Progression of GA with subsequent exudative NV-AMD

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Disclosures

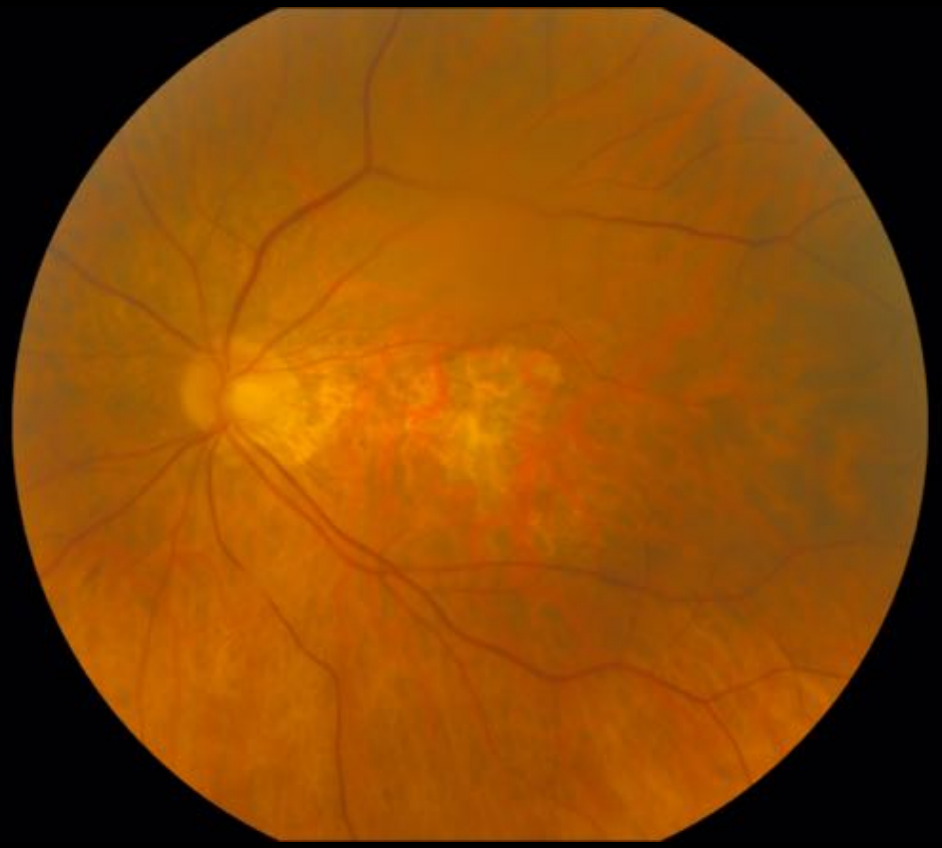
- None

Summary

- In AREDS2, in eyes that developed GA during the study (incident cohort), GA enlargement was significantly slower with subsequent exudative NV-AMD (0.20 vs 0.29 mm, p=0.037)
- This was not observed in those who had GA at baseline (prevalent cohort)
- The potential association of decreased rate of GA enlargement with the presence of subsequent exudative neovascularization found in this subgroup (incident cohort) requires replication from future longitudinal studies

Purpose

- To examine whether the rate of GA enlargement is influenced by subsequent exudative NV-AMD

