Progression of Atrophy and Phenotypic Variability in Autosomal Dominant Stargardt-like Macular Dystrophy due to *PROM1* mutation

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Financial disclosures

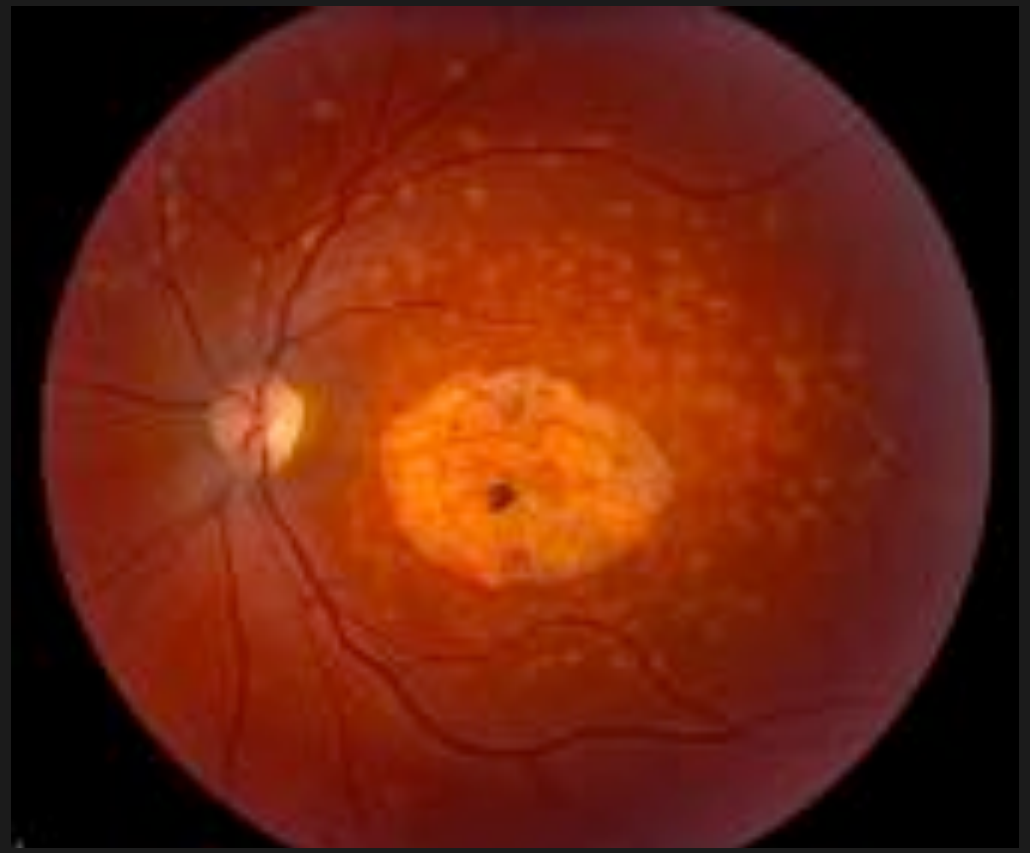
- None

Summary

- Macular dystrophy that looks like Stargardt disease and AMD can be caused by a dominant mutation in PROM1 (p.R373C)
- Rates of atrophy progression are similar to those reported for *ABCA4*-related Stargardt disease and less than AMD
- Rates of atrophy vary based on early macular phenotype
  - Geographic atrophy > multi-focal GA > bulls-eye maculopathy

