Case study

Stargardt's Disease Diagnosed in Adults. Case report.

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ABSTRACT

Aims: To describe a Stargardt disease, (STGD1) is an autosomal recessive inherited disease often associated with mutations in ABCA4 and characterized by the accumulation of autofluorescent lipofuscin deposits in the retinal pigment epithelium (RPE).
Presentation of Case: J.A.D.L, male, 52 years old, foreman, born in Rio de Janeiro, attends the ophthalmologic consultation complaining of progressive low visual acuity, noticed at around 31 years of age
Discussion: Stargardt disease is the most common hereditary macular dystrophy, representing 7% of retinal dystrophies. The first and only clinical manifestation is the decrease in central vision, which predominantly starts between six and fifteen years of age.
Methodology: Case report
Results: Therefore, the referral of young patients with visual complaints without initial abnormalities of the fundus of the eye for ophthalmological evaluation is essential, since the diagnosis of patients at an early stage of the disease is increasingly important with the advent of new therapeutic possibilities .
Conclusion: Although many factors contribute to the phenotype of patients with STGD1, the expression and residual activity of ABCA4 mutants play an important role in determining disease severity.
Retinal thickness and disease duration influence the visual prognosis of patients. Patients with Stargardt's disease have a smaller macular thickness when compared to normal individuals, and this reduction is related to the duration of the pathology. Therefore, OCT is fundamental for the follow-up of these patients, contributing to a better prognostic assessment of the disease.

Keywords: Autosomal recessive inheritance; Stargardt's Disease; retinal dystrophy, pisciform deposits, lipofuscin accumulation.

1. **INTRODUCTION**

Stargardt disease (STGD1) is the most common recessive macular dystrophy and is characterized by decreased central vision, atrophy of the macula and the underlying retinal pigment epithelium, and is associated with disease-causing sequence variants in the ABCA4 gene. [1-4]
It is usually inherited in an autosomal recessive way by mutations in the ABCA4 gene, located on chromosome 1, region p13-p21, whose protein product is involved in ATP-dependent membrane transport of both cones and rods, however there is great genetic heterogeneity. [2-5]
Genetically, STGD is a heterogeneous disorder usually inherited as an autosomal recessive disorder, but rarely presents as an autosomal dominant trait with a later onset of clinical symptoms. A recessive locus has been mapped to chromosome 1p (STGD type 1). [1-3] This

gene encodes a retina-specific transmembrane protein, ABCA4, which belongs to the family of membrane transporters of the ATP Binding Cassette (ABC) type. [2,3]

The retinal pigment epithelium (RPE) and the macular region's photoreceptor layer are the most compromised sites. The classic funduscopic aspect of the disease is of beaten bronze macular lesions and yellowish-white pisciform lesions known as "flecks", corresponding to the accumulation of lipofuscin in the apical pole of the RPE cells. [2,4,6,7]

The clinical features of the disease vary according to the severity of its genotype and the sensitivity of the foveal cones and retinal pigment epithelium (RPE) to this genotype. Low visual acuity is the most common clinical manifestation, ranging from 20/30 to 20/200, while the age of onset can range from 5 to 50 years of age. [2,4,6,7]

The dispersed pisciform deposits ("flecks") in the posterior pole may extend to the middle periphery, and macular alterations may be found in 50% of patients. Decreased visual acuity often precedes funduscopic changes and depends on the age of onset of symptoms, so that the later the onset, the less likely there is to be visual loss. In the late stage of the disease, far visual acuity stabilizes at approximately 20/200. [4,6,7,8]

The diagnosis of Stargardt's disease is based on clinical history and fundus changes, and complementary tests are essential in this context. Fluorescein angiography (FFA) is a widely used diagnostic method and can confirm the diagnosis of Stargardt, as hyperfluorescent pisciform lesions, varying degrees of macular atrophy, which can present an aspect of target maculopathy and choroidal silence, are more evident. it is a hypofluorescence by choriocapillary blockage, due to the accumulation of lipofuscin in the RPE, present in around 80% of the cases, which practically seals the diagnosis, although the absence does not exclude this disease.[5,8,9,10,11] Standard electroretinogram (ERG) and electrooculogram do not represent valuable diagnostic tools, as functional loss is initially restricted to retinal focal areas. Multifocal ERG has been shown to be useful in detecting foveal dysfunction in Stargardt's disease, even at early stages, being important in the diagnosis and helping to describe the topography of loss of cone activity more precisely. [2,12,13,14]

Optical coherence tomography (OCT) provides high resolution images of the retinal layers and is used to detect macular changes in retinal dystrophies. Multifocal ERG and OCT have the ability to quantify intraretinal changes in early stages of the disease, which aids in the patient's prognosis. [9.15-18]

2. CASE REPORT

J.A.D.L, male, 52 years old, foreman, born in Rio de Janeiro, attends the ophthalmologic consultation complaining of progressive low visual acuity, noticed at around 31 years of age. The picture initially manifested itself as difficulty reading traffic signs. Reports an episode of sudden visual loss lasting about 5 seconds for 8 years with spontaneous improvement.

