



Indocyanine Green Angiography in Classic Choroidal Neovascularization

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Abstract: The indocyanine green (ICG) angiographic features of classic choroidal neovascularization (CNV) were evaluated in the 66 consecutive patients (70 eyes) by ICG angiography using the scanning laser ophthalmoscope. All patients had classic CNV documented by fluorescein angiography. Indocyanine green angiographic findings of classic CNV were as follows: Vessel architecture in 66% (46 of 70) of eyes, feeding vessels in 29% (20 of 70), and late hyperfluorescence in 93% (65 of 70) of eyes. Borders of classic CNV were found well-defined in 47% (33 of 70), and ill-defined in 49% (34 of 70) of eyes. In the remaining 4% (3 of 70) of eyes ICG angiography did not detect CNV. Our study indicates that fluorescein angiography remains the method of choice in the diagnosis of classic CNV. Indocyanine green angiography provides more information in the detection of feeding vessels of classic CNV. *Jpn J Ophthalmol* 1998;42:300-303 © 1998 Japanese Ophthalmological Society

Key Words: Age-related macular degeneration, choroidal neovascularization, feeding vessel, fluorescein angiography, indocyanine green angiography, scanning laser ophthalmoscope.

Introduction

The Macular Photocoagulation Study Group has reported the beneficial effects of laser photocoagulation in the treatment of classic choroidal neovascularization (CNV).¹⁻³ Detection of classic CNV is one of the most important criteria for laser treatment, and fluorescein angiography has been the method of choice for diagnosis. Recent advances in imaging technology have made indocyanine green (ICG) angiography a popular diagnostic tool in addition to fluorescein angiography.⁴⁻¹¹ Indocyanine green angiography, because of the biophysical properties of ICG dye, offers the theoretical advantage of better visualization of the choroidal vasculature. In the following study, we evaluated whether the ICG angiographic features of classic CNV would provide addi-

tional information that might help in diagnosis and treatment of CNV.

Materials and Methods

The study included 66 consecutive patients (70 eyes) examined at the University Eye Clinic of Tübingen between January 1993 and December 1994. Inclusion criteria were: (1) Clinical evidence of choroidal neovascularization and (2) presence of classic CNV based on fluorescein angiography. Exclusion criteria were: (1) Clinical and/or fluorescein angiographical evidence of occult CNV; (2) prior laser treatment of the CNV; (3) patients with ocular opacities that precluded the interpretation of fluorescein and ICG angiography; and (4) patients with known allergy to fluorescein or ICG dye.

Each patient underwent a complete eye examination including slit-lamp biomicroscopy with a Goldmann contact lens. A scanning laser ophthalmoscope (SLO, Type 101, Rodenstock, Munich, Germany) with a 780-nm infrared diode laser and a 830-nm barrier filter was used for ICG angiography. All the ICG angiographies were obtained using a 10-mm aperture, confocal mode, infrared laser energy of 1880

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mW and helium-neon laser for positioning the instrument. After injection of 50 mg/4 mL of ICG (Pulsion, Munich, Germany) intravenously, ICG angiographies were recorded on an S-VHS videotape (Panasonic AG 7500, Osaka). Indocyanine green angiographic images were recorded continuously during the first minute, and at the 10th and 30th minute after injection of the dye. Analysis of the angiograms was performed on the observing monitor while playing the videotape. Fluorescein angiography was obtained with either a SLO or a conventional fundus camera (Topcon 50 VC, Tokyo) after injection of 5 mL of 10% sodium fluorescein into a cubital vein. Stereoscopic color photographs were taken on the same day.

Classic CNV was classified according to the definition of the Macular Photocoagulation Study Group.² Indocyanine green angiograms were analyzed based on the delineation of the border of CNV. In addition, detection of the vessel architecture, feeding vessels, and late hyperfluorescence of CNV were recorded.