Autosomal dominant Stargardt-like macular dystrophy

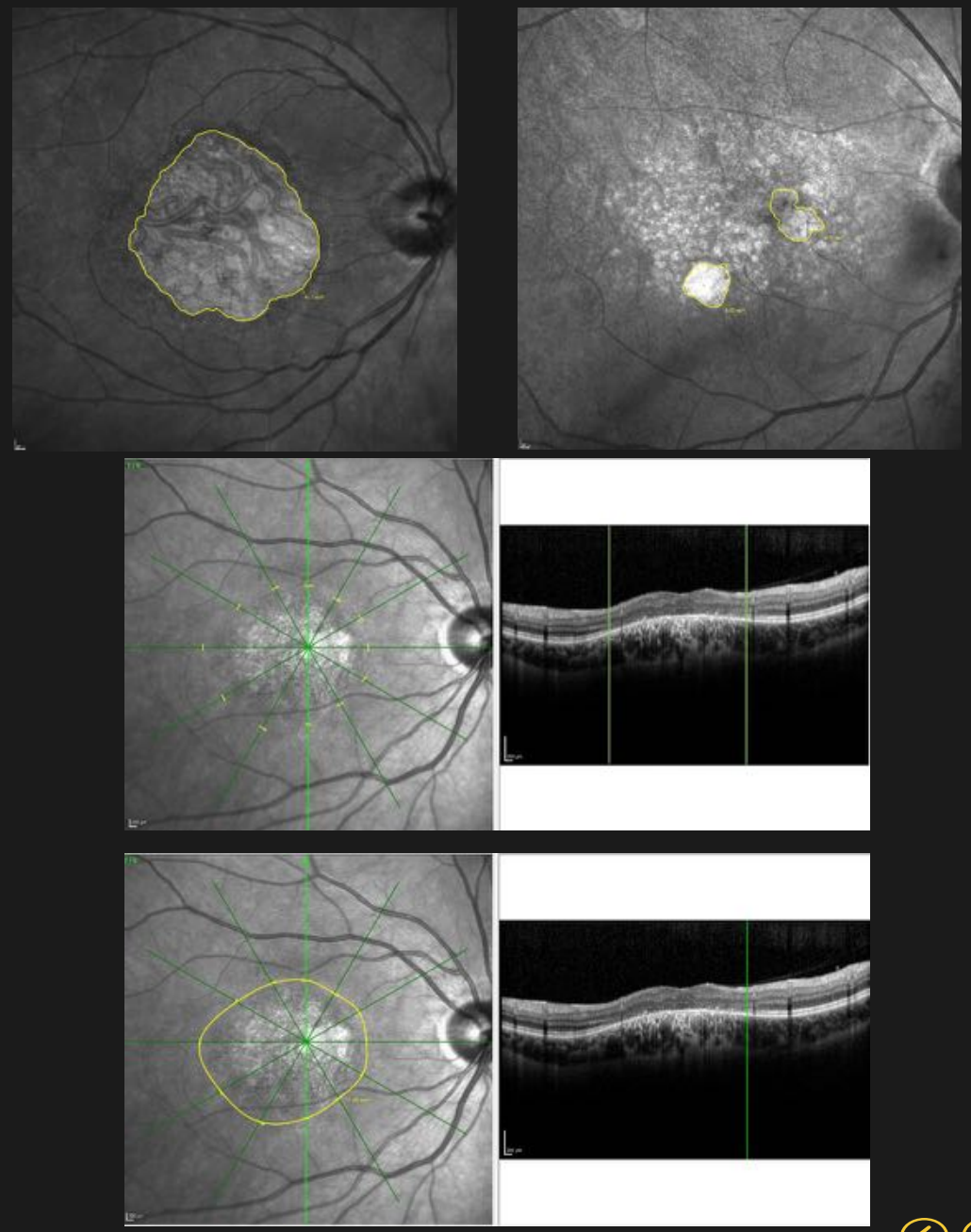
- Rare, progressive retinal dystrophy, reduced acuity 2nd - 5th decade of life, macular atrophy and fundus flecks
- Known mutations:
  - ELOVL4 – more common mutation
  - PROM1 – mutation heterogeneity
- Goals
  - Describe clinical spectrum of disease
  - Quantify rate of progressive macular atrophy



Cibis et al. *Archives of Ophth* 1980. Stone et al. *Archives of Ophth* 1994. Michaelides et al. *IOVS* 2010.