The patient reported that, over the years, there was a worsening of visual acuity in both eyes, which was indolent and progressive, even having sought medical help, but without success. Claims good peripheral vision and a lot of difficulty focusing on objects, as central vision is blurry.

In the past pathological history, he claims to have systemic arterial hypertension. Denies diabetes, eye trauma, previous eye surgeries and any eye pathologies. Denies previous ophthalmic procedures, daily use of eye drops and family members with glaucoma.

Visual acuity (VA) with the best correction for central vision was finger count (CD) at 2.0 meters in the OD and CD at 1.0 meter in the OE. Peripheral vision was 20/150 in both eyes.

Biomicroscopy was within normal limits.

Intraocular pressure: 11/11mmHg at 12:00

Funduscopy showed regular optic discs, excavation/physiological disc ratio in AO, vascular arcades without alterations, posterior pole with bilateral white-yellow lesions of various sizes and shapes, such as round, oval or in a pisciform shape that did not extend to the middle

periphery retinal, areas of atrophy of the pigmented epithelium, without choroidal neovascularization. Retinas applied, no areas of detachment. (Figures 1 and 2)
The visual field examination had the reliability indices within normal parameters, showing areas of central scotoma in the AO and the RE with already loss of peripheral vision. (Figures 3 and 4)
Fluorescein angiography showed areas of diffuse hypofluorescence compatible with “choroid silence” and “bulls eye” hyperfluorescence in the macular region, being compatible with Stargardt's Disease in both eyes. (Figures 5 and 6)
The patient is under regular follow-up at the retinal outpatient clinic, with visual acuity maintained since the last consultation under conservative treatment. Therefore, the referral of young patients with visual complaints without initial abnormalities of the fundus of the eye for ophthalmological evaluation is essential, since the diagnosis of patients at an early stage of the disease is increasingly important with the advent of new therapeutic possibilities .

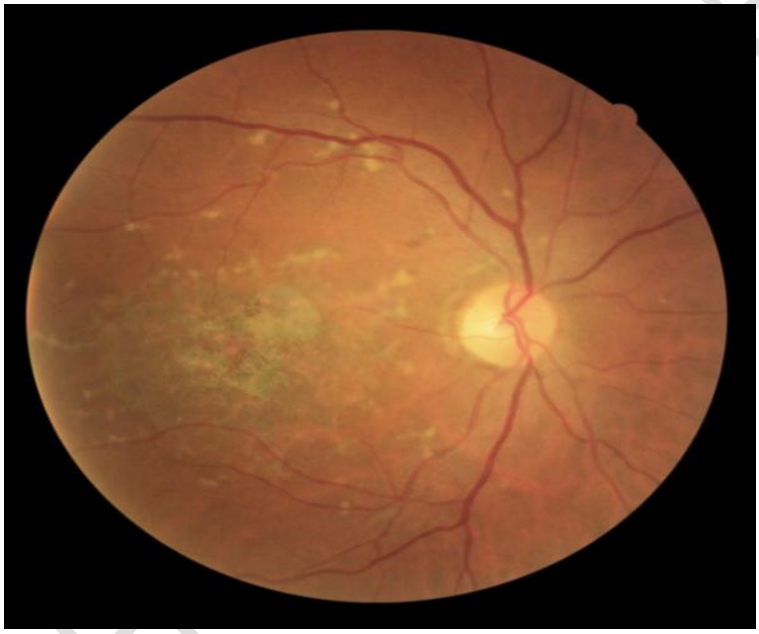

Figure 1 (Right eye retinogram)

