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Risk Characteristics of the Combined Geographic Atrophy and Choroidal Neovascularisation Phenotype in Age-Related Macular Degeneration

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Abstract

Aim—To investigate the risk characteristics of the combined geographic atrophy (GA) and choroidal neovascularization (CNV) phenotype of age-related macular degeneration (AMD) compared to GA or CNV.

Methods—Patients with advanced AMD were identified and divided into three groups using multimodal imaging: patients with GA in at least one eye, patients with CNV in at least one eye, and patients with simultaneous GA and CNV in at least one eye. Epidemiologic and clinical factors were gathered from patient questionnaires. Genotypes for age-related maculopathy susceptibility 2 (*ARMS2*) and complement factor H (*CFH*) were determined.

Results—42 patients with GA or CNV and 16 patients with combined GA/CNV were identified. Patients with the combined phenotype were older (86.4 vs. 81.8 years, $p=0.049$) and had a higher prevalence of advanced AMD in the fellow eye (81.3% vs. 31.0%, $p<0.001$). *CFH* and *ARMS2* risk alleles were not associated with the combined phenotype.

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Conclusion—The combined GA/CNV phenotype has similar epidemiologic, clinical, and genetic features as GA and CNV but occurs at an older age and is more associated with advanced AMD in the fellow eye, suggesting that all these phenotypes are part of the same spectrum of disease and that the combined phenotype represents an even more advanced form of AMD than either GA or CNV.

Keywords

age-related macular degeneration; geographic atrophy; choroidal neovascularisation

INTRODUCTION

Age-related macular degeneration (AMD) is the leading cause of blindness worldwide, affecting 30–50 million people. A recent report from the World Health Organization global eye disease survey estimated that 14 million people are blind or severely visually impaired due to AMD.[1] The disease is chronic and progressive and is characterized by death of the photoreceptors and eventually the underlying retinal pigment epithelium (RPE). The late stage of AMD is divided into two types. The first, called “dry” AMD or geographic atrophy (GA), refers to the death of the RPE and photoreceptors and is characterized by a defined area of RPE degeneration in which choroidal blood vessels are visible.[2] The second, called “wet” AMD or choroidal neovascularization (CNV), refers to the proliferation of new vessels either under the RPE, breaking through the RPE, or within the retina, leading to death of the photoreceptors from exudative damage.[2] CNV accounts for approximately 60–65% of all advanced AMD cases, and GA accounts for the other 35–40%.[3, 4]

Although GA and CNV are generally considered to be phenotypically different entities, they have a similar risk profile with regard to the environmental, clinical, and genetic factors related to late AMD. Older age, cigarette smoking, low intake of antioxidants, elevated body mass index, family history of AMD, hypertension, large soft drusen, and reticular lesions are associated with both forms of advanced AMD.[5–11] More recently, genetic variants have also been shown to be associated with advanced AMD, especially variants in the age-related maculopathy susceptibility 2 (*ARMS2*) and complement factor H (*CFH*) genes; the *CFH* Y402H variant was associated with both forms of late AMD in some reports,[12,13] whereas other studies found the *ARMS2* A69S variant to be a risk factor for late AMD.[11,14] However, the treatment for each form is quite different. Nutritional supplements are the only available treatment that might marginally delay the onset or progression of GA,[15, 16] which normally causes irreversible gradual vision loss. In contrast, when an eye develops CNV, there is usually an abrupt drop in visual acuity, but anti-vascular endothelial growth factor (anti-VEGF) agents can be effective in active CNV and as a maintenance therapy.[17]

GA and CNV can occur simultaneously in the same eye. The Age-Related Eye Disease Study found that 0.4% of 3,212 eyes developed both GA and CNV after 5 years of follow-up.[18] Furthermore, histopathological studies have shown the coexistence of GA and CNV in eyes where it may not have been evident clinically.[19, 20] Few studies have focused on the simultaneous occurrence of GA and CNV in the same eye. Sunness et al. reported that an

eye with GA whose fellow eye has CNV is at significant risk for the development of CNV, with 2-year and 4-year incidences of 18% and 34%, respectively.[21] Other studies found the 5-year incidence of developing CNV in an eye with GA to be 45–49%.[22, 23] Nevertheless, little is yet known about this combined GA/CNV subtype of AMD and its risk factors.

