FEEDER VESSEL DETECTION BY MEANS OF DYNAMIC INDOCYANINE GREEN ANGIOGRAPHY OF SUBFOVEAL CHOROIDAL NEOVASCULARIZATION SECONDARY TO AGE-RELATED MACULAR DEGENERATION

ANGIOGRAFÍA DINÁMICA CON VERDE INDOCIANINA EN EL DIAGNÓSTICO DE VASOS NUTRICIOS DE COMPLEJOS NEOVASCULARES SUBFOVEALES COROIDEOS EN LA DEGENERACIÓN MACULAR ASOCIADA A LA EDAD

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ABSTRACT

Purpose: This study aimed to assess the detection and characteristics of feeder vessels (FV) of subfoveal choroidal neovascularization (CNV) in age-related macular degeneration (ARMD).

Methods: A retrospective study of 59 consecutive eyes presenting subfoveal CNV secondary to ARMD was performed. Feeder vessels were detected by means of indocyanine green video angiography using a confocal scanning laser ophthalmoscope. The following factors were analyzed: patient age, visual acuity using Snellen lines and/or ETDRS, fluorescein angiographic (FA) patterns, size of CNV, and time of evolution. The following characteristics of FV also were evaluated: FV pattern (umbrella or racquet-like pattern), number, width and the location with respect to the fovea.

Results: FV were detected in 36 subfoveal CNV (61%). No significant differences were noted between the presence of FV in terms of visual acuity (U Mann-Whitney, p=0.816), FA patterns (Fisher’s...
exact probability test \( p=0.265 \), size of the CNV (U Mann-Whitney, \( p=0.267 \)) and time of evolution (U Mann-Whitney, \( p=0.099 \)).

The most common pattern FV was a the racquet-like pattern, inserted in the subfoveal CNV from an extrafoveal origin on the nasal side after a variable course of approximately 1.27 mm (range 0.1-2.9 mm), with a diameter of 83.3 \( \mu \)m (range 20-150 \( \mu \)m).

**Conclusions:** FV were detected in 36 subfoveal CNV (61\%) in ARMD. Only 16 subfoveal CNV (25.4\%) were considered eligible for FV treatment (*Arch Soc Esp Oftalmol* 2006; 81: 79-84).

**Key words:** Feeder vessels, CNV, ARMD.

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**INTRODUCTION**

Age related macular degeneration (ARMD) is the most frequent cause of legal blindness in patients over 65 in developed countries (1). The presence of a choroidal neovascular complex (CNV) is less frequent but it produces faster and more severe loss of vision than the atrophic form. Direct photo-coagulation of the entire CNV is efficient but only allows an acceptable functional result in the extrafoveal forms, while photo-dynamic therapy achieves permanent closure of the membrane but produces poor functional results (2). Even though macular translocation of CNVs produces satisfactory functional results in selected cases, it presents a very high percentage of severe complications (3).

In recent years different groups have demonstrated the possibility of locating the afferent feeder vessels (ANV) of the CNV utilizing videoangiography with indocyanine green (ICG) and, after direct photocoagulation of said vessels, the closure of the neovascular membrane (4,5).

The purpose of this study is to evaluate the detection capacity of ANVs in subfoveal CNVs by means of high-speed ICG videoangiography as well as to analyze the characteristics of ANVs in what concerns the behavior of subfoveal CNVs and the possibility of photocoagulation thereof.

**SUBJECTS, MATERIAL AND METHODS**

Fifty-nine videoangiographies of exudative ARMD due to CNV were taken from 53 consecutive patients from July 2000 to August 2002.

Mann Whitney, \( p=0.267 \), o el tiempo de evolución (U Mann Whitney, \( p=0.099 \)). El patrón de la AFG más común fue el tipo raqueta, con nacimiento nasal extrafoveal, con un recorrido medio de 1,27 mm (rango 0,1-2,9) y un diámetro medio de 83,3 \( \mu \)m (rango 20-150).

**Conclusiones:** Se pudo identificar VNA en el 61\% de una población con CNV bien o mal delimitadas, y solo 16 NVC subfoveales (25.4\%) reunieron las características necesarias para realizar tratamiento con láser del VNA.

**Palabras clave:** Vasos nutricios, NVC, DMAE.

After signing the informed consent form, all patients took a complete ophthalmologic exploration, including visual acuity with Snellen equivalent (ETDRS and/or Snellen), funduscopy, retinography (CANON CF-60, Canon Inc. USA), fluorescein angiography (AGF) (Canon CF-60 or Heidelberg Retina Tomograph, HRT), and dynamic ICG. The latter was made injecting 2.5 ml of an indocyanine green 10\% solution (ICG-pulsion, Pulsion Medical System) in the cubital vein followed by 5ml of saline solution. Recordings with the HRT were initiated 4 seconds after the injection of the dye and were maintained for 15 seconds. The ICG videoangiography obtained comprised 12 images per second with a resolution of 512 x 512 pixels and a fields of 20º to 30º and photographs at 15, 30, 60 seconds, 5 and 15 minutes from the test. We excluded the cases with poor quality of the angiographic study due to lack of cooperation or blurry medium, as well as the cases with vascularized serous detachment or severe hemorrhage hiding the membrane.