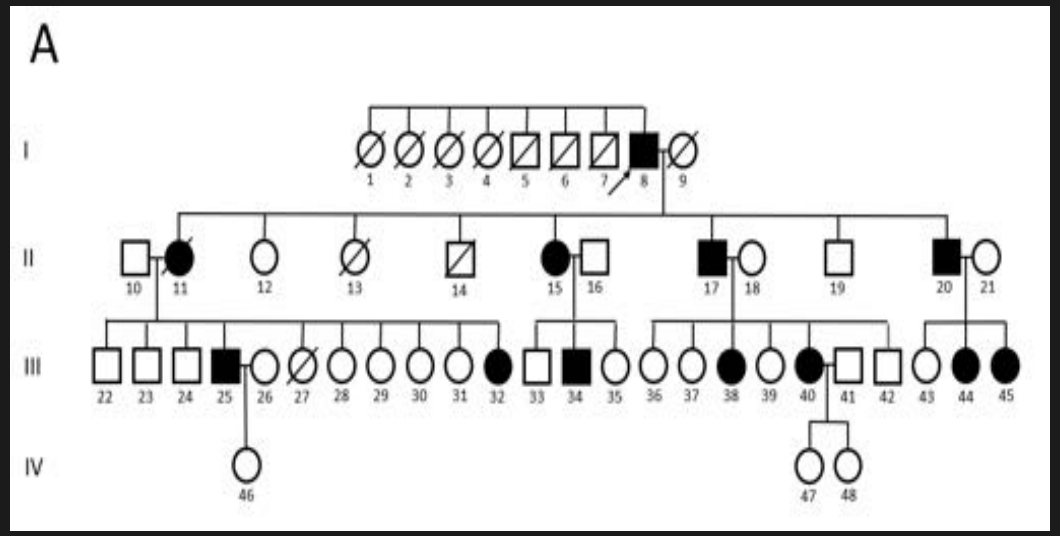
Methods

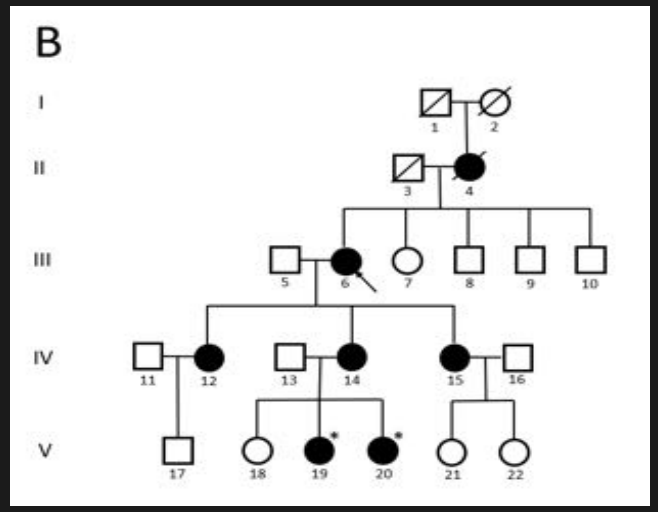
- Single center, longitudinal retrospective case series
- Clinical data collected for patients with Arg373Cys (p.R373C) mutation in *PROM1*
- Areas of atrophy measured on Heidelberg Eye Explorer (version 6.3.2.0)

