FLUORESCEIN ANGIOGRAPHY IN AGE RELATED MACULAR DEGENERATION

[1]L. LEVAI, [2]GENOVEVA OLARU

[1,2]"Constantin Papilian" Military Hospital, Cluj-Napoca

Abstract: *Age Related Macular Degeneration is a degenerative condition of the macula and is increasingly pervasive in our country, encountered unfortunately in patients even younger than 55. The current work is trying to present the importance of fluorescein angiography in this disease.*

Keywords: *fluorescein angiography, fluorescence, age related macular degeneration*

Rezumat: *Degenerescenţa maculară senilă este o afecţiune maculară tot mai răspândită la noi în ţară care, din păcate, este întâlnită la persoane tot mai tinere, cu vârste chiar sub 55 de ani. Lucrarea de faţă îşi propune o prezentare a utilităţii angiofluorografiei în această afecţiune.*

Cuvinte cheie: *angiofluorografie, fluorescenţă, degenerescenţa maculară senilă*

INTRODUCTION

Since 1874, when it was first described in the medical literature as "symmetrical central choroido-retinal disease occurring in senile persons," age-related macular degeneration (ARMD) has also been referred to as senile, or diskiform, macular degeneration, among many other terms.(1) In fact ARMD presents a multifactorial pathology of the macula that includes most of all, age,(2) smoking,(3) hypertension,(4) and family history of the disease.(5) Other potential risk factors include cardiovascular disease,(6) sunlight exposure,(2,7) diets low in lutein, zeaxanthin and other dietary antioxidants or diets high in fats.(8,14) Inflammation has also received attention as a potential risk factor for this disease.(15)

There are two main clinical forms of the disease: the dry form, which represents 80% of cases and the wet or exudative form, with more serious consequences, which represents 20% of cases.(16)

Fluorescein angiography (FA) dates to the early 1960s and provides a valuable tool in the diagnostics of retinal vascular disease, being a safe procedure and is easily performed in the confines of a physician's office,(16) being indispensable in the diagnostics and establishment of the clinical form of ARMD.

Sodium fluorescein (SF) is used for this investigation. After intravenous (IV) injection of SF, it reaches the choroidian circulation, where, following excitation with blue light, it emits green light (fluorescence), which passes through a filter and then is photographed. Zeiss Visucam is one of the most popular FA devices which use digital photography. Zeiss Visucam is equipped with:

- a continuous light source for fundus visualization;
- another powerful light source for SF excitation;
- filters: blue excitation filter, barrier filter located in front of the digital camera, red free filter;
- digital camera.

Fluorescence is the ability of a substance to emit light of a longer wavelength when continuously excited by light of a shorter wavelength. The properties of excitation occur when SF is exposed to and absorbs wavelength of approximately 465 to 490 nm (short blue wavelength). The molecular structure of SF becomes altered and emits a new wavelength (fluoresces) of 520-630 nm (greenish-yellow). Additionally, fluorescence depends on blood pH value, an optimum fluorescence occurs with a blood pH of 7.4. After SF injection the retinal and large choroidal vessels do not normally leak fluorescein because of the tight junctions between the endothelial cells. After SF binds with albumin in serum protein it is eliminated from the kidneys in approximately 24-48 hours. The most noticeable effects are coloration of the skin and urine for 12-24 hours after injection.

Adverse effects are usually mild: nausea, vomiting, sneezing, pruritus, most frequent being nausea. Sometimes trombophlebitis, pyrexia, skin eruption and nerve palsy may occur. The rarest and most serious complications include: cardiovascular, respiratory and neurological complications.

As a working technique one can follow the next protocol:

- Before SF injection a red free photo is taken of each fundus, thus providing an excellent high contrast picture of the retina to compare against the later fluorescein structures.
- Green filter is deactivated while the blue and the barrier filters are activated and again each fundus is photographed, thus pseudofluorescence and autofluorescence are assessed. Pseudofluorescence is caused by a poorly matched filter combination or older filters that have started to deteriorate. Sclera and scar tissue may demonstrate this defect. Autofluorescence is caused by structures in the retina

(optic nerve drusen, astrocytic hamartomas) that emit fluorescent light when excited by the blue excitation light.