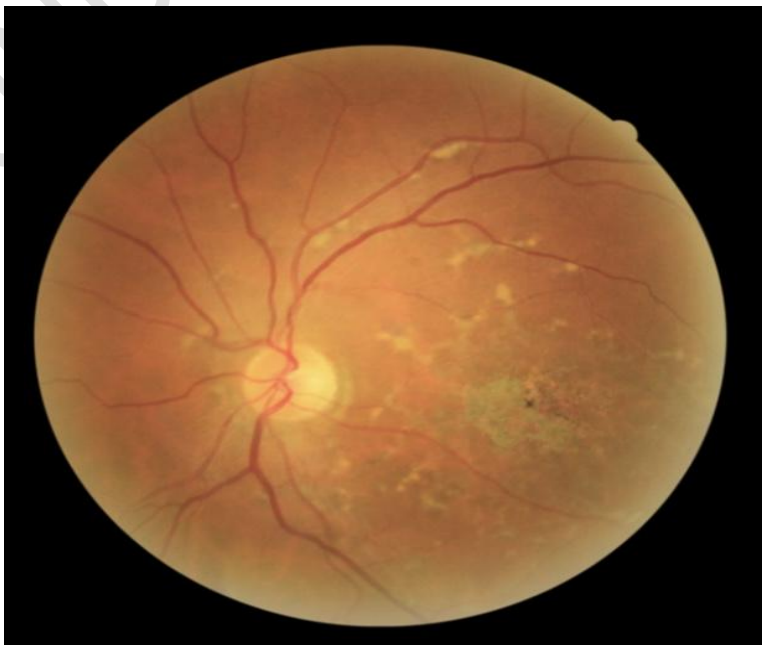

Figure 2 (Left eye retinogram)

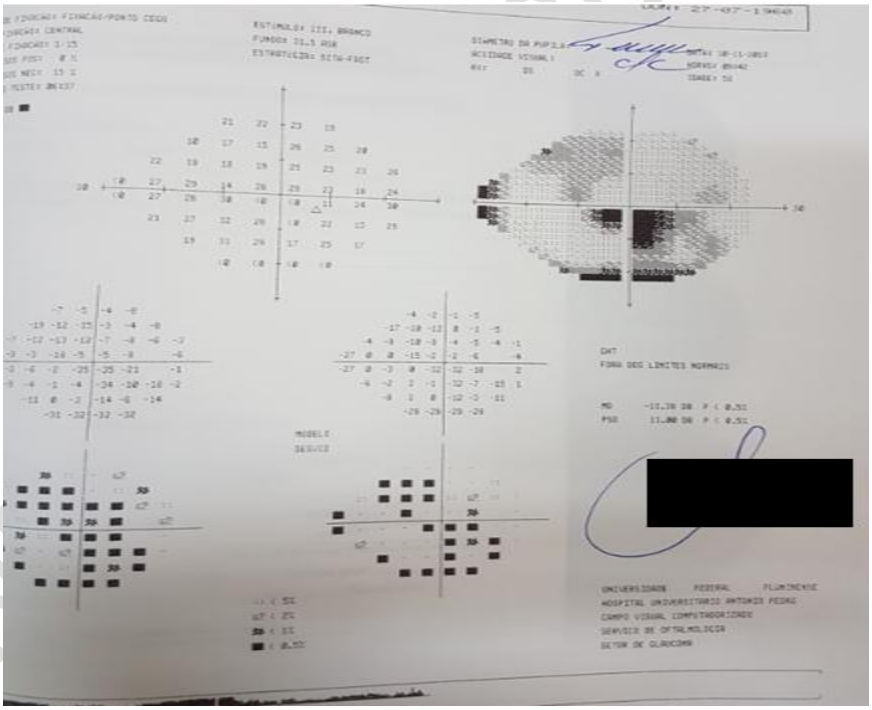

Figure 3 (Visual field 24.2 of the right eye)