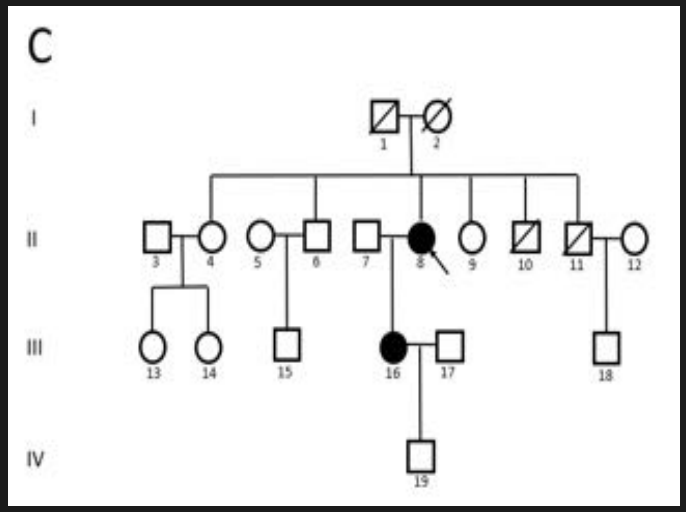


Demographics

- 15 patients, 5 different families
- Age range – 8 to 82
- 3 males, 12 females
- Average f/u 5.1 years (range 0-12)
- 3 types of macular atrophy
  - GA
  - Multi-focal GA
  - BEM