The purpose of the present study is to determine whether there are any correlations between specific epidemiologic, clinical, and genetic factors and the combined GA/CNV form of advanced AMD. Knowing the risk characteristics of this entity might help to predict its occurrence, encourage frequent follow up, and help in its early management.

MATERIALS AND METHODS

Population

Our research group had conducted a prospective imaging and genetics study of AMD which included 93 consecutive patients in a retinal specialist's practice (KBF) and was approved by the Institutional Review Board of New York University Langone Medical Center. Informed consent had been obtained from all individuals for participation in the study and for review of the study data for publication. For the current study, 58 patients diagnosed with advanced AMD in at least one eye were identified from the original study and divided into three groups based on colour photographs, spectral domain optical coherence tomography (SD-OCT), infrared (IR) imaging, fluorescein angiography (FA), and/or indocyanine green angiography (ICG) (Figure 1): patients with GA in at least one eye (no CNV in either eye), patients with CNV in at least one eye (no GA in either eye), and patients with simultaneous GA and CNV in at least one eye (GA, CNV or early AMD in the fellow eye). Exclusion factors included presence of CNV in one eye and GA in the fellow eye, diabetic retinopathy, pathological myopia, idiopathic CNV, angioid streaks, central serous chorioretinopathy, and other macular dystrophies. GA was defined as the presence of round or oval areas of RPE atrophy that exceeded one-third of a disc diameter in size and through which large choroidal vessels were visible in colour and IR images. The diagnosis of CNV was based on the presence of either CNV or its components (such as intraretinal fluid, subretinal fluid, serous pigment epithelial detachment, or hemorrhage) on FA, ICG, and/or SD-OCT. The diagnosis of classic multilobular GA in eyes with CNV was based on multimodal imaging in order to differentiate GA from other CNV sequelae, such as fibrotic tissue and scarring, or atrophy resulting from treatment. An eye was diagnosed with early AMD if it had no signs of advanced AMD and at least one large soft drusen ($>125\text{ }\mu\text{m}$) or more than five intermediate drusen ($63\text{--}125\text{ }\mu\text{m}$). Reticular pseudodrusen were defined as a yellowish interlacing pattern of $125\text{ }\mu\text{m}$ to $250\text{ }\mu\text{m}$ wide in colour photographs or as hyperreflective deposits above the RPE in SD-OCT. The study eye was considered to be the eye with advanced AMD and was designated arbitrarily when both eyes had advanced AMD (bilateral GA, bilateral CNV or bilateral GA and CNV).

In the original study, patients had been given a detailed questionnaire regarding their cardiovascular, medical, and family history. In addition, genetic information had been obtained from all patients. DNA was originally isolated from peripheral blood leukocytes using a DNA blood kit and screened for haplotype-tagging single-nucleotide polymorphisms

in the *CFH* (Y402H, rs1061170) and *ARMS2* (A69S, rs10490924) genes. Genotyping was performed by polymerase chain reaction-restriction fragment length polymorphism analysis using a genotype assay (TaqMan, Life Technologies, Norwalk, CT, United States) and 4.50 ng of DNA. The thermal cycling conditions consisted of an initial hold at 95° C for 10 minutes, followed by 40 cycles of a 15-s 92° C denaturation step and a 1-minute 60° C annealing and extension step. Plates were read in a sequence-detection system (Applied Biosystems ViiA7 RUO Software, Life Technologies, Norwalk, CT, United States).

For the current study, epidemiologic and clinical information (gender, age, smoking history, diagnosis of hypertension, diagnosis of diabetes, diagnosis of dyslipidemia, and family members diagnosed with AMD) was gathered by reviewing patients' questionnaires. Previously obtained genotypic data for the *CFH* and *ARMS2* genes were collected for the current analysis.

