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STARGARDT'S DISEASE - A RARE CASE STUDY

Ophthalomology

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ABSTRACT

We present a case of a 13-year-old female who has had a diminution of vision in both eyes since childhood. Fundus examination shows numerous flecks giving a beaten metal appearance, a circular lesion on the macula suggestive of macular dystrophy, and an appearance of bull's eye maculopathy suggestive of Stargardt disease. It is an autosomal recessive, heterogeneous disease with many clinical presentations, which vary vastly in the age of onset and the rate of progression. Patients present with progressive visual impairment, usually beginning in the first or second decades of life. Due to the advancement of technology and newer diagnostic modalities, there has been significant improvement in the detection of this disease at the initial stages.

KEYWORDS

Stargardt disease, macular dystrophy, maculopathy, autosomal recessive.

INTRODUCTION

The term "macular dystrophy" is historically used for a group of heritable disorders that present with retinal abnormalities between the temporal vascular arcades (1). Stargardt disease (STGD1) is one of the most common causes of inherited macular dystrophy in both adults and children. It has an onset during the early second decade of life and presents initially with central vision loss, yellow flecks around the macula and retinal mid-periphery, and there is progressive atrophy of the retinal pigment epithelium (RPE) (2-4). It is characterized by bilateral and symmetrical maculopathy with autosomal recessive transmission linked to the ABCA4 gene. The earlier the age of onset, the more severe the disease course, better prognosis generally associated with a later onset (5).

The ABCA4 gene encodes for the ABCA4 protein, which is responsible for removing toxic substances from the photoreceptors (6). In a patient with this mutation, the ABCA4 protein is defective, accumulating a toxic substance known as lipofuscin within the retinal cells. This ultimately results in cell death (7).

Stargardt-like diseases are retinal diseases with phenotypes like STGD1 but with an autosomal dominant inheritance (8). It includes STGD2, STGD3, and STGD4. STGD2 was erroneously linked to chromosome 13q34 (9).

The phenotypic heterogeneity makes the clinical diagnosis of STGD1 challenging. Reports from the Progression of Atrophy Secondary to Stargardt Disease (ProgStar) study have described the natural history of the disease with the help of various structural and functional investigative modalities (10). Noble and Carr classified STGD based on fundus appearance into 4 groups (11)

- Group 1: Macular degeneration without flecks
- Group 2: Perifoveal flecks with macular degeneration (Stargatdt disease)
- Group 3: Diffuse flecks with macular degeneration (fundus flavimaculatus with macular degeneration)
- Group 4: Diffuse flecks, absent macular degeneration (pure fundus flavimaculatus)

Fundus fluorescein angiography is the investigation of choice as it evidences "silence choroidien". It appears dark in FFA most probably due to lipofuscin accumulation in RPE. The retinal vessels appear clearer against a hypo-fluorescent choroid. In late stages, ERG and EOG also become subnormal, and visual fields get diminished.

Here we report a case of a 13-year-old young student with Stargardt's disease in both eyes

A 13-year-old female presented with chief complaints of diminution in vision in both eyes since childhood. She also reported a gradual and progressive loss in distinguishing between faces and colours. There was no history of similar complaints in any other family member. She did not have a history of any chronic illness and did not receive any prolonged medical treatment.

Her general physical examination and systemic examination results were normal. Visual acuity was 6/60 in both eyes which did not improve by refractive correction during the ocular check-up.

	Right eye	Left eye
Conjunctiva	Normal	Normal
Cornea	Clear	Clear
Anterior chamber	Normal in-depth and content	Normal in-depth and content
Iris	Normal in colour and texture	Normal in colour and texture
Pupil	Round regular reactive	Round regular reactive
Lens	Clear	Clear
Extraocular movements	Full in all directions	Full in all directions

On distant direct ophthalmoscopy, the media and red fundal glow were normal in both eyes. Both eye's optic discs were normal on indirect ophthalmoscopy; neither eye's foveal reflex was appreciated. The optic discs in both eyes were of normal size and had clearly defined edges. In both eyes, vessels had a normal arterio-venous ratio of 2:3 and emerged from the disc's centre in a dichotomous branching pattern. An ill-defined circular lesion was visible at the macula suggestive of macular dystrophy. It was surrounded by multiple pisciform flecks in both eyes as evidenced by fundus photographs. These tiny yellowish flecks were present in all four quadrants of both eyes It was more noticeable in red-free fundus images. [Figure-1(a,b)].

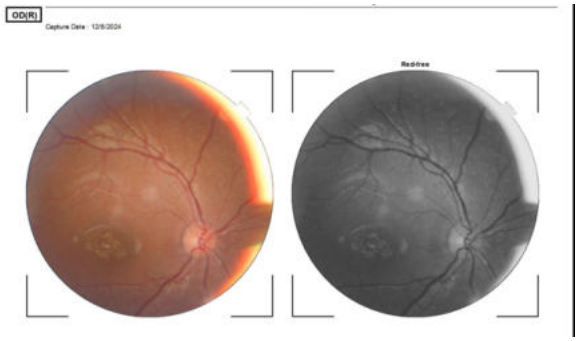

Figure 1(a)- Right Eye

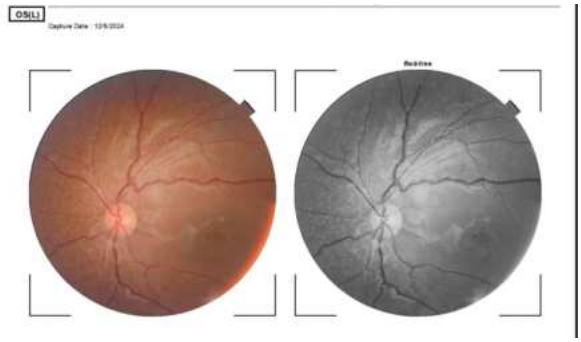

Figure 1(b) –Left Eye

Figure 1 (a,b) shows multiple flecks in all four quadrants (red free image)and macular dystrophy giving the appearance of a bull's eye.