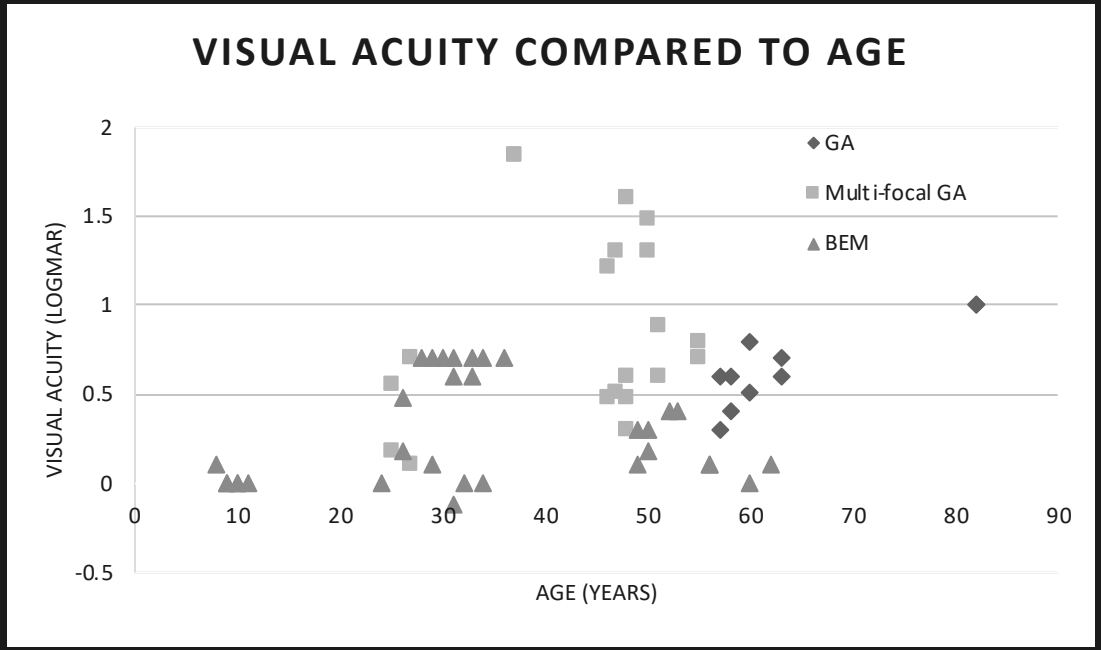


		Initial Exam		Final Exam		Type of atrophy	Yellow flecks	Peripheral pigment clumping	Vascular attenuation
	Gender	Age	BCVA	Age	BCVA				
Patient A:I,8	Male	82	20/200 OD 20/200 OS	Same	Same	Central GA	No	Yes	No
Patient A:II,15	Female	58	20/40 OD 20/80 OS	63	20/80-1+1 OD 20/100 OS	Central GA	Yes	Yes	Yes
Patient A:III,25	Male	49	20/25-1 OD 20/25-2 OS	50	20/30 OD 20/20-1 OS	BEM	No	No	No
Patient A:III,38	Female	46	20/60+2 OD 20/320 OS	51	20/100-2 OD 10/300 OS	Multi-focal GA	No	Yes	Yes
Patient A:II,20	Male	25	20/30+2-2 OD 20/70 OS	37	20/1400 OD 20/1400 OS	Multi-focal GA	No	Yes	No
Patient B:IV,12	Female	24	20/20 OD 20/125 OS	33	20/100-1 OD 20/100-1 OS	BEM	No	Yes	No
Patient B:IV,15	Female	31	20/15 OD 20/15 OS	34	20/20+2 OD 20/15-3 OS	BEM	No	No	No
Patient B:IV,14	Female	26	20/60-2 OD 20/60-1 OS	36	20/100+2 OD 20/80+1-2 OS	BEM	No	Yes	No
Patient B:III,6	Female	49	20/40-2 OD 20/20-1 OS	53	20/50+2 OD 20/25+2 OS	BEM→multi-focal GA	No	Yes	No
Patient B:V,19	Female	9	20/20-2 OD 20/20- OS	11	20/20 OD 20/20+ OS	BEM	No	No	No
Patient B:V,20	Female	8	20/25+ OU	10	20/20 OD 20/20 OS	BEM	No	No	No
Patient C:III,16	Female	32	20/20-1 OD 20/25-1 OS	Same	Same	BEM	No	Yes	No
Patient C:II,8	Female	56	20/25 OD 20/20 OS	63	20/25-3 OD 20/20-2 OS	BEM	Yes	Yes	No
Patient 14	Female	48	20/40 OD 20/60+2 OS	55	20/125+2 OD 20/100-2 OS	Multi-focal GA	No	Yes	No
Patient 15	Female	56	20/25-2+2 OD 20/25-2 OS	Same	Same	BEM	No	Yes	Yes

Patient characteristics		
	Percentage of patients	Number of patients
Gender		
Male	20%	3
Female	80%	12
Type of atrophy		
BEM	67%	10
Multi-focal GA	20%	3
GA	13%	2
Fundus findings		
Yellow flecks	13%	2
Pigment clumping	73%	11
Vascular attenuation	20%	3
	Percentage of eyes	Number of eyes
Refractive error*		
Myopia	69%	18
Hyperopia	23%	6
Emmetropia	8%	2
OCT findings*		
Hyporeflective spaces	8%	2

***Refractive error and OCT analysis was not available for all eyes, percentages calculated based on total number of available eyes**

Rates of atrophy progression		
	Rate of atrophy (mm^2/year)	Standard deviation
Type of atrophy		
BEM	0.23	0.14
Multi-focal GA	0.53	0.31
GA	1.08	0.29
All patients	0.36	0.32



