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Zwyrodnienie plamki związane z wiekiem (AMD) – epidemiologia XXI wieku

Streszczenie

Wprowadzenie. Zwyrodnienie plamki związane z wiekiem (AMD) jest najczęstszą przyczyną ślepoty u ludzi po 50-tym roku życia w krajach rozwiniętych. Pomimo intensywnych prac na patogenezę, przebiegiem i leczeniem tej choroby wciąż pozostaje wiele niewiadomych.

Cel. Ocena epidemiologiczna występowania zwyrodnienia plamki związanego z wiekiem (AMD) w południowo-wschodniej Polsce, ze szczególnym uwzględnieniem integralności warstwy nabłonka barwnikowego siatkówki i fotoreceptorów w poszczególnych stadiach AMD na podstawie otrzymanych obrazów autofluorescencji dna oka.

Materiał i metody. Badaniami objęto 200 chorych (322 oczy) skierowanych do Kliniki Okulistyki w Lublinie z różnymi formami AMD. Średni wiek chorych wynosił 70 lat (od 49 do 91 lat). Chorzy badani byli co 6 miesięcy przy użyciu konfokalnego skaningowego oftalmoskopu laserowego (Heidelberg Retina Angiograph 2- HRA2) oraz mieli wykonane pełne badanie okulistyczne. Okres obserwacji wynosił od 1 do 40 miesięcy (średnio 18 miesięcy).

Wyniki. W 116 oczach (84%) z wczesnym stadium AMD stwierdzono punktowe zmiany w obrazie autofluorescencji dna oka a w 22 oczach (16%) nie stwierdzono istotnych zmian. W 52 oczach (62%) z wysiękową formą AMD występował normalny lub zbliżony do normy sygnał autofluorescencji, a w 34 oczach (38%) w miejscu błony sygnał autofluorescencji był zmieniony. Wszystkie oczy z blizną tarczową charakteryzował nierównomierny spadek autofluorescencji w miejscu blizny oraz wzrost autofluorescencji w obszarze otaczającym. Oczy z zanikiem geograficznym cechował brak sygnału autofluorescencji w miejscu zaniku nabłonka barwnikowego a w 40 przypadkach (95%) w obszarze przylegającym do zaniku stwierdzono wzmożony sygnał autofluorescencji.

Wnioski. Częstsze rozpoznanie zwyrodnienia plamki związanego z wiekiem u chorych zamieszkałych w obszarze miejskim, może wynikać ze znacznie większej dostępności lekarza okulisty w terenach miejskich w porównaniu z wiejskimi. Występowanie poszczególnych form zwyrodnienia plamki związanego z wiekiem nie odbiega od danych zawartych w literaturze. Obrazy autofluorescencji dna oka chorych z AMD wykazują dużą różnorodność, mogą być pomocne w monitorowaniu przebiegu AMD

Słowa kluczowe: zwyrodnienie plamki związane z wiekiem (AMD), autofluorescencja dna oka, konfokalny skaningowy oftalmoskop laserowy.

Age-related macular degeneration (AMD) – epidemiology of the 21st century

Abstract

Introduction. Age-related macular degeneration (AMD) is the leading cause of legal blindness in the industrialized world over the age of 50. Despite intensive efforts to understand AMD pathogenesis, the course and treatment options for this disease remain basically unknown.

Aim. The aim of the study is the epidemiological evaluation of age-related macular degeneration (AMD) occurrence in south-east Poland with particular consideration of retinal pigment epithelium layer and photoreceptors integrity in various AMD stages according to the obtained fundus autofluorescence images of the eye.

Material and methods. Two hundred patients (322 eyes) with different forms of AMD sent to the Ophthalmology Clinic in Lublin were included in the study. Mean age was 70 years (49-91 years). Apart from the complete ophthalmological examination the patients were examined every 6 months by using a confocal scanning ophthalmoscope (Heidelberg Retina Angiograph 2- HRA2). The follow-up period was from one to 40 months (mean – 18 months).