The recordings were assessed by two retinaologists (EGU, FCC) experienced in HRT videoangiography.

The MPS (6) classification was utilized to separate CNS as classical and hidden type 1, with fibrovascular detachment and type 2, with late ooze of the dye due to non-determined causes.

The membranes were subdivided in three groups according to the evolution time (under 6 months, between 6 months and one year, and over one year) and according to size (under 5 mm², between 5 and 15 mm², and over 15 mm²).

We determined the presence or absence of ANV(s), the location with respect to the fovea, the length of the main trunk (considering it from the
beginning of the vessel up to the first bifurcation) and its diameter. The type of ANV was classified according to the neovascular pattern described by Staurenghi (5), in racquet (R) when the main trunk appeared in the plane of the membrane (fig. 1), and in umbrella shape (P) when the ANV began below the CNV (fig. 2), showing the section of the main trunk. The measures were made utilizing the HRT software. The presence of ANV was correlated to the type of neovascular membrane by means of Fisher’s exact test, while the Mann-Whitney test allowed us to analyze the presence or absence of ANV as regards the evolution time, the membrane size and visual acuity. Statistical tests were made with the SPSS (Statistical Package for the Social Sciences, SYSTAT software, version 11 for Macintosh).

RESULTS

Population characteristics

The study included 34 women and 19 men, mean age 72.4, SD 9.8 and a range between 50 and 91 years of age. Forty-seven patients exhibited a unilateral subfoveal CNV membrane while 6 were bilateral. Of the 59 eyes, 54.4% had visual acuity below 0.16, with the mean being 0.21 SD 0.91 in Snellen equivalent. 38.2% of patients had a history of arterial high pressure or cardiovascular disease.

Characteristics of the membranes

The classic form was described in eight cases (13.6%), the mixed form in six (10.1%) and 45 patients (76.3%) exhibited hidden CNV, of which 32 were of type 1 (54.2%) and 13 of type 2 (22%).

The mean size was under 5 mm² in 12 patients (20.4%), 23 had a membrane between 5 and 15 mm² (39%), and a further 24 over 15 mm² (40.6%).

The evolution time was under 6 months in 29 patients (49.1%), between 6 months and one year in 12 cases (20.4%), and over one year in 18 cases (30.5%).

Characteristics of the ANVs

Identification of the ANV with videoangiography was possible in 36 subfoveal CNV membranes (61%). In four cases it was possible to recognize two nutrition vessels, and in one 3 ANV were identified in the same CNV.

A R (racquet) pattern was found in 18 CNV (50%), in one case with two ANV and in another
case with three. In 16 cases (45.5%) an umbrella pattern was described, one of which had two ANV. In two eyes both patterns were identified in the same membrane (5.4%).

The mean length of the main trunk was 127 SD 88 microns, with extreme values of 100 and 290 microns, while the mean diameter was 83.3 SD 43.3 microns with a range between 20 and 150 microns.

The main ANV was extrafoveal (XF) in 12 cases (33.3%), juxtafoveal (JF) in 14 cases (38.9%), and subfoveal (SF) in 10 cases (27.8%). It was most frequently found nasal vis-à-vis the macula, (11 cases), followed by temporal in 6 cases, upper half-field in 4 and lower half-field in 5.

Particularly, the racquet pattern was localized in 11 cases as being XF, in five JF and in four SF. The capacity to detect ANVs with visual acuity is seen in table I, the ARMD type in table II, the lesion size in table III and the evolution time in table IV.

**DISCUSSION**

The studied population exhibits the typical characteristics found in an ARMD population. In addition, the findings of AGF are compatible with the results of a recently published study (7).

The identification of the ANV was heralded in 1991 by the Macular Photocoagulation Study Group (MPS) which recommended focal photocoagulation thereof, if visible, in relapsing retro-foveal of juxtafoveal CNVs (6).

However, the identification of said ANV, in subfoveal CNV, presents important difficulties mainly due to the low visibility of said vessels within the neovascular mesh and because they are visible for a very short period of the angiogram (1-4 seconds). In 1998, due to the high-speed, high resolution angiography by means of confocal scan laser, the first results were published about the identification of

<table>
<thead>
<tr>
<th>Table I. Correlation between the identification of an afferent nutrition vessel (ANV) and visual acuity (VA)</th>
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<tbody>
<tr>
<td><strong>VA</strong></td>
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<tr>
<td>≥ 0.3</td>
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<tr>
<td>&gt; 0.1 and &lt; 0.3</td>
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<tr>
<td>≤ 0.1</td>
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<tr>
<td>total</td>
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Mann-Whitney Test, p=0.861.