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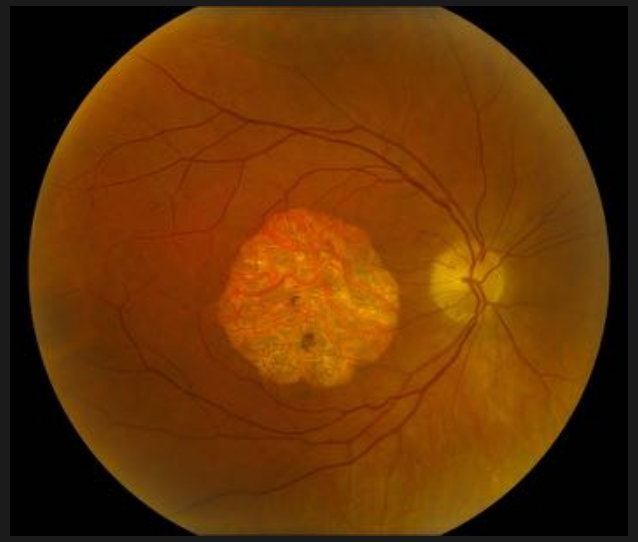
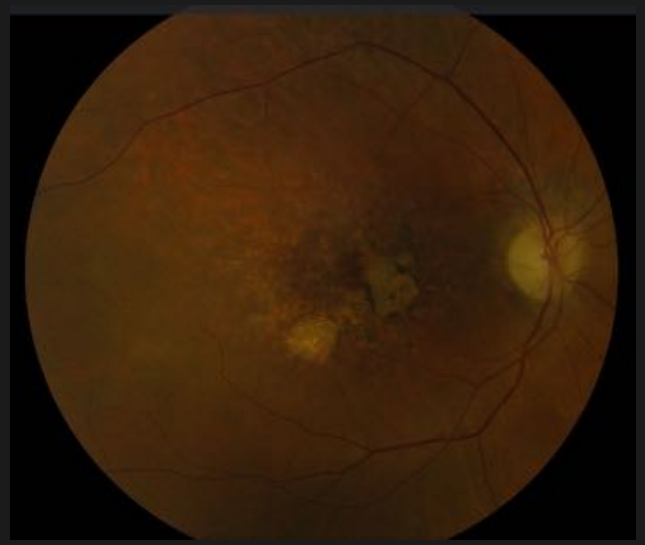
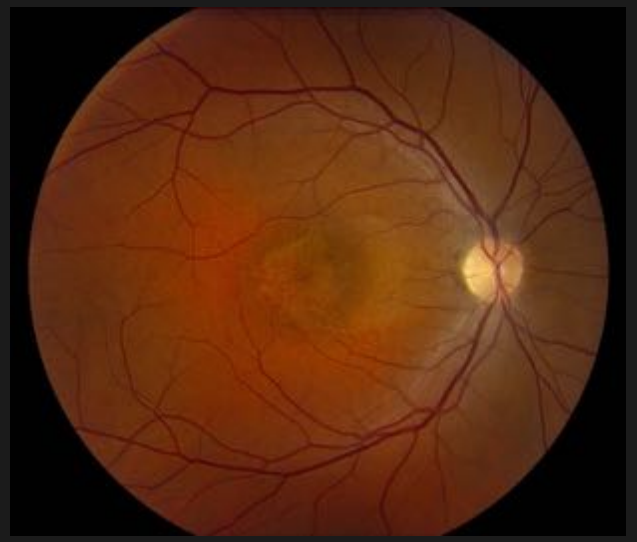
Patient A:II,15