Results. In 116 eyes with early AMD punctuate changes in autofluorescence images and in 22 eyes (16%) no distinct changes were observed. In 52 eyes (62%) with wet AMD, normal or near normal autofluorescence signal was present and the rest – 34 eyes (38%) had changes in the autofluorescence signal corresponding with the CNV area. All the eyes with disciform scar were characterized by uneven autofluorescence signal decrease in the scar area with an increased signal in the surrounding area. Eyes with geographic atrophy (GA) lacked the autofluorescence signal corresponding to RPE atrophy and in 40 cases (95%) increase autofluorescence signal junctional to GA was noted.

Conclusion. The fact that AMD is more often diagnosed among city inhabitants comparing to inhabitants of rural regions may be due to better accessibility of ophthalmologists in urban than in agricultural areas. The presence of respective AMD forms in our study does not differ from those in the literature. Fundus autofluorescence images of the AMD eyes vary greatly and may be helpful in monitoring the course of AMD.

Key words: age-related macular degeneration (AMD), fundus autofluorescence, confocal scanning laser ophthalmoscope.

Age-related macular degeneration (AMD) is a disease causing constant changes in the choroid and retina which leads to an irreversible complete or partial loss of vision. It can occur in two forms. The “dry” form is mild with slow progression (85-90% of patients) characterized by the presence of drusen and in an advanced stage – geographic atrophy with the destruction of the pigmented epithelium and photoreceptors. The other – “wet” form (10-15%) often develops very fast and is characterized by the choroidal neovascularization (CNV) occurrence. AMD affects people over the age of 45-50, when the incidence is about 8%. It will become increasingly prevalent along with aging and in the population of 80-year-olds, it is about 40%. In Poland the estimated number of patients is from about 1.2 to 1.5 million people, in 10-15% of which a more destructive – “wet” form is observed. The essential role in the diagnosis and monitoring of the course of the age-related macular degeneration plays the so-called fundus autofluorescence. Recent studies indicate that the autofluorescence phenomenon comes from the retinal pigment epithelium (RPE) level and results from excessive lipofuscin accumulation in these cells [1-7].

Topographic fundus autofluorescence detection in vivo is possible using a confocal scanning laser ophthalmoscope. The published studies show that early and late stages of AMD are attributable to differences in the autofluorescence signal distribution as well as to a distinct fundus autofluorescence pattern in some cases [8-11].

Several findings suggest that increased fundus autofluorescence corresponds to a higher risk of advanced AMD stages development. Therefore, detection of changes in fundus autofluorescence probably may allow the identification of eyes with a high risk of AMD different form development such as geographic atrophy of the retinal pigment epithelium (GA) or the choroidal neovascularisation (CNV).

AIM

The purpose of our study was epidemiologic evaluation of age-related macular degeneration (AMD) occurrence in south-east Poland with particular consideration to the retinal pigment epithelium layer and photoreceptors integrity in various AMD stages according to obtained visual acuity.

MATERIALS AND METHODS

Two hundred patients (322 eyes) with different diagnosed forms of AMD sent to the Ophthalmology Clinic in Lublin during the years 2006 – 2009 were included in the study. An additional qualifying criterion was the clarity of optical media allowing obtaining a good quality fundus autofluorescence image. This group consisted of 104 women (52%) and 96 men (48%). The mean age was 70 years (49-91 years). Patients were examined according to the standard protocol using the same confocal scanning ophthalmoscope (Heidelberg Retina Angiograph 2-HRA2) and underwent a complete ophthalmologic examination. Patients were examined every 6 months or more often, if needed. The follow-up period was from 1 to 40 months (mean – 18 months).

Regarding the clinical data, the examined eyes were classified into three groups. In the first group eyes with early signs of AMD (soft drusen accompanied, or not, by RPE changes) were qualified and this group consisted of 138 eyes (43%). The second group contained 84 eyes (26%) with the choroid neovascularisation. The third group consisted of eyes with advanced stages of AMD. In this group, 42 eyes (13%) with geographic and 58 (18%) disciform scar were noted.