OCT showed thinning of the fovea with disorganized and loss of integrity of the RPE line. There were multiple deposits from degenerated photoreceptors noted at the retinal pigment epithelial (RPE) layer as well as central macula thinning in both eyes; also, there was thinning of the ganglion cell complex within the macula.

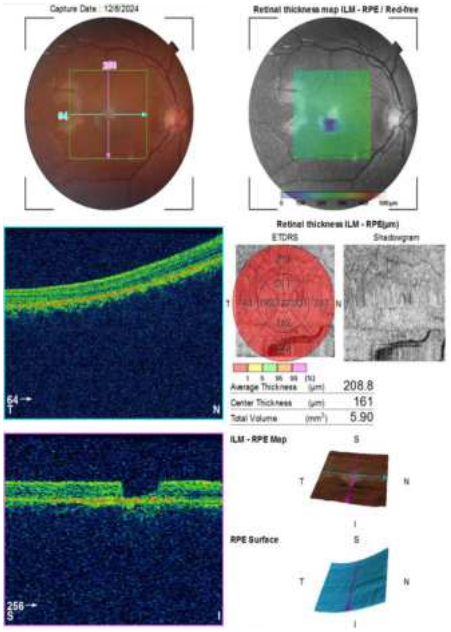

Figure 2(a)- OCT Right Eye

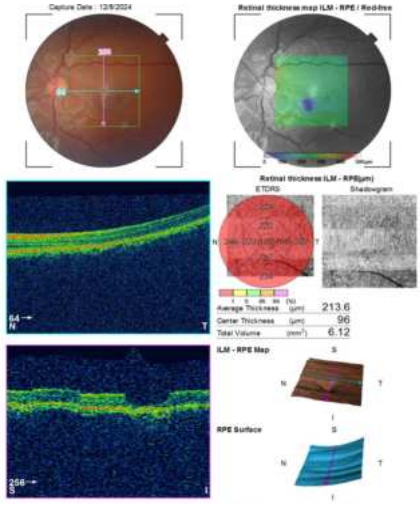

Figure 2(b)- OCT Left Eye

Figure 2 (a,b) shows the OCT images of the right eye(a) and left eye(b) depicting thinning of the fovea and disorganization of the inner segment and outer segment junction.

DISCUSSION

STGD is named after the German ophthalmologist Karl Stargardt who first reported the disease in 1909. Stargardt disease is a genetic condition caused due to ABCA4 large gene mutations. These mutations prevent the ABCA4 (ABCR) gene from production of transmembrane transporter protein which is expressed by rod outer segments. This protein is needed for vision and its deficiency eventually leads to the collection of lipofuscins in the retina (12,13). The accumulation of lipofuscin leads to the formation of flecks. In vivo, study results have shown that patients with STGD1 have 2 to 5 times the amount of lipofuscin compared to the age-matched controls (14). The disease is associated with slow, progressive damage to the RPE cells and overlying photoreceptors, leading to decreased central visual function, color vision, and dark adaptation, developing within the first two decades of life (15).

The age of onset, the clinical presentations, the fundal findings, and the degree of progression markedly affect the course of the disease (1). A landmark project, The Progression of Atrophy Secondary to Stargardt Disease (ProgStar) study, based on prospective and retrospective analyses, reported no significant change in best corrected visual acuity (BCVA) during a 12-month follow-up (16) and a clinically small BCVA loss over 24 months (17).

Another disorder called Stargardt-like disease occurs due to a mutation in the ELOVL4 gene at 6q14.1. It is associated with autosomal dominant spinocerebellar ataxia, autosomal recessive disorder congenital ichthyosis, spastic quadriplegia, and impaired intellectual development (18).

No treatment modality is recommended to prevent or reverse visual loss in patients with STGD1. Photoprotection can be used to delay the disease progression and low vision aids for those with visual field loss. Proper refractive correction should be prescribed. Intravitreal anti-vascular endothelial growth factor (VEGF) injections are the preferred treatment modality for patients who develop CNVM (18). Various ongoing Pharmacological Therapy, Gene Therapy, and Stem-cell therapy are investigating various novel therapeutic modalities for this condition (19). Genetic counseling is an integral part of managing this condition. Genes can help predict the prognosis and progression of the disease.

CONCLUSION

Stargardt disease represents one of the major causes of inherited childhood and adulthood irreversible visual impairment. Due to its high phenotypic and genotypic heterogeneity, it is a complex disease to understand. Increasingly improved non-invasive imaging techniques and biochemical and genetic advances have led to substantial forward steps in the monitoring and management of patients.

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