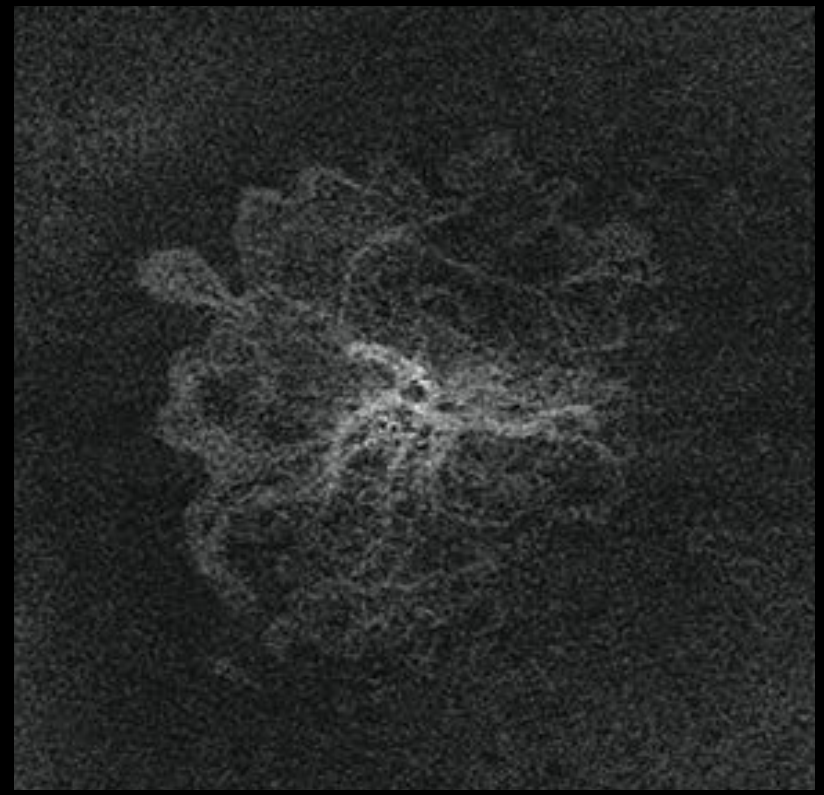


Background

- Late AMD is the disease stage with substantial risk for visual loss.
- Unlike for NV-AMD, there is no treatment for GA.
- GA lesions enlarge and coalesce relentlessly over time, and the central involvement is almost inevitable over time.

Background

- GA and NV-AMD can coexist in the same eye.
- Our previous study demonstrated that the risk of NV-AMD in eyes with new GA was 29% after 4 years.
- de Oliveira Dias *et al.* (2018)
  - Showed that large % of exudative MNV pre-existed as non-exudative MNV



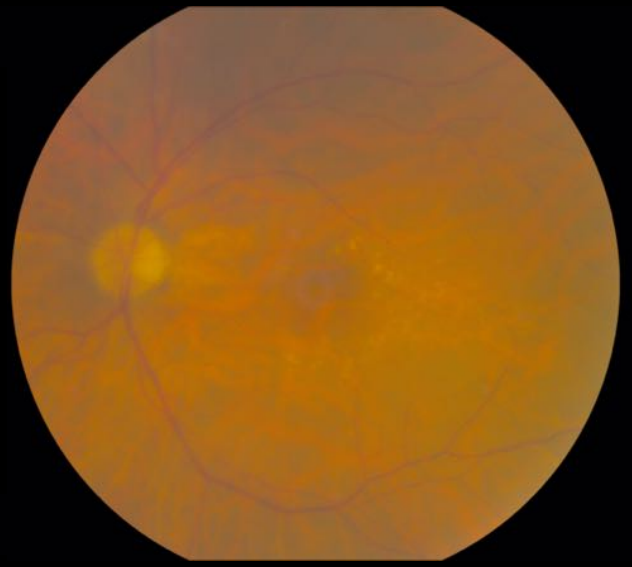
Background

- Keenan *et al*. (2018) presented the hypothesis that the presence of non-exudative MNV adjacent to a GA lesion might slow GA enlargement in AREDS2.
- Other small studies before and after this have reported potential associations between the presence of MNV (exudative and/or non-exudative) and decreased incidence and/or enlargement of macular atrophy.
- The goal of this study was to use the AREDS2 data to characterize the natural history of GA with subsequent NV-AMD development.

Age-related Eye Disease Study 2 (AREDS2)

- Enrollment from 2006 to 2008 at 82 clinical sites in the US

- Criteria:
  - Bilateral large drusen, or
  - Late AMD (neovascular AMD or central geographic atrophy) in 1 eye and large drusen in the fellow eye



AREDS2

- Enrollment from 2006 to 2008 at 82 clinical sites in the US
- Criteria:
  - Bilateral large drusen, or
  - Late AMD (neovascular AMD or central geographic atrophy) in 1 eye and large drusen in the fellow eye
- Study population
  - 4203 patients
  - Age 50-85