Results

Of the 66 patients, 36 were female (55%) and 30 were male (45%). The mean age of the patients was 64.5 years (range, 22–88 years). The etiology of CNV was age-related macular degeneration (AMD) in 51 eyes, idiopathic in 10, and myopia in 6 eyes. Presumed ocular histoplasmosis syndrome (POHS) was present in 3 eyes.

The borders of the CNV were well-defined by ICG angiography in 47% (33 of 70) of eyes, and ill-defined in 49% (34 of 70) of eyes (Figures 1 and 2). In 4% (3 of 70) of eyes, CNV could not be detected on ICG angiography (Figure 3). Of these three eyes, CNV was secondary to AMD in two eyes, and to idiopathic CNV in 1 eye.

Indocyanine green angiography revealed the vessel architecture of CNV in 66% (46 of 70) of eyes. Hyperfluorescence of the CNV in the late phase of the ICG angiography was detected in 93% (65 of 70) of eyes. Feeding vessels of the CNV were identified in 29% (20 of 70) of eyes. Fluorescein angiography revealed feeding vessels in only 11% (8 of 70) of eyes (see Table 1).

Discussion

Indocyanine green dye has its absorption and reflection peak in the near infrared spectrum. Secondly, it binds rapidly to 98% of the serum proteins.¹² These unique properties of ICG angiography are advantageous for better imaging of choroidal vasculature.

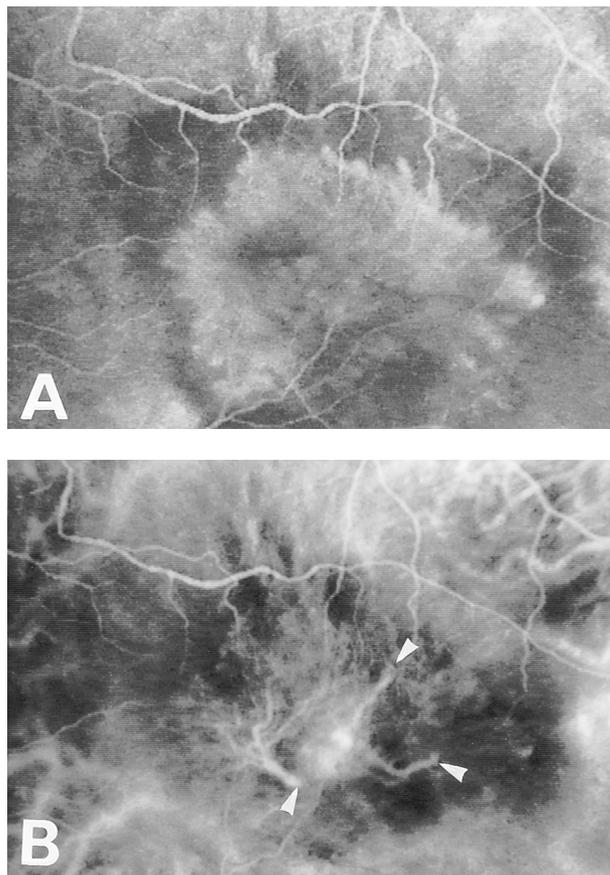


Figure 1. (A) Fluorescein angiogram (arteriovenous phase) of left eye demonstrates classic choroidal neovascularization. (B) Early phase of indocyanine green angiogram of left eye demonstrates vessel architecture of well-defined choroidal neovascularization. Note feeding and draining vessels (arrowheads).

The high temporal resolution of SLO makes dynamic evaluation of choroidal circulation possible and contributes to the superiority of the SLO in comparison to other cameras. This is because the 780-nm infrared laser of the SLO is the most suitable for detection of free ICG dye before it binds to plasma protein. It takes only about 10 seconds for free ICG dye to bind to plasma protein within the blood.

