover, because the OCT image shows only the two-dimensional, restrictive boundaries of CNV, demonstrating the three-dimensional images of the entire lesion is impossible. Added to these considerations, some other problems in using OCT as diagnostic modality had occurred. Firstly of all, because a slice of OCT is observed as a line on FA or ICG, detection of an extremely small CNV lesion is not easy. Secondly, deciding on the accurate location of height, which is believed to represent CNV activity on OCT, requires further investigation. Thirdly, the way of detecting boundaries of an occult lesion on OCT, one that shows no definite boundaries by FA, also required investigation. Fourth, repeating the present investigation and confirming lesion changes in cases of follow up loss is not possible due to the retrospective nature of the present study. It is hope that such problems will be further defined and resolved by further investigations.

The present study demonstrates that the real type and the actual size of choroidal neovascularization may differ from lesion size by FA or ICG. In cases of larger lesion sizes by OCT than by FA or ICG, we guess that histologically altered structures as identified by OCT are not observable by FA or ICG. The OCT image is more reliable than FA or ICG for evaluating RPE detachment

and the associated exudative changes in the retina, and an effective diagnostic tool for evaluating the presence of a lesion and the boundaries in combination with ICG and FA. However, using OCT only CNV cannot be diagnosed and treated. If penetration is increased to pass severe hemorrhage and exudative materials, and differentiate all layers of retina, it will give more information to diagnosis of CNV and morphological study around the lesion. Also, the three-dimensional image of the entire lesion can be used as a sole therapeutic guide by increasing the angles of the two-dimensional slices. In cases of occult CNV in AMD, ICG and OCT proved to be effective tools for diagnosis, but fluorescein angiography remains as an essential tool for the diagnosis of CNV. Regardless of types of CNV, FAG, ICG and OCT will elevate the specificity of a diagnosis if their findings are compared during diagnosis.

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