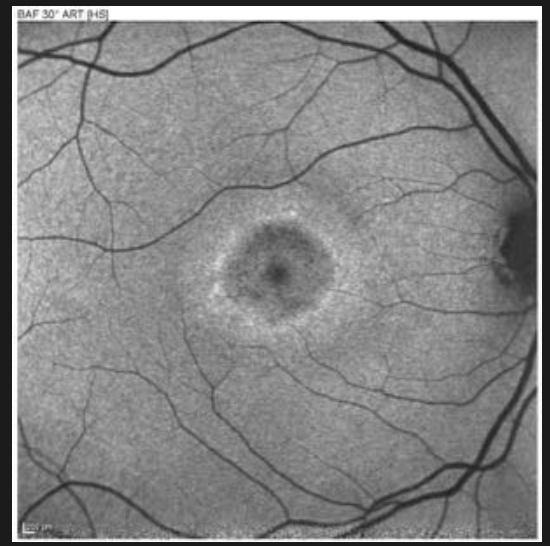


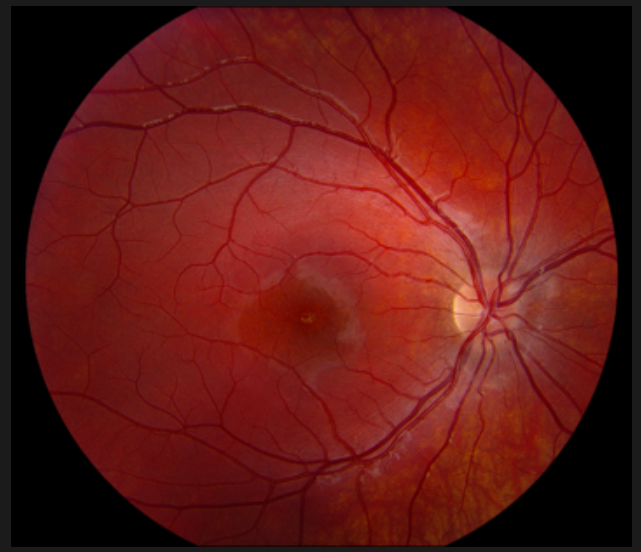
Patient A:III,38

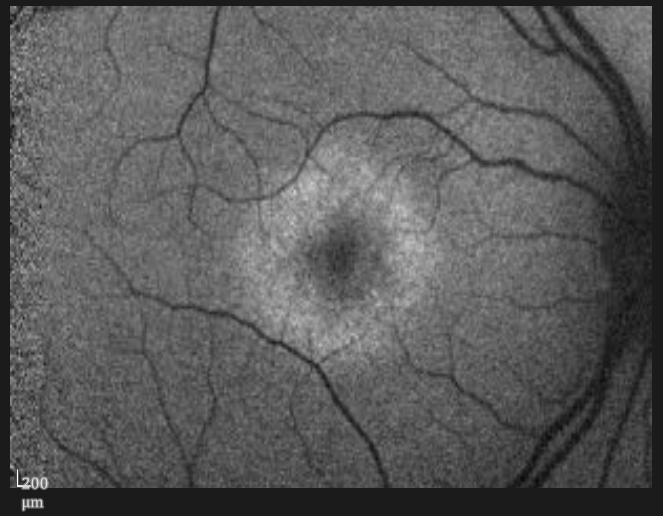


Patient A:III,25





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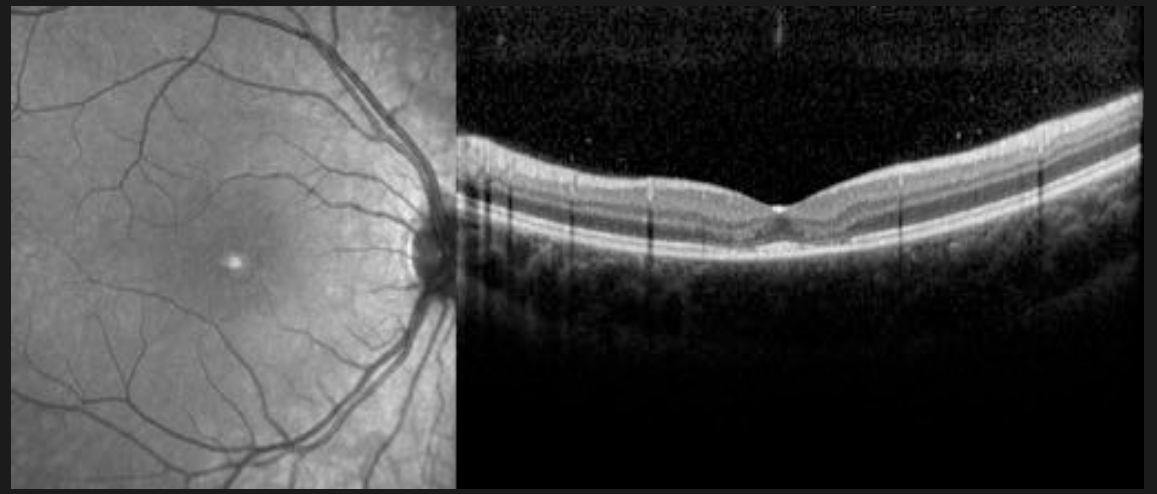

