A 48-Year-Old Woman Referred for Macular Degeneration in Both Eyes

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Introduction:

A 48-year-old woman was referred for macular degeneration in both eyes. She reports having multiple blind spots in both eyes as well as difficulty focusing over the last 4-5 years. She had never sought care or been evaluated for visual disturbances up until her most recent appointment with an optometrist several weeks prior. She does note a family history of macular degeneration although she believes the diagnosis was made at an older age.

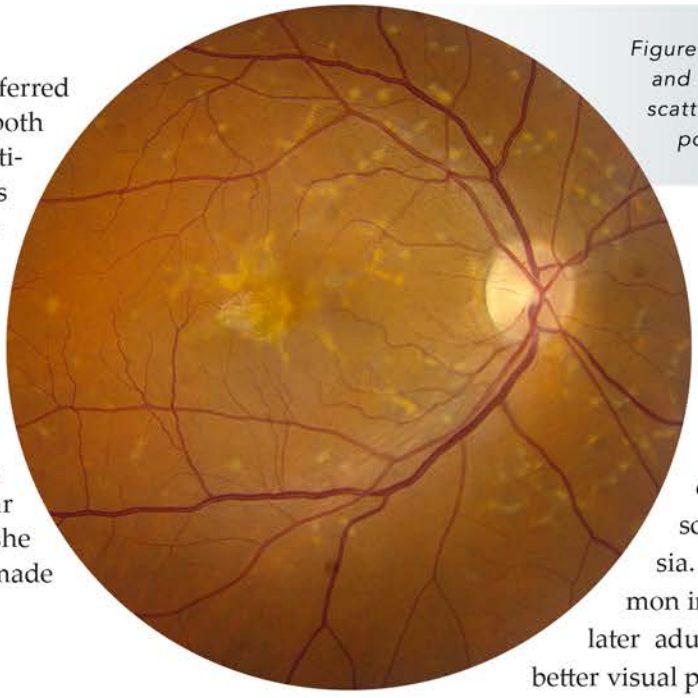
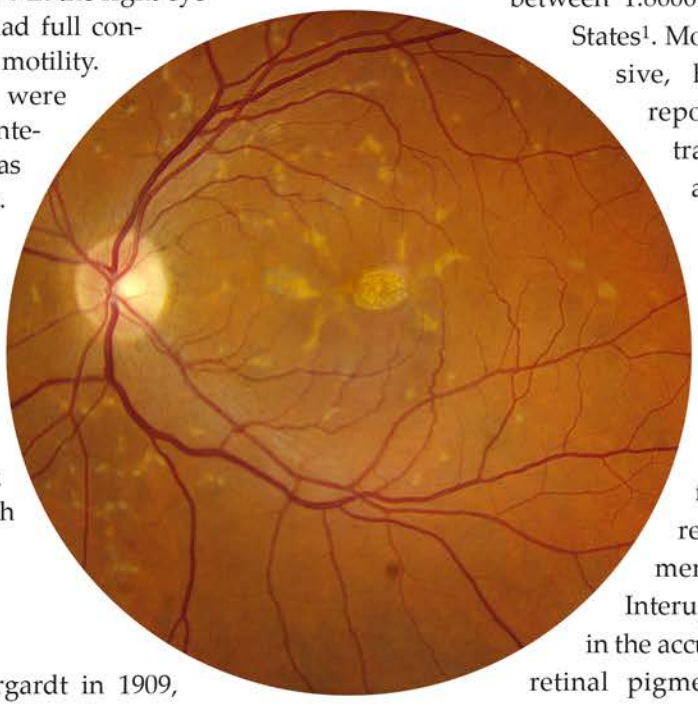


Figure 1: Fundus photos of the right and left eye. Note pisciform flecks scattered throughout the posterior pole along with central atrophy.

Exam:

On exam the patient was 20/50 in the right eye and 20/150 in the left. She had full confrontational fields and full motility. Her intraocular pressures were within a normal range. An anterior segment examination was remarkable for mild cataracts. Fundus examination revealed central atrophy with yellow/white flecks scattered throughout the posterior pole. An OCT revealed atrophy without edema and a fluorescein angiogram revealed a dark choroid consistent with Stargardt disease.



Discussion:

First described by Karl Stargardt in 1909, Stargardt disease is the most common macular dystrophy in adults under 50 years of age and is a common cause of central vision loss in this population[1]. Symptoms include bilateral central vision loss along with scotomata and dyschromatopsia. Although onset is more common in childhood, it can present in later adulthood and generally has a better visual prognosis than the early childhood forms. It has an estimated prevalence of between 1:8000 and 1:10000 in the United States[1]. Most cases are autosomal recessive, however there have been reported pedigrees in which transmission was found to be autosomal dominant. The mutation is found in the ABCA4 gene encoding an ATP binding cassette transporter protein expressed in rod outer segments. The gene is believed to play a role in the visual cycle by facilitating the transport of retinoids across the outer segment disc membrane[2,3,4]. Interuptions in this process result in the accumulation of lipofuscin in the retinal pigment epithelium (RPE). The

pathophysiology of Stargardt is believed to be related to this accumulation of byproduct and damage to photoreceptors and ultimately to RPE.