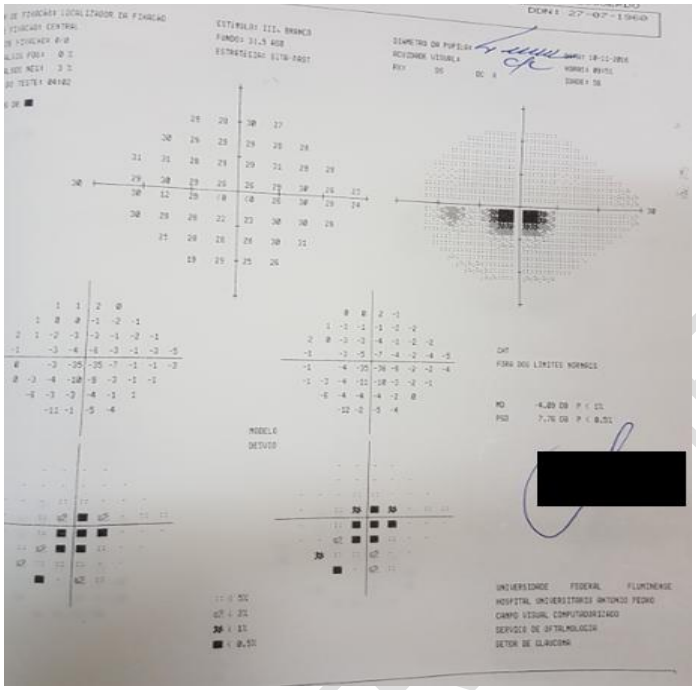

Figure 4 (Visual field 24.2 of the left eye)

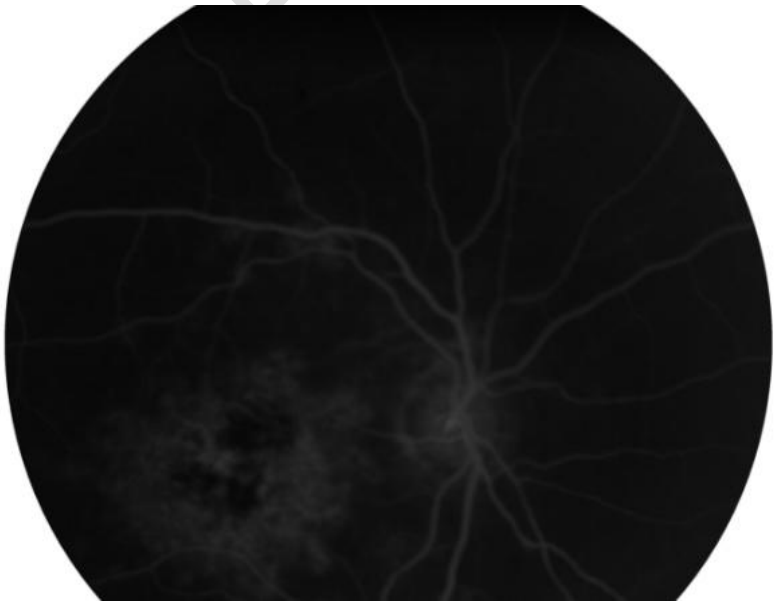

Figure 5 (Fluorescein angiography of the right eye)

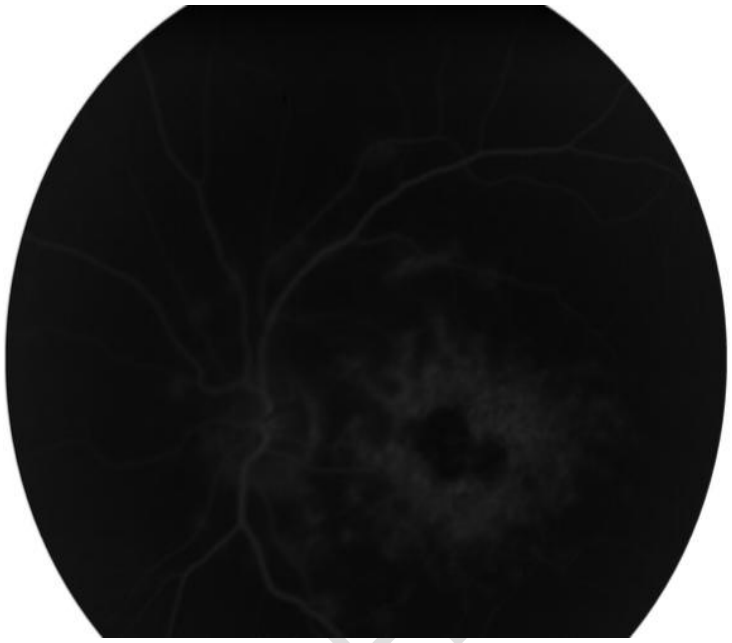

Figure 6 (Fluorescein angiography of the left eye)

3.**DISCUSSION**

Stargardt disease is the most common hereditary macular dystrophy, representing 7% of retinal dystrophies. The first and only clinical manifestation is the decrease in central vision, which predominantly starts between six and fifteen years of age.[17,19-22] In exceptional cases, as in our report, symptoms start in the third decade of life.

Findings in the fundus of the eye depend on the form of presentation and clinical course of the disease, and may, in some cases, affect older patients. In advanced stages, visual acuity varies between 20/200 to finger count. [18,21,23-25] The current visual acuity of the patient presented is similar to that found in the literature in advanced cases of the pathology, which shows that early diagnosis, good ammnesis and detailed examination are essential for early diagnosis.