- 5cc of 10% SF is injected in a rapid bolus, to ensure an overall good contrast of the retinal structures.
- After approximately 7 seconds the photographic sequence should begin at the rate of one picture every 2 seconds until dye is seen in the early choroidal phase, then photography should be accelerated to one frame per second. Choroidal phase is extremely brief, lasting only 2-3 seconds.
- The primary area of interest should be documented through the arterial-venous phase before a switch to the opposite eye, in the first 20-30 seconds.
- Late photographs are taken depending on the suspected pathology after 5, 10, 15, or 20 minutes.(16)

A normal fluorescein angiography is made up the following phases :(17)

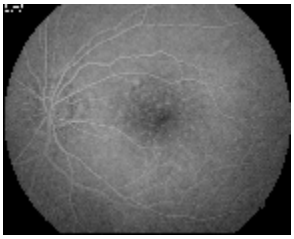
- Choroidal
- Arterial
- Early arterio-venous
- Arterio-venous
- Recirculation
- Late

Fluorescein angiography aspects in ARMD

In the dry form we encounter:

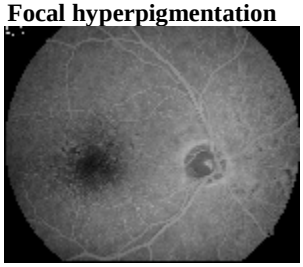
- Drusen Hard drusen: this generally show up as window defects in the region of the drusen in the early phase due to atrophy of the overlying retinal pigment epithelium (RPE), (picture no. 1) The fluorescence fades in the late phase of the angiogram. Soft drusen: the fluorescein ngiographic pattern in soft drusen varies depending on their content. In general they hyperfluorescence later and either fade or stain in the late phase of the angiogram.(17)

Picture no. 1. Hard drusen

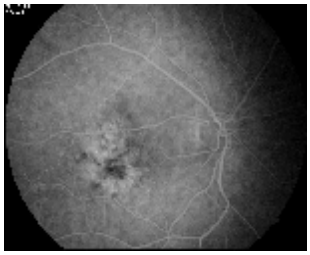


- Focal hyperpigmentation*:* These areas of focal pigment block the background choroidal fluorescence, (picture no. 2).
- Diffuse stippled hyperfluorescence is noted in the region of pigment mottling at the posterior pole (picture no. 3). A pattern of reticular or punctate blockage is seen corresponding to areas of pigment clumps.(17)
- Early hyperfluorescence is noted within the areas of geographic atrophy due to the window defect in the RPE (picture no. 4). The choriocapillaries fill slowly within the lesion. However the choriocapillaries may be entirely absent and filling of the larger choroidal vessels may be easily visualized. The extent of the lesion does not change in the late phases. In the latephase angiogram, hyperfluorescence due to staining of the choroidal tissue and the sclera is seen in the region of the geographic atrophy.(17)

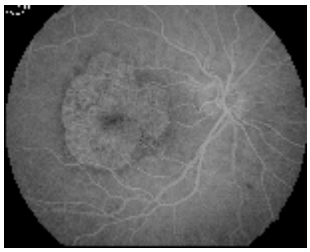
Picture no. 2. Focal hyperpigmentation



Picture no. 3. Nongeographic atrophy of retinal pigment epithelium



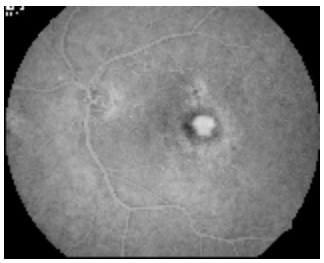
Picture no. 4. Geographic atrophy of the retinal pigment epithelium



In the wet form we encounter:

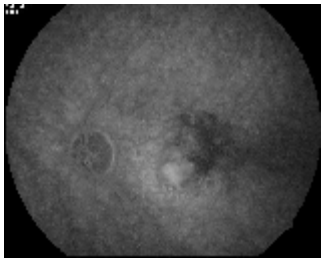
- Classic choroidal neovascular membrane *(*CNVM) (picture no. 5) shows up in the early phase as a bright, well demarcated area of hyperfluorescence which increases in intensity and extent in the mid and late films due to progressive leakage of the dye which obscures the boundaries of the CNVM.