Statistical Methods

Risk allele and genotype frequencies were calculated. χ^2 tests and two-tailed Fisher's exact tests were used to compare the prevalence of the different categorical variables (e.g., gender, presence of dyslipidemia, presence of hypertension, etc.) between the study groups, and student's t-test was used to analyze differences between two means of continuous variables (e.g., the patients' ages between the two study groups). Binary logistic regression was used to analyze the association between epidemiologic and clinical factors and the combined GA/CNV form. Statistical analyses were performed with Excel 2007 software (Microsoft, Inc., Redmond, WA, United States), QI Macros 2013 (KnowWare International, Inc., Denver, CO, United States), and XLSTAT 2013.4 (Addinsoft, New York, NY, United States). For all tests, a *p*-value less than 0.05 was considered statistically significant.

RESULTS

Fifty-seven of 58 patients included in this study identified themselves as Caucasian, and one person was of Hispanic origin. The mean age was 83 ± 2.1 years (range 61–98 years), and the median age was 88 years. 65.5% were female. Demographic, epidemiologic, clinical, and genetic characteristics were not statistically different between patients with GA and those with CNV. Thus, the first two groups (patients with GA and patients with CNV) were combined into a newly defined Group 1 (*n*=42). The patients with the combined GA/CNV phenotype formed Group 2 (*n*=16).

Epidemiologic and Clinical Factors

There was a statistically significant difference in age (*p* = 0.049), but not in gender or length of onset of late AMD, between the two groups. The groups' characteristics are listed in Table 1. Environmental factors (hypertension, diabetes, dyslipidemia, smoking status, and family history of AMD) were not significantly different between the groups. The number of intravitreal injections of anti-VEGF was not statistically different between both groups. Reticular lesion prevalence was not statistically different between the groups, though its frequency was higher in Group 2 (the combined GA/CNV group). With regard to the status of the fellow eye, advanced AMD was significantly more frequently diagnosed in Group 2

than in Group 1 (the GA or CNV group). In a binary logistic regression model, the status of the fellow eye remained significantly different between the groups (95% confidence interval (CI): 1.613–38.357, $p = 0.011$), whereas age did not remain significant (95% CI: 0.977–1.239, $p = 0.116$).

Genetic Factors

Table 2 shows the genotype and allele frequencies among Groups 1 and 2. The frequencies of the risk allele (C) for *CFH* and the risk allele (T) for *ARMS2* were not significantly different between the two groups. Genotypic frequencies for each gene were not statistically different between the groups. The frequency of having at least one risk allele for each gene was not significantly different between the groups (66.7% vs 56.3%, $p = 0.46$).

DISCUSSION

This study investigated the epidemiologic, clinical, and genetic characteristics of the combined GA/CNV form of advanced AMD in individual patients. There was no statistically significant difference between a group of patients with this form of advanced AMD and a group with other subtypes of advanced AMD (GA or CNV) with regard to epidemiologic and clinical factors, with the exception of age and status of the fellow eye. The mean age was statistically different between the groups; patients with the combined GA/CNV phenotype were older. However, older age was not associated with this phenotype using binary logistic regression. The prevalence of advanced AMD in the fellow eye in the combined GA/CNV group was significantly higher compared to the other group in a logistic regression model that included the AMD (GA or CNV) status of the fellow eye. A possible explanation for these results is that this combined GA/CNV form occurs at a later stage of AMD than either GA or CNV. In 2012, Querques et al. demonstrated that treatment of GA-associated CNV with ranibizumab did not improve the functional outcome after 24 months of follow-up despite an anatomic response of the CNV.[24] This finding suggests a more severe subtype of late AMD with a partial response to treatment, as only the exudative part is targeted.

To the authors' knowledge, no other studies have investigated the epidemiologic and clinical factors of the combined GA/CNV phenotype included in the present study; therefore, the data of the present study could not be compared to that of other studies. In the Macular Photocoagulation Study (MPS), the clinical risk factors mentioned for developing CNV were hypertension, one or more large drusen, five or more drusen of any size, and focal hyperpigmentation.[22, 23] In the present study, hypertension was not found to be linked to the prevalence of simultaneous GA and CNV.