After a preliminary examination consisting of anamnesis, detailed ophthalmologic examination and a fundus autofluorescence examination, patients had follow-up visits every 6 months. Some patients also had fluorescein angiography and optical coherent tomography (OCT) examination performed. During control visits best corrected visual acuity, fundus examination, fundus photography, fundus autofluorescence and fluorescein angiography examination in cases of exudative changes presence or suspicion were performed.

RESULTS

Among the patients from the study group, 153 (76.5%) patients were inhabitants of cities (Lublin – 76, other cities from the Lublin region – 46, cities outside the Lublin region – 31) and the rest of them – 47 (23.5%) patients inhabited rural territories. In 138 eyes (43%) the early stage of AMD was detected and in 84 eyes (26%) there were typical signs of the exudative AMD form with the subretinal neovascular membrane. The rest of the eyes presented the advanced stage of AMD, among them 42 eyes (13%) with geographic atrophy and 58 (18%) with disciform scar. In 116 eyes (84%) with early AMD punctuate changes of decreased or increased signal in autofluorescence images and in 22 eyes (16%) no distinct changes were observed.

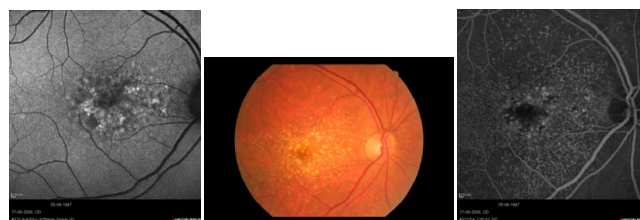


FIGURE 1. A. Fundus autofluorescence image with focal signal changes in early AMD. B. Fundus photography. C. Fluorescein angiography.

In 10 eyes (8.6%) with detected autofluorescence changes, progression towards exudative AMD form was noted and in 2 (1.7%) geographic atrophy developed.

In 52 eyes (62%) with “wet” AMD, normal or near normal autofluorescence signal was present and the rest 34 eyes (38%) had changes in the autofluorescence signal (decreased or increased signal) corresponding with the CNV area. In 85% eyes (29) with signal changes in the membrane region visual acuity was <0.4. On the other hand, in 90% (47) eyes with no autofluorescence change over membrane had visual acuity >0.4.

Additionally, in 60 eyes (71%) the CNV region was surrounded by an increased autofluorescence signal area considerably exceeding hyperfluorescence quantity present on the fluorescein angiography.



FIGURE 2. A. Fundus autofluorescence image with decreased signal in neovascular area surrounded by increased signal in exudative AMD. **B.** Fundus photography. **C.** Fluorescein angiography.

All eyes with disciform scar were characterized by uneven autofluorescence signal decrease in the scar area with an increased signal in the surrounding area.

Observation and digital analysis of fundus autofluorescence images of the eyes with geographic atrophy affirmed a relatively even lack of autofluorescence signal in the pigmented epithelium atrophy area and showed mean growth of this area of 0.75mm² /6 months. In this group in 40 cases (95%) an increased autofluorescence signal junctional to GA was noted.

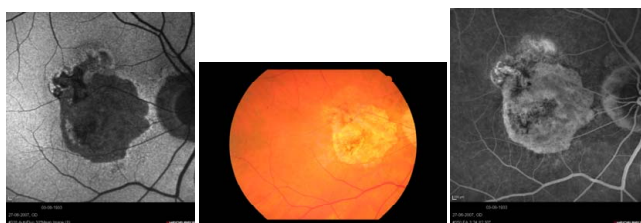


FIGURE 3. A. Fundus autofluorescence image with decreased signal in geographic atrophy area surrounded by increased signal of the junctional zone in atrophic AMD. **B.** Fundus photography.

