**Purpose**

Variants in the complement factor H (CFH), the complement component 3 (C3) and the age-related maculopathy susceptibility 2 (ARMS2) genes have been established to confer significant risks of susceptibility for age-related maculopathy degeneration (AMD). Their role for AMD disease progression was investigated.

**Methods**

- Patients with GA secondary to AMD were included from the longitudinal natural history arm of the multicenter FAM–Study (registration www.clinicaltrials.gov: NCT00393692). A total of 619 patients with dry (early or late) AMD in the study eye were enrolled (mean age, 73.9 years; mean follow-up, 35 months) and were recruited at 6 centres in Germany. [1] 612 unrelated individuals of German origin served as controls.

Using a two-level-random effects model, a single variable of GA progression rate was computed based on longitudinal observations of both eyes for every patient studied. [2] The variable represents a continuous, biology-based quantitative phenotype and was used for association analysis with genetic data.

UNPHASED was used to test for association between the quantitative trait variable “geographic atrophy progression” and SNP alleles and haplotypes. [3] P-values were adjusted for the covariates age, BMI, and smoking, using the “modifiers” option of the UNPHASED software package. Posthoc power values for single SNPs were computed with the R software package (http://www.r-project.org).

- In a subset of 99 cases with pure bilateral GA, variants in CFH, ARMS2 and C3 were strongly associated with disease susceptibility (Table 1).

- Median progression rate of geographic atrophy over a mean follow-up of 3.0 years was 1.61 mm²/year.

- There was no association between GA progression rate and the genetic risk variants at the three loci (Table 2) – despite sufficient power (Table 3).

**Results**

- In a subset of 99 cases with pure bilateral GA, variants in CFH, ARMS2 and C3 were strongly associated with disease susceptibility (Table 1).

- Median progression rate of geographic atrophy over a mean follow-up of 3.0 years was 1.61 mm²/year.

- There was no association between GA progression rate and the genetic risk variants at the three loci (Table 2) – despite sufficient power (Table 3).

**Conclusions**

- Variants at CFH, C3, and ARMS2 confer high risks for the susceptibility of geographic atrophy due to AMD, but not for AMD disease progression.

- Therapeutic options specifically addressing these three susceptibility factors may not be promising once late atrophic AMD has developed.

- Other so far unknown susceptibility factors may be involved.

**References:**


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