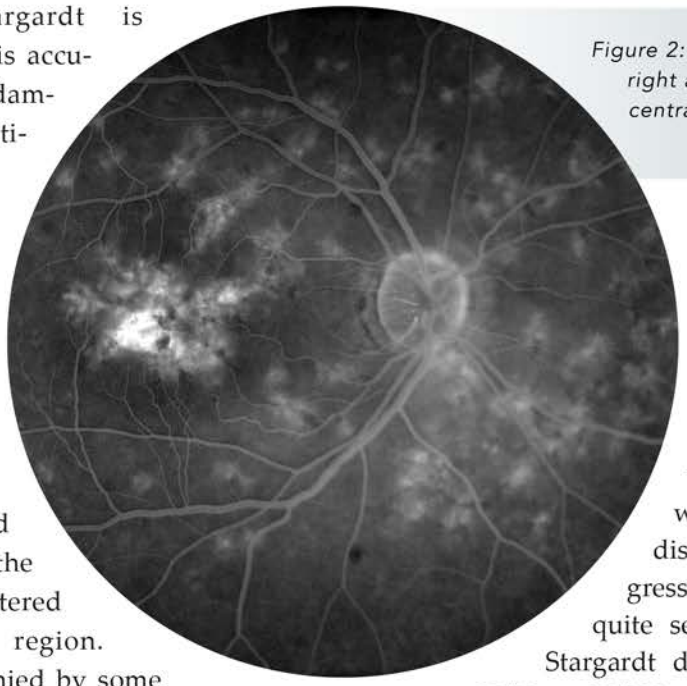
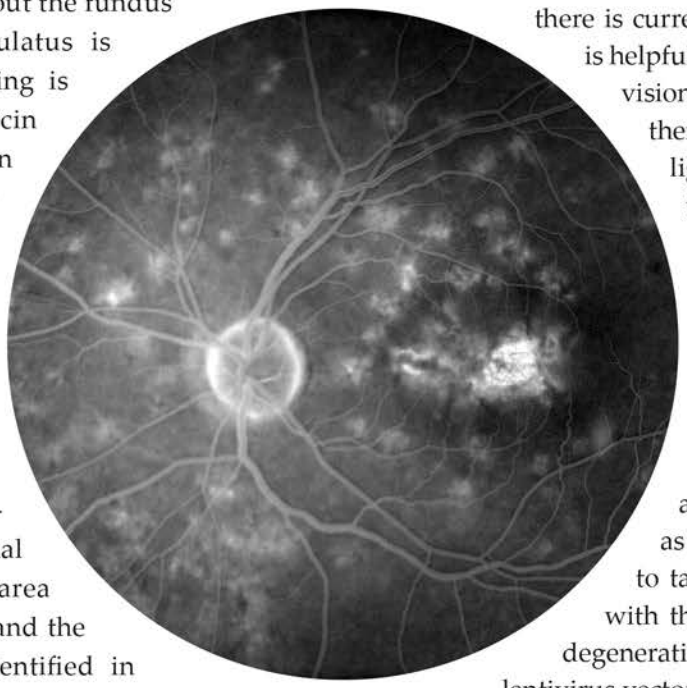


Figure 2: Fluorescein angiogram of the right and left eye. Hyperfluorescent central atrophy and flecks against a dark choroid.

Stargardt disease has a wide range of phenotypic manifestations ranging from bull's eye maculopathy to retina-wide degeneration[1,5]. Despite this heterogeneity there are several clinical characteristics shared by all cases, most notably the yellow pisciform flecks scattered around the peripapillary region. This is commonly accompanied by some degree of foveal atrophy. If the flecks are predominant and scattered throughout the fundus the term fundus flavimaculatus is commonly used[6]. This finding is likely the result of lipofuscin like pigment accumulation in the RPE blocking transmission. The hyperfluorescent may actually be lipofuscin engorged RPE cells accumulating in the subretinal space.



OCT in Stargardt disease typically demonstrates central loss of the outer retinal layers. A thickening of the area between Bruchs membrane and the ellipsoid zone has been identified in patients with the disease as well. This was found in areas devoid of atrophy and without flecks. The thickening extended beyond the posterior pole and was actually found to be more prominent peripherally[6]. Fundus autofluorescence reveals hyper auto fluorescent flecks, which are a result of accumulated lipofuscin within the RPE. Fluorescein angiography can confirm the diagnosis with the finding of a dark choroid. This phenomenon describes the prominent retinal circulation against a dark, hypo fluorescent choroid and is found in 80% of patients.