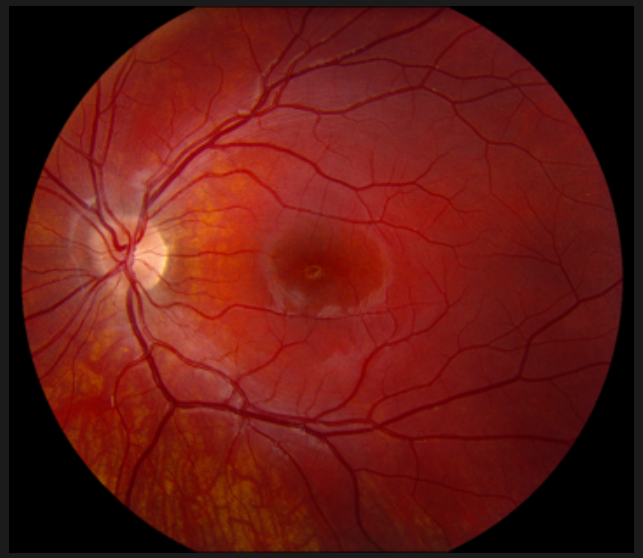

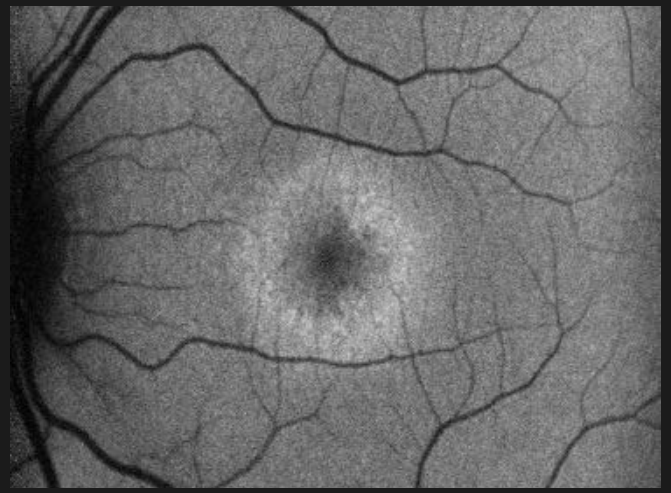

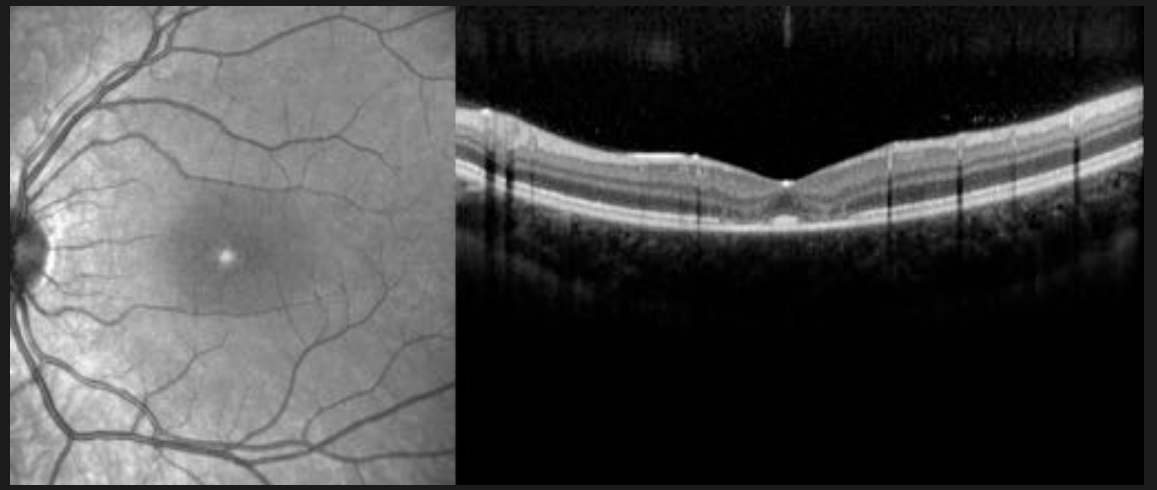

Conclusions

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- Rates of atrophy progression are similar to those reported for *ABCA4*-related Stargardt disease and less than AMD
- Rates of atrophy vary based on early macular phenotype
  - Geographic atrophy > multi-focal GA > bulls-eye maculopathy
- Early findings best seen on FAF and OCT and late findings variable

Thanks

- Co-authors and mentors
  - Ian Han MD
  - Jeremy Hoffman
  - Edwin Stone, MD, PhD
  - Elliott Sohn, MD