With regard to genetics, there was no association in the present study between the *ARMS2* and *CFH* genes and the combined GA/CNV form of late AMD, a result which is concordant with the study by Grob et al., which found no association between the combined GA/CNV phenotype of 20 patients and the following genes: high temperature requirement factor A1 (*HTRA1*), complement component 3 (*C3*), complement component 2 (*C2*), *ARMS2*, and *CFH*. [25] However, Grob et al. found that patients with the combined GA/CNV phenotype had a higher frequency of the *ARMS2* and *HTRA1* risk alleles compared to 154 patients with

GA and 154 patients with CNV. In the present study, there was a lower frequency of the *ARMS2* risk allele in the combined GA/CNV group compared to the GA or CNV group, whereas there was a higher frequency of the *CFH* risk allele in the combined GA/CNV group. Nevertheless, the findings of the Grob et al. study and the present study did not reach statistical significance with regard to risk allele frequencies.[25] This suggests that other genes might be responsible for the GA/CNV phenotype and that further studies are warranted.

CNV and GA have generally been considered two different entities. However, they have a similar genetic and environmental risk profile[5–14] and may be two possible advanced manifestations of a single disease process whose outcome is controlled by a balance of factors yet to be determined. The combined GA/CNV form could then represent the outcome when all these factors are involved. The current study, which did not identify differentiating epidemiological or genetic features between AMD subtypes and the combined form, is consistent with this hypothesis. This model would also provide a rationale to consider the simultaneous occurrence of GA and CNV as an even more advanced form of AMD than either form separately.

This study has some limitations. The number of studied eyes was small, and clinical factors that were not included in this study, such as the size and number of drusen, might be involved in the risk profile of the combined GA/CNV form of late AMD. Further investigations are required to elucidate the characteristics of this subtype in order to improve our knowledge of the patients at risk. On the other hand, this study is the first to shed light on the epidemiologic and clinical characteristics of the combined GA/CNV form and suggests that environmental factors or genes other than those already studied might be involved.

In conclusion, the finding of GA and CNV simultaneously in the same eye occurs in older patients and is more associated with advanced AMD in the fellow eye compared to eyes with GA or CNV. This suggests that this combined entity should be characterised as an even more advanced form of AMD than the GA and CNV subtypes. Further study of this combined entity may provide insight into the environmental and genetic risk factors that drive this form of advanced disease.

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References

1. Resnikoff S, Pascolini D, Etya'ale D, et al. Global data on visual impairment in the year 2002. *Bull World Health Organ.* 2004; 82:844–51. [PubMed: 15640920]
2. Klein R, Davis MD, Magli YL, et al. The Wisconsin age-related maculopathy grading system. *Ophthalmology.* 1991; 98:1128–34. [PubMed: 1843453]