There is a great deal of variability within the age on onset and the timing of visual symptoms in patients with Stargardt disease. The disease is generally slowly progressive and can be fairly mild to quite severe. The visual acuity in Stargardt disease usually ranges from 20/50 to 20/200, although most retain better than 20/100 vision in at least one eye[7]. While there is currently no medical treatment it is helpful to refer these patients to low vision specialists, and to counsel them regarding avoiding bright lights and sunlight. Although treatment options are currently limited, the possibility of future therapies is present. There is great deal of research and resources examining the potential role of stem cell therapy, gene replacement therapy, and pharmacologic therapy as well. Gene therapy attempts to target healthy photoreceptors, with the aim being to slow further degeneration. Subretinal injection of a lentivirus vector delivering ABCA4 to its target cells is currently undergoing phase I/II clinical trials. Human embryonic stem cell derived RPE cells have been transplanted subretinally in eyes with advanced Stargardt also in a phase I/II trial.

References:

1. Stargardt disease: clinical features, molecular genetics, animal models and therapeutic options.

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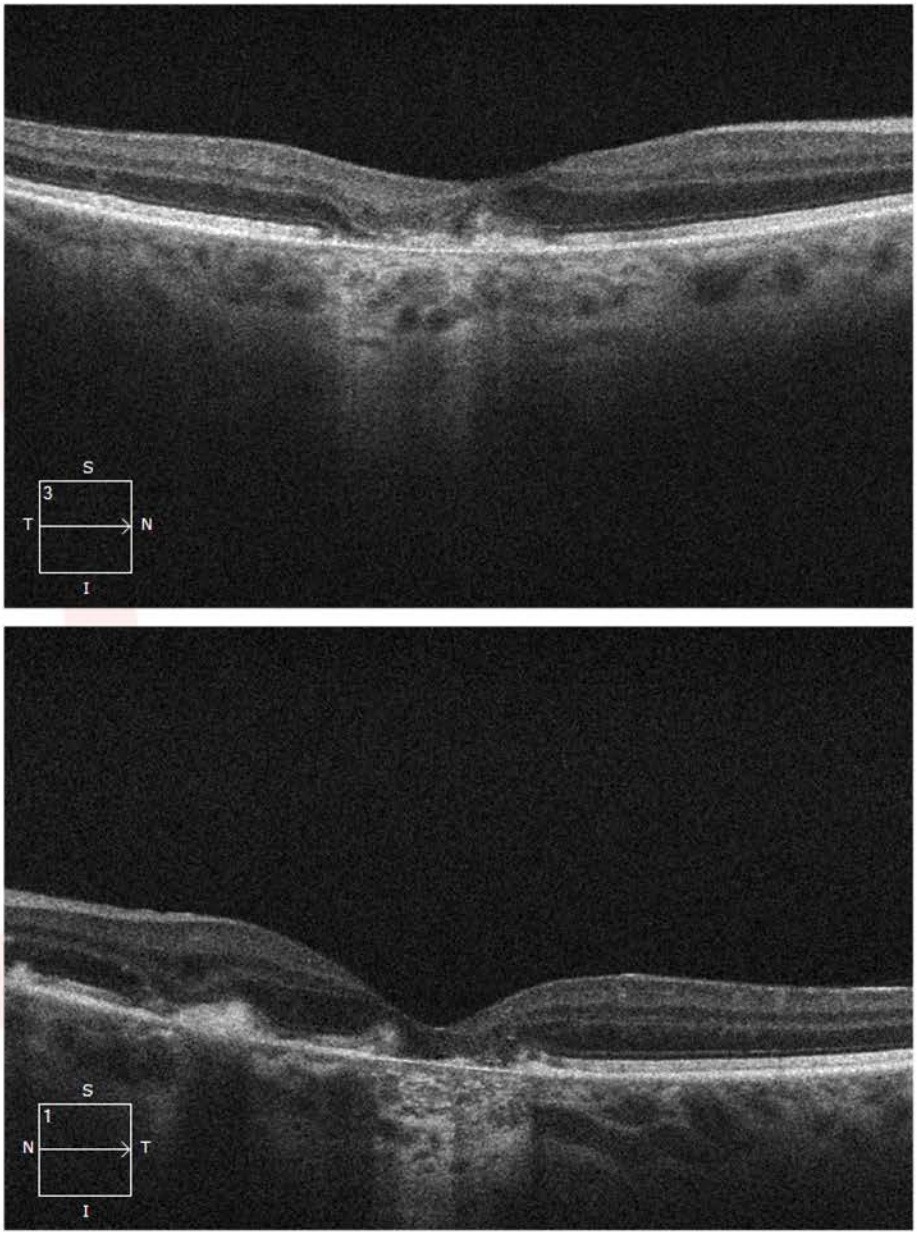

Figure 3: OCT of the right (top) and left (below) eyes with central atrophy .

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