Study Design

- Two cohorts
  - Eyes that developed GA during the study (incident cohort)
  - Eyes that had pre-existing GA at baseline (prevalent cohort)
- Two subgroups within each cohort
  - GA that subsequently developed exudative NV-AMD
  - GA that never developed exudative NV-AMD
- GA growth rate
  - Based on measurements from at least two follow-up visits
  - Measurements from GA with coexisting exudative NV-AMD were not included

Results

Baseline systemic factors of AREDS2 Participants

Characteristic	Incident GA without subsequent exudative NV-AMD	Incident GA with subsequent exudative NV-AMD	P	Prevalent GA without subsequent exudative NV-AMD	Prevalent GA with subsequent exudative NV-AMD	P
Age (years), mean (SD)	74.4 (SD 7.0)	75.5 (6.7)	0.21	75.3 (7.1)	77.3 (5.3)	0.09
Female sex, %	58.4	60.9	0.58	57.0	66.7	0.15
Smoking history, % - Never - Former - Current	 43.1% 49.9% 7.0%	 28.8% 65.8% 5.5%	0.02	 35.1% 57.5% 7.4%	 44.4% 50.8% 4.8%	0.32

Baseline Ocular Characteristics

Characteristic	Incident GA without subsequent exudative NV-AMD	Incident GA with subsequent exudative NV-AMD	P	Prevalent GA without subsequent exudative NV-AMD	Prevalent GA with subsequent exudative NV-AMD	P
Eyes, n	684	73		393	63	
GA area (initial, mm^2), mean (SD)	1.69 (2.5)	1.77 (2.6)	0.76	3.58 (4.3)	3.06 (4.0)	0.28
Central GA, %	33.5	23.3	0.08	33.3	33.3	1.00
GA configuration, % - Small (single patch <1 DA) - Multifocal - Horseshoe or ring - Solid - Indeterminate	 58.8 23.8 2.5 12.6 2.3	 57.5 17.8 2.8 20.6 1.4	0.35	 34.4 23.9 9.4 26.2 6.1	 39.7 20.6 4.8 31.7 3.2	0.48
Fellow eye with GA, %	70.3	61.1	0.17	84.0	88.9	0.40

Genetic Association with GA Enlargement

Characteristic		Incident GA without subsequent exudative NV-AMD	Incident GA with subsequent exudative NV-AMD	P	Prevalent GA without subsequent exudative NV-AMD	Prevalent GA with subsequent exudative NV-AMD	P
Genetic data available, n		350	39		136	29	
ARMS2 rs10490924, % (0=G, 1=T)	0/0	35.7	35.9	0.90	36.0	37.9	0.98
	0/1	43.4	46.2		43.4	41.4	
	1/1	20.9	17.9		20.6	20.7	
C3 rs2230199, % (0=C, 1=G)	0/0	49.1	53.8	0.19	55.1	58.6	0.62
	0/1	42.6	30.8		36.0	37.9	
	1/1	8.3	15.4		8.8	3.4	
APOE rs73036519, % (0=G, 1=C)	0/0	49.7	43.6	0.29	54.4	51.7	0.94
	0/1	42.3	41.0		34.6	37.9	
	1/1	8.0	15.4		11.0	10.3	

No significant genetic interaction found

	Change per year in square root of GA area		
	Estimate (mm)	95% CI (mm)	P*
Incident GA - without subsequent exudative NV-AMD	0.29	0.27-0.30	0.037
Incident GA - with subsequent exudative NV-AMD	0.20	0.12-0.28	
Prevalent GA - without subsequent exudative NV-AMD	0.28	0.26-0.29	0.37
Prevalent GA - with subsequent exudative NV-AMD	0.31	0.24-0.37	

Discussion

- The main difference between the two cohorts was the baseline GA size
- The potential effect of non-exudative MNV on GA enlargement might be relatively small and localized

Study Limitations

- Post-hoc analyses (unplanned a priori)
- This study relied on using subsequent exudative MNV as a proxy for a period of presumed non-exudative MNV.
- No direct diagnosis or visualization of non-exudative MNV

Conclusions

- In AREDS2, in eyes that developed GA during the study (incident cohort), GA enlargement was significantly slower with subsequent exudative NV-AMD (0.20 vs 0.29 mm, p=0.037)
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- Wai Wong, MD, PhD
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