3. Smith W, Assink J, Klein R, et al. Risk factors for age-related macular degeneration: pooled findings from three continents. *Ophthalmology*. 2001; 108:697–704. [PubMed: 11297486]
4. Klein ML, Ferris FL 3rd, Armstrong J, et al. Retinal precursors and the development of geographic atrophy in age-related macular degeneration. *Ophthalmology*. 2008; 115:1026–31. [PubMed: 17981333]
5. Risk factors for neovascular age-related macular degeneration. The Eye Disease Case-Control Study Group. *Arch Ophthalmol*. 1992; 110:1701–8. [No authors listed]. [PubMed: 1281403]
6. Tomany SC, Wang JJ, Van Leeuwen R, et al. Risk factors for incident age-related macular degeneration: pooled findings from 3 continents. *Ophthalmology*. 2004; 111:1280–7. [PubMed: 15234127]
7. Pumariega NM, Smith RT, Sohrab MA, et al. A prospective study of reticular macular disease. *Ophthalmology*. 2011; 118:1619–25. [PubMed: 21550118]
8. Complications of Age-related Macular Degeneration Prevention Trial (CAPT) Research Group. Risk factors for choroidal neovascularization and geographic atrophy in the complications of age-related macular degeneration prevention trial. *Ophthalmology*. 2008; 115:1474–9. [PubMed: 18502512]
9. Clemons TE, Milton RC, Klein R, et al. Risk factors for the incidence of advanced age-related macular degeneration in the Age-Related Eye Disease Study (AREDS): AREDS report no. 19. *Ophthalmology*. 2005; 112:533–9. [PubMed: 15808240]
10. Klein R, Peto T, Bird A, et al. The epidemiology of age-related macular degeneration. *Am J Ophthalmol*. 2004; 137:486–95. [PubMed: 15013873]
11. Francis PJ, George S, Schultz DW, et al. The *LOC387715* gene, smoking, body mass index, environmental associations with advanced age-related macular degeneration. *Hum Hered*. 2007; 63:212–8. [PubMed: 17347568]
12. Gangnon R, Lee K, Klein B, et al. The Y402H Variant in the Complement Factor H Gene Affects Incidence and Progression of Age-Related Macular Degeneration: Results from Multi-State Models Applied to the Beaver Dam Eye Study. *Arch Ophthalmol*. 2012; 130:1169–76. [PubMed: 22965593]
13. Magnusson KP, Duan S, Sigurdsson H, et al. *CFH* Y402H confers similar risk of soft drusen and both forms of advanced AMD. *PLoS Med*. 2006; 3:e5. [PubMed: 16300415]
14. Schwartz SG, Agarwal A, Kovach JL, et al. The *ARMS2* A69S variant and bilateral advanced age-related macular degeneration. *Retina*. 2012; 32:1486–91. [PubMed: 22481475]
15. Evans JR, Lawrenson JG. Antioxidant vitamin and mineral supplements for preventing age-related macular degeneration. *Cochrane Database Syst Rev*. 2012; 6:CD000253. [PubMed: 22696317]
16. Kansagara, D.; Gleitsmann, K.; Gillingham, M., et al. Nutritional supplements for age-related macular degeneration: a systematic review [Internet]. Washington (DC): Department of Veterans Affairs (US); 2012 Jan. <http://www.ncbi.nlm.nih.gov/books/NBK84269/>. Published January 2012. Accessed October 2, 2013
17. Kaiser PK. Emerging therapies for neovascular age-related macular degeneration: drugs in the pipeline. *Ophthalmology*. 2013; 120(5 Suppl):S11–5. [PubMed: 23642781]
18. Davis MD, Gangnon RE, Lee LY, et al. The Age-Related Eye Disease Study severity scale for age-related macular degeneration: AREDS Report No. 17. *Arch Ophthalmol*. 2005; 123:1484–98. [PubMed: 16286610]
19. Green WR, Key SN 3rd. Senile macular degeneration: a histopathologic study. *Trans Am Ophthalmol Soc*. 1977; 75:180–254. [PubMed: 613523]
20. Green WR, Enger C. Age-related macular degeneration histopathologic studies: The 1992 Lorenz E. Zimmerman Lecture. *Ophthalmology*. 1993; 100:1519–35. [PubMed: 7692366]
21. Sunness JS, Gonzalez-Baron J, Bressler NM, et al. The development of choroidal neovascularization in eyes with the geographic atrophy form of age-related macular degeneration. *Ophthalmology*. 1999; 106:910–9. [PubMed: 10328389]
22. Five-year follow-up of fellow eyes of patients with age-related macular degeneration and unilateral extrafoveal choroidal neovascularization. Macular Photocoagulation Study Group. *Arch Ophthalmol*. 1993; 111:1189–99. [No authors listed]. [PubMed: 7689826]

23. Risk factors for choroidal neovascularization in the second eye of patients with juxtafoveal or subfoveal choroidal neovascularization secondary to age-related macular degeneration. Macular Photocoagulation Study Group. Arch Ophthalmol. 1997; 115:741–7. [No authors listed]. [PubMed: 9194725]
24. Querques G, Massamba N, Coscas F, et al. Choroidal neovascularisation complicating geographic atrophy in age-related macular degeneration. Br J Ophthalmol. 2012; 96:1479–83. [PubMed: 23077229]
25. Grob S, Luo J, Hughes G, et al. Genetic analysis of simultaneous geographic atrophy and choroidal neovascularization. Eye (Lond). 2012; 26:1106–13. [PubMed: 22699975]

Fig. 1.