DISCUSSION

Nowadays, the number of AMD patients amounts to 30-40 million people globally, and the statistical data indicate constant increase of morbidity. AMD is associated, among others, with an increase of mean life span [1,2]. Therefore it appears that the term “epidemiology of the 21st century” is fully justified. Our study comprised the population from east-south Poland, mainly the Lublin region. As regards the number of the patients examined, it is the biggest AMD study in the Polish literature up to now. More than ¾ of the examined group comprised of urban inhabitants. Probably it does not mean that the same proportion is for the whole population. It may be due to better accessibility to ophthalmologist in the city area in comparison with rural areas and as a result- more patients referred to the clinic from the urban region. Some influence may be presented by the level of awareness among urban inhabitants, but such hypothesis is hard to prove. Proportion of different AMD forms presented in our study is in accordance with the literature data [12,13].

Fundus autofluorescence is a very important parameter in diagnosing and observing natural history of AMD. Fundus autofluorescence imaging is a noninvasive and quick examination giving additional information as compared with conventional imaging techniques. The information concerns lipofuscin topographic distribution in the retinal pigment epithelium layer. It is known that excessive lipofuscin granules accumulation in the RPE liposomal compartment leads

to one of the stages of pathogenesis of AMD and of other retinal diseases.

Heterogenic fundus autofluorescence in subsequent AMD forms probably represents various metabolic stages of the retinal pigment epithelium status. During early AMD, patients observation using fundus autofluorescence imaging were divided into a subgroup with punctate signal changes and without changes. Previous studies showed that locally increased or decreased autofluorescence signal correlates in all AMD forms with visible microperimetry disturbances and coincides with retinal sensitivity deterioration in these spots [14].

From the very beginning of autofluorescence studies it is known that lack of or decreased autofluorescence signal is correlated with retinal pigment cells and photoreceptor destruction. As other studies revealed it, using this technique may be helpful in prognosing and monitoring anti-vascular drugs (anti-VEGF) therapies. It is ascertained that eyes with CNV, in which increased autofluorescence signal over membrane area was present, had worse visual acuity after treatment [15]. It is partially in accordance with our observations indicating that in the group with decreased or increased autofluorescence signal over the CNV area visual acuity was worse comparing eyes with normal autofluorescence signal over the CNV area. Despite many intensive efforts in many clinical centers, pathogenesis of AMD still remains unclear. Most probably, there exists a complex, multifactor mechanism initiating disease and its progression. The study we conducted contributes to research concerning this problem in the Polish population. Especially substantial it is to explore the phenomenon of fundus autofluorescence since our results distinctly suggest that any interventional studies with pharmacologic treatment, that may inhibit disease progression to the level of useful visual acuity before irreversible blindness stage, should make use of the information contained in the fundus autofluorescence imaging.

CONCLUSIONS

The fact that AMD is more often diagnosed in urban inhabitants comparing to inhabitants of rural regions in the group that we analyzed may be due to better ophthalmologist accessibility in urban than in agricultural areas and is proportionally visible in the number of patients referring to our clinic. The presence of respective AMD forms in our study does not differ from these in the literature. Early AMD stages may be or not accompanied by different local fundus autofluorescence signal changes. The presence of these changes correlates with deterioration of visual acuity. Similar correlation in eyes with exudative AMD was observed. In eyes with central decrease of autofluorescence signal worse visual acuity was noted.

All eyes with advanced AMD stages had distinct autofluorescence signal decrease in the lesion area. Eyes with geographic atrophy were characterized by even signal decrease in contrary to eyes with exudative AMD having irregular decrease of autofluorescence signal. Bigger or smaller increase of signal surrounding lesions was a common feature.

The presented fundus imaging technique distinctly and relatively early displays retinal pigment epithelium atrophy,

which means photoreceptor deterioration in this area. This method also detects areas of metabolic inefficient epithelium, in which atrophic changes will soon occur.

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