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<tr>
<th>Table II. Correlation between the identification of an afferent nutrition vessel (ANV) and the type of neovascular complex (CNV): classic, mixed, hidden with fibrovascular detachment (OC1) and hidden with belated ooze of non-determined origin (OD2)</th>
</tr>
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<tbody>
<tr>
<td><strong>CNV</strong></td>
</tr>
<tr>
<td>Classic</td>
</tr>
<tr>
<td>Mixed</td>
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<tr>
<td>OC1</td>
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<td>OC2</td>
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<td>total</td>
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Fisher’s exact test, p=0.265.

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<tr>
<th>Table III. Correlation between the identification of an afferent nutrition vessel (ANV) and the size of the neovascular complex (CNV)</th>
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<tbody>
<tr>
<td><strong>CNV size</strong></td>
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<tr>
<td>&lt;5 mm²</td>
</tr>
<tr>
<td>&gt;5 and &lt;15 mm²</td>
</tr>
<tr>
<td>&gt;15 mm²</td>
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<tr>
<td>total</td>
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Mann-Whitney Test, p=0.267.

**Table IV. Correlation between the identification of an afferent nutrition vessel (ANV) and the evolution time**

<table>
<thead>
<tr>
<th><strong>Evolution</strong></th>
<th>Without ANV</th>
<th>With ANV</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td>&lt; 6 m</td>
<td>8</td>
<td>21</td>
<td>29</td>
</tr>
<tr>
<td>&gt;6 m and &lt;12 m</td>
<td>6</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>&gt;12 m</td>
<td>9</td>
<td>9</td>
<td>18</td>
</tr>
<tr>
<td>total</td>
<td>23</td>
<td>36</td>
<td>59</td>
</tr>
</tbody>
</table>

Mann-Whitney Test, p=0.09.

ANV and its selective photocoagulation as a treatment for sub-foveal CNV in ARMD (4).

It is surprising to find such a low number of studies and the variability of their data in what concerns the identification of ANVs in ARMD.

In our work, where hidden membranes predominate (45 of 59 eye), the identification of said vessels by means of dynamic ICG with HRT has been achieved in 61% of the 59 eyes with MCNV secondary to ARMD. Said results are in contrast with those supplied by other authors in literature because they are remarkably higher than those found by Shiraga, who was able to identify ANV in 22%, 37 patients out of a population of 170 patients with
subfoveal membrane CNV (27 with classic membrane and 10 hidden) (4). In addition, Piermarocchi obtained very similar results identifying ANV in 35 (22.4%) out of 156 eyes with predominantly classic subfoveal MCNV (8). On the other hand, a pilot study by Staurenghi detected ANV in 19 of 22 classic subfoveal CNV membranes (86%) (5), while Glaser visualized ANV in over 75% of hidden CNVs (data presented in Course 308 of the American Ophthalmology Academy, Dallas, Texas, November 2000). All these data are higher than those of this study.

The explanation for this discrepancy can be due to several facts, firstly to the evolution time (which is not mentioned in other studies). In the patients of our series we have found a tendency to a better visualization of ANVs if the evolution time was under 6 months (p<0.099). With lower evolution times, the neovascular mesh is less dense and therefore it is easier to find the ANV. This has also been described by Piermarocchi who demonstrated how he detected 84.2% of ANVs in 112 eyes after treatment with dynamic phototherapy. This produces a rarefaction of the coriocapillary, as demonstrated by Flower (9), associated to a localized reduction of vascular flow, producing a reduction of the angiographic noise inside and around the coroidal membrane, thus facilitating the identification of said vessels.

Secondly, said differences can be due to the type of membrane (classic or hidden). Even though statistically significant differences have not been found, the visualization of said vessels is somewhat higher in classic membranes (10 cases out of 14 patients) and in hidden membranes with fibrovascular detachment (19 of 32 cases).

Finally, the higher prevalence of detection in our work with regard to that found by Shiraga or Piermarocchi can also be explained by a possible slant in the diagnostic criteria for the ANV. Said authors have only assessed vessels with the main trunk in the same plane of the neovascular complex. If we restrict the search to the racquet pattern (which is more likely to be photoagulated), in our results the existence of ANVs is reduced to 30% of patients.

The detection of ANV is not enough; it must be photoagulated and therefore being placed preferably extrafoveal or at least juxtafoveal, over 300 microns from the fovea. Thus, the cases selected for treatment in our group were reduced to 16 patients (25.4%). In the reduced group of five patients we utilized the Staurenghi criteria, who considered cases for treatment those with ANV diameters under 85 microns, i.e., five(8.4%). It is not surprising that four of these patients had an evolution under 6 months.

The following factors did not prove either a statistically significant association with the presence of ANV: patient age, visual acuity or size of the lesion.

From the results of this study it can be concluded that ANV was identified in 61% of a population with clearly or vaguely limited CNVs, and in 24.5% of cases said vessel was extra- or juxtafoveal and therefore susceptible to treatment with laser.

REFERENCES