Among the differential diagnoses considered, macular diseases are included, such as: X-linked retinoschisis; vitelliform macular dystrophy; progressive cone dystrophy; familiar druse; and fundus albipunctatus. [14,22,24-27] All these pathologies were excluded in the patient in the present report.

Retinal degeneration observed in Stargardt's disease is believed to be caused by the accumulation of lipofuscin in the RPE, resulting in death of RPE cells and photoreceptors, leading to atrophic lesions seen in the macula in the late stage of the disease. described.[12, 24-28]

The characteristics of STGD1 vary widely due to the marked phenotypic heterogeneity associated with the large number of disease-causing sequence variants identified in ABCA4. There are several manifestations of the disease, resulting in a spectrum of clinical

presentations, progression rates, imaging tests, psychophysical and electrophysiological findings, and variable prognosis.[15,19,22,26-29]

STGD1 commonly presents as progressive bilateral central vision loss, most often onset in childhood and a second peak incidence in early adulthood. 15-17,22,26 There is growing evidence that onset is related to the severity of underlying ABCA4 variants with childhood-onset STGD1 being associated with more deleterious variants compared with adult-onset or late-onset. [18,26,28-30]

Initially, ophthalmoscopy may reveal a normal fundus or mild retinal abnormalities, including loss of the foveal reflex or mild RPE disturbance, with or without loss of vision. Diagnosis can therefore be delayed unless retinal images with background autofluorescence, OCT and an electrophysiological assessment are performed, just as happened with our patient, being diagnosed late and documented with imaging exams already in advanced stages of the disease. illness. [14-19.30.31]

OCT provides a quantitative assessment of the retinal layers, with a good correlation between the images obtained and the corresponding anatomical structure, allowing for a better assessment of macular alterations. OCT provides high-resolution images, proving to be of great help in the assessment of macular diseases, since it is possible to objectively and accurately quantify retinal thickness, thus aiding in diagnosis and follow-up. [22.28-31]

OCT can show the loss of normal retinal architecture starting in the central macula with relative preservation of the peripheral macula in the early stages of the disease. Importantly, up to a third of children at initial presentation may not show “flecks” on funduscopy or autofluorescence.[13,18,20,22] These pisciform deposits develop over time and are associated with increased macular atrophy. another reason why the diagnosis is usually delayed, which probably happened to our patient. [2,26,29,30]

4. **CONCLUSION**

Stargardt's disease is an autosomal recessive retinal dystrophy, characterized by a dysfunction of the cones in the central region before the appearance of pisciform deposits, RPE atrophy or abnormalities in complementary exams such as OCT, fluorescein angiography, autofluorescence and full-field electroretinography. The progressive loss of bilateral central vision that can later progress to impairment of peripheral vision is characteristic.

Although many factors contribute to the phenotype of patients with STGD1, the expression and residual activity of ABCA4 mutants play an important role in determining disease severity.

Retinal thickness and disease duration influence the visual prognosis of patients. Patients with Stargardt's disease have a smaller macular thickness when compared to normal individuals, and this reduction is related to the duration of the pathology. Therefore, OCT is fundamental for the follow-up of these patients, contributing to a better prognostic assessment of the disease.

Therefore, the referral of young patients with visual complaints without initial abnormalities of the fundus of the eye for ophthalmological evaluation is essential, since the diagnosis of patients at an early stage of the disease is increasingly important with the advent of new therapeutic possibilities .

Competing interests

Authors have declared that no competing interests exist.

Authors’ Contributions

Thiago Sande Miguel : concept, design, definition of intellectual content, literature search, clinical studies, experimental studies, data acquisition.

Felipe Bekman Diniz Mitleg Rocha: design, definition of intellectual content, literature search, clinical studies, experimental studies, manuscript preparation, manuscript editing
Tais Cristina Rossett: concept, design, definition of intellectual content, literature search, clinical studies, experimental studies, data acquisition, data analysis, manuscript preparation, manuscript editing
Maurício Bastos Pereira : concept, design, definition of intellectual content, l, clinical studies, experimental studies, data acquisition, data analysis, manuscript preparation, manuscript editing and manuscript review.
Daniel Almeida da Costa: definition of intellectual content, clinical studies, manuscript preparation, manuscript editing and manuscript review.

Consent

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images

Ethical approval

It is not applicable.

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