Picture no. 5. Classic choroidal neovascular membrane



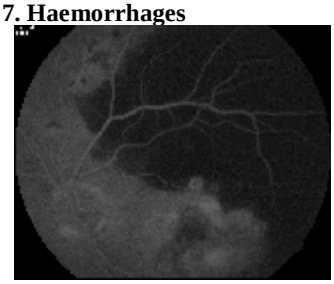
- Occult CNVM on angiography reveals an area of diffuse ooze but no lacy pattern of a classic CNVM. Leakage and punctuate staining may be seen in the late views (picture no. 6)

Picture no. 6. Occult CNVM



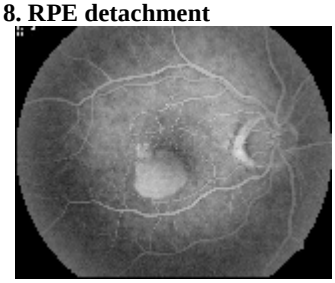
- Hemorrhages: Subretinal haemorrhages block the underlying choroidal fluorescence, being hypofluorescent; retinal vessels are seen above them (picture no. 7)

Picture no. 7. Haemorrhages



- RPE detachment: Fluorescein angiography reveals a hyperfluorescent area with rapid and uniform filling (picture no. 8).

Picture no. 8. RPE detachment



CONCLUSION

Fluorescein angiography is a very efficient tool in the diagnosis and monitoring of patients with ARMD providing valuable data upon the post treatment evolution of the patients. The most important advantage of this technique is the line it draws between the dry and the wet form, bringing major contribution in correct decision of treatment. The iconography is part of the research study, performed by the author, who assesses the epidemiologic factors of ARMD and the above described working technique was respected during FA.

REFERENCES

1. Paulus T, de Jong, Age-Related Macular Degeneration, The New England Journal of Medicine 2006 Oct 5;355(14):1474-1485.
2. Klein R, Peto T, Bird A, Vannewkirk M. The epidemiology of age-related macular degeneration. Am J Ophthalmol. 2004;137:486-495.
3. Mitchell P, Wang J, Smith W, Leeder S. Smoking and the 5-year incidence of age-related maculopathy: the Blue Mountains Eye Study. Arch Ophthalmol. 2002;120:1357-1363.
4. Klein R, Peto T, Bird A, Vannewkirk MR. The epidemiology of age-related macular degeneration. Am J Ophthalmol. 2004;137:486-495.
5. Klein M, Mauldin W, Stoumbos V. Heredity and age-related macular degeneration: observations in monozygotic twins. Arch Ophthalmol. 1994;112:932-937.
6. Vingerling J, Dielemans I, Bots M, Hofman A, Grobbee D, de Jong P. Age-related macular degeneration is associated with atherosclerosis: the Rotterdam Study. Am J Epidemiol. 1995;142:404-409.
7. Taylor H, West S, Munoz B, Rosenthal F, Bressler S, Bressler N. The long-term effects of visible light on the eye. Arch Ophthalmol. 1992;110:99-104.
8. Mares J. Carotenoids and eye disease: epidemiologic evidence. In: Krinsky NI, Mayne S, eds. Carotenoids in Health and Disease. New York, NY: Marcel Dekker Inc; 2003:19.
9. Mares-Perlman J, Millen A, Ficek T, Hankinson SE. The body of evidence to support a protective role for lutein and zeaxanthin in delaying chronic disease. J Nutr. 2002;132:518S-524S.
10. van Leeuwen R, Boekhoorn S, Vingerling J et al. Dietary intake of antioxidants and risk of age-related macular degeneration. JAMA. 2005;294:3101-3107.
11. Mares-Perlman J, Brady W, Klein R, VandenLangenberg G, Klein B, Palta M. Dietary fat and age-related maculopathy. Arch Ophthalmol. 1995;113:743-748.
12. Smith W, Mitchell P, Leeder S. Dietary fat and fish intake and age-related maculopathy. Arch Ophthalmol. 2000;118:401-404.
13. Seddon JM, Cote J, Rosner B. Progression of age-related macular degeneration: association with dietary fat, transunsaturated fat, nuts, and fish intake. Arch Ophthalmol. 2003;121:1728-1737.
14. Seddon J, Rosner B, Sperduto R et al. Dietary fat and risk for advanced age-related macular degeneration. Arch Ophthalmol. 2001;119:1191-1199.
15. Wirostko E, Wirostko W, Wirostko B. Age-related macular degeneration is an inflammatory disease possibly treatable with minocycline. Acta Ophthalmol Scand. 2004;82:243-244.
16. Hampton G, Nelsen T. Age Related Macular Degeneration Principles and Practice. Raven Press, New York 1992;3:101-135.
17. Shetty N, Sharma T, Shanmugam M, Bhende M, Gopal L, Samant P, Gopal L. Atlas of Fundus Fluorescein Angiography. Japee Brothers, New Delhi 2004:4-7,69,79.