Combined geographic atrophy (GA) and choroidal neovascularization (CNV) in a patient with age-related macular degeneration. **A.** Multilobular GA is visible on infrared as small round or oval atrophic areas of increased reflectance (green arrows). **B.** Occult CNV is shown on spectral domain optical coherence tomography as fibrovascular material below the retinal pigment epithelium (red arrows). **C.** The color photograph clearly shows the atrophic depigmented oval and round areas of GA (yellow arrows). **D.** GA is seen in the intermediate phase of the fluorescein angiogram as hyperfluorescent lobular lesions due to window defects (blue arrows). **E)** Occult CNV is characterized by an ill-defined area of irregular leakage and stippled hyperfluorescence in the late phase of the fluorescein angiogram (red circle).

Table 1

Demographic, environmental, and clinical characteristics of the two study groups

	Group 1 ^[a]	Group 2 ^[b]	P-Value ^[c]
Number	42	16	–
Mean age, years (SD) ^[d]	81.8 (2.5)	86.4 (3.4)	0.05 ^[e]
Onset of late AMD (months)	52.1 (6.8)	58.3 (13.1)	0.68
Number of anti-VEGF, ^[f] injections	23.5 (3.2)	18.5 (4.6)	0.38
Female, n (%)	28 (66.7)	10 (62.5)	0.77
Diagnosis of hypertension, n (%)	27 (64.3)	8 (50.0)	0.32
Diagnosis of diabetes, n (%)	3 (7.1)	2 (12.5)	0.61
Diagnosis of dyslipidemia, n (%)	22 (52.4)	8 (50.0)	0.87
Family history of AMD, ^[g] n (%)	11 (26.2)	6 (37.5)	0.40
History of smoking, n (%)	27 (64.3)	10 (62.5)	0.90
Presence of reticular lesions, n (%)	17 (40.5)	9 (56.2)	0.28
Advanced AMD in fellow eye, n (%)	13 (31.0)	13 (81.3)	< 0.001

^a Patients with age-related macular degeneration (AMD) and either geographic atrophy (GA) or choroidal neovascularisation (CNV).

^b Patients with AMD and both GA and CNV simultaneously in the same eye.

^c P-values resulted from χ^2 tests and two-tailed Fisher's exact tests.

^d Standard deviation.

^e The p-value is 0.049 but has been rounded to 0.05.

^f Anti-vascular endothelial growth factor.

^g Age-related macular degeneration.

Table 2

Genotype and allele frequencies of the two study groups

	Group 1 ^[a]	Group 2 ^[b]	P-Value ^[c]
<i>CFH</i> ^[d]			
Genotype frequency			
TT, n (%)	7 (16.7)	1 (6.2)	0.42
CT, n (%)	26 (61.9)	9 (56.3)	0.69
CC, n (%)	9 (21.4)	6 (37.5)	0.21
Risk allele frequency (C)	0.52	0.66	0.20
<i>ARMS2</i> ^[e]			
Genotype frequency			
GG, n (%)	11 (26.2)	6 (37.5)	0.40
GT, n (%)	24 (57.1)	7 (43.8)	0.36
TT, n (%)	7 (16.7)	3 (18.7)	1.00
Risk allele frequency (T)	0.45	0.41	0.65

^a Patients with age-related macular degeneration (AMD) and either geographic atrophy (GA) or choroidal neovascularisation (CNV).

^b Patients with AMD and both GA and CNV simultaneously in the same eye.

^c P-values resulted from χ^2 tests and two-tailed Fisher's exact tests.

^d Complement factor H gene.

^e Age-related maculopathy susceptibility 2 gene.