In our study using ICG angiography, the borders of classic CNV could be defined in only 47% of eyes. In the remaining 53%, neovascular lesions were either ill-defined or could not be detected. In other studies using digital ICG angiography; 20% to 59% of eyes had been found to have ill-defined or nondetectable CNV, whereas fluorescein angiography revealed well-defined classic CNV.^{7,13–15} Differences in inclusion criteria, such as previous laser treatment, heterogeneity

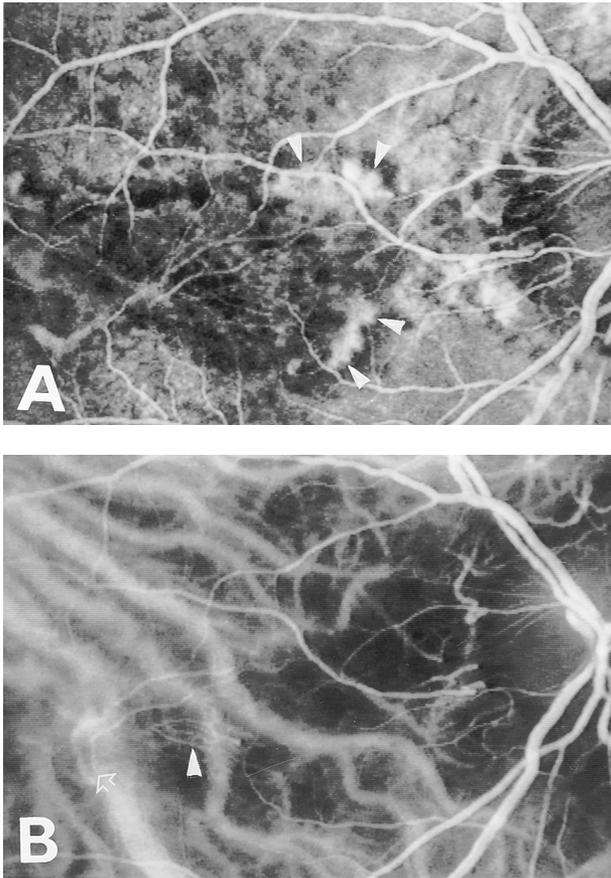


Figure 2. (A) Fluorescein angiogram (arteriovenous phase) of right eye demonstrates well-defined choroidal neovascularization (CNV). Arrowheads indicate active leaking components of CNV. (B) Indocyanine green angiogram (early phase) of right eye demonstrates vessel architecture of choroidal neovascularization (CNV) incompletely. Arrowhead indicates vessel net in center of CNV. Borders of CNV remain ill-defined. Note feeding and draining vessels (open arrow).

of etiology for CNV, use of different angiographic systems for ICG angiography, and small sample size make it difficult to compare these studies. We share the opinion that, generally, when detectable in ICG angiography, classic CNV was less visible than in fluorescein angiography.⁶⁻¹⁰ Because the infrared light penetrates the retinal pigment epithelium easily, this layer does not create a dark background against the CNV in ICG angiography as happens in fluorescein angiography. The increased choroidal background hyperfluorescence in ICG angiography could interfere with visualization of the hyperfluorescence of the CNV. The lower fluorescence of ICG (4% of fluorescein dye) was reported as a contributing factor to this feature.^{7,13} However, the detector or the CCD

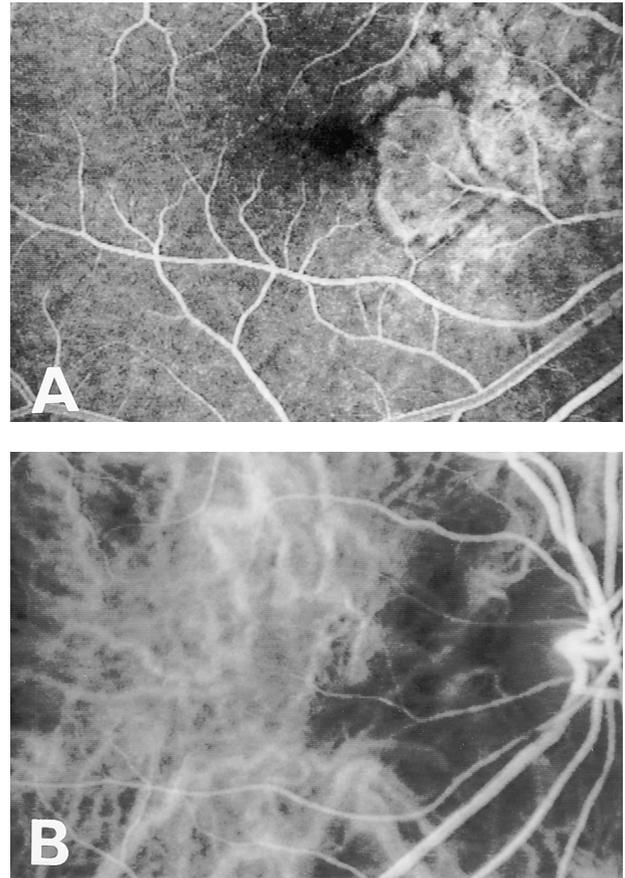


Figure 3. (A) Fluorescein angiogram (arteriovenous phase) of right eye demonstrates well-defined classic choroidal neovascularization. (B) Indocyanine green angiogram (early phase) of right eye fails to demonstrate choroidal neovascularization.

camera used in ICG angiography is more sensitive than that used in fluorescein angiography. For this reason, the same phase of fluorescein and ICG angiograms could provide the same brightness of retinal vessels. Capillaries of the retina can be observed in ICG angiography when the fluorescence of the choroidal vessels is out of focus. As mentioned above, the strong background fluorescence of choroidal vessels may interfere with detection of the delicate vessels of CNV in ICG angiography.

Compared with other ICG studies, we found the detection of vessel architecture to be an important finding in our ICG angiography of CNV. This could result from the use of the SLO instead of the digital fundus camera for ICG angiography.^{8,9,16} However, we noted difficulties in localizing the CNV in the late phase of ICG angiography in relation to the foveal center. This is a drawback of the SLO. Generally, the image quality of the late phase ICG angiograms

Table 1. Indocyanine Green Angiographic Characteristics of Classic Choroidal Neovascularization ($n = 70$)

Etiology	<i>n</i>	Well-Defined	Ill-Defined	Not Detected	Vessel Net	Feeding Vessel	Late Hyperfluorescence
AMD	51	21	28	2	35	16	52
Idiopathic	10	6	3	1	5	2	8
Myopia	6	4	2	—	5	2	3
POHS	3	2	1	—	1	—	2
Total <i>n</i> (%)	70	33 (47%)	34 (49%)	3 (4%)	46 (66%)	20 (29%)	65 (93%)

AMD: age-related macular degeneration. POHS: presumed ocular histoplasmosis syndrome.

is better when using a digital fundus camera or Heidelberg type SLO.

Indocyanine green angiography was superior to fluorescein angiography in detection of the feeding vessels of classic CNV (29% vs. 11%). Less and slower leakage of ICG dye through fenestrated choriocapillaris permits precise evaluation of the vessel structure of CNV. However, ICG dye leaks only from immature vessels of CNV that are not enclosed by retinal pigment epithelium.¹⁷ On the other hand, fluorescein dye is known to leak from all areas of CNV with an overlying fluid-filled subretinal space.¹⁸ The more active components of neovascular lesions, which were distinctly observed by fluorescein angiography, could be successfully detected on the late-phase ICG angiography.

Our study indicates that ICG angiography cannot replace fluorescein angiography in the diagnosis of classic CNV. Therefore, ICG angiographic interpretation of CNV without performing fluorescein angiography has some limitations. The main advantage of ICG angiography in the evaluation of classic CNV was the detection of feeding vessels. Analysis of the choroidal vasculature using ICG angiography may provide additional clues concerning the effects of new therapeutic approaches for CNV.

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