Case Report

Late-Onset Stargardt disease; A clinical condition may be misdiagnosed: A case report

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ABSTRACT

Stargardt disease (SD) is a rare condition primarily represented by a progressive visual acuity impairment. This macular dystrophy has a wide clinical spectrum leading to a false diagnosis and may be neglected. We report a case of late-onset SD that was misdiagnosed to raise awareness of ophthalmologists about SD special in patients without fundus abnormalities. A 35-year-old female presented with progressive bilateral vision loss from 2 years ago. She had a medical history of photorefractive keratectomy (PRK) 5 years prior to presentation. All retinal and corneal medical records before PRK were normal. In the retinal exam, bilateral numerous sub-retinal yellow deposits were seen in the fovea. Optical coherence tomography showed retinal thinning and retinal pigment epithelium irregularity of fovea. Fluorescein angiography revealed a dark choroid pattern. SD is typically described in young patients but may develop later in adulthood and masquerade other macular dystrophies. We recommend referring children and young adults with ambiguous visual complaints without initial fundus abnormalities to a specialized ophthalmologic center.

Keywords: Stargardt disease, Visual acuity, Macular dystrophy, Fovea, Fundus

Introduction

Stargardt disease (SD) or Stargardt macular dystrophy has been primarily explained by a German ophthalmologist, Karl Stargardt in 1909 [1]. This autosomal recessively inherited disorder has an approximate incidence rate of 10-12.5 per 100000 persons and occurs due to mutations in the ABCA4 gene [2]. More recent investigations have described its autosomal dominant phenotypes related to mutations in PRPH2, ELOVL4, and PROM1[3]. This macular dystrophy has a wide clinical presentation leading to clinical diagnosis challenges. Progressive impairment in the visual acuity (VA) is the most significant complaint of patients that usually commences in their first or second decades of life. However, evidence has presented that late-onset SD is accompanied by better prognosis [4]. Atrophic irregular lesions in the macula and yellow-white lesions at the level of the retinal pigment epithelium (RPE), referred to as flecks are the characteristics of this disorder detected through fundus examination. The diagnosis of SD may be challenging especially in the early stage of the disease due to a lack of fundus abnormalities and clinical signs [4, 5]. Nevertheless, the information about the diagnosis, prognosis, and therapeutic approaches for this disorder is limited; although, by the emergence of new technologies including fundus autofluorescence (FAF), fluorescence angiography (FA), and spectral-domain (SD) optical coherence tomography (OCT) and psychophysical testing methods such as microperimetry a better insight regarding the development and progression of SD is available [5].

In the current study, we report a young female with progressive VA impairment who was misdiagnosed to highlight the clinical presentations and imaging features to help an ophthalmologist in timely and accurate diagnosis.

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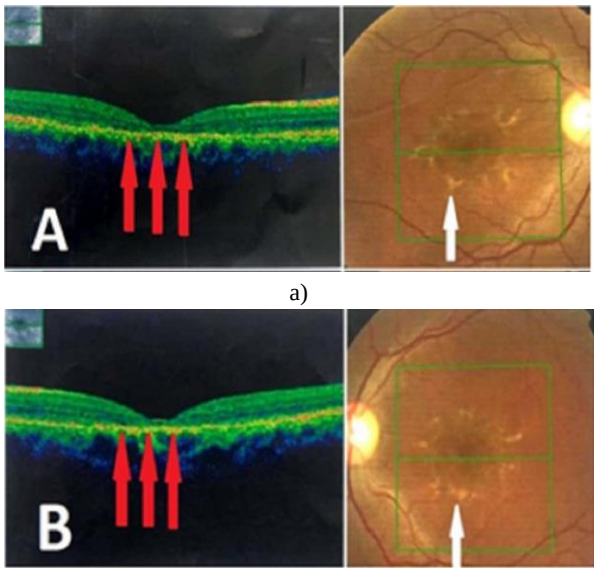
Case presentation

A 35-year-old female was referred to the Ocular Emergency Center affiliated with Yazd University of Medical Sciences with progressive bilateral painless vision loss for the past two years. The patient had a previous history of refractory surgery 5 years before. She underwent photorefractive keratectomy (PRK) for correction of a myopic refractive disorder. According to the pre-operation of her medical records; her refraction was -3 - 1× 180 degrees in the right eye and was -2.75 -0.75 ×10 degrees in the left eye without any signs of keratoconus in the corneal imaging. Fundus examination has been normal. The examination was performed using the Snellen chart in which her right and left eye's best-corrected VA were 20/30 and 20/40 respectively. The Slit-lamp examination revealed normal cornea without haze or scar and a clear lens. Dilated fundus examination showed bilateral multiple yellow flecks in the fovea **(Figure 1)**.

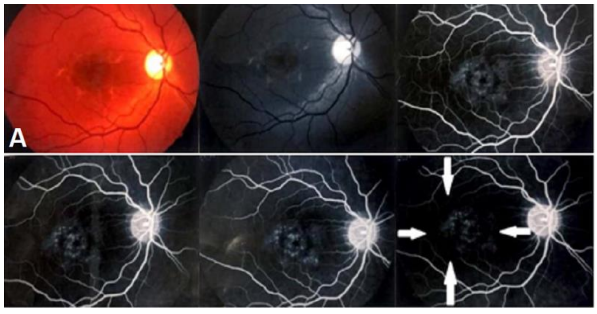


a)

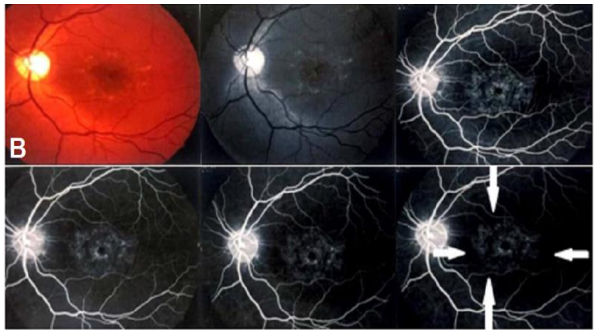
b)

Figure 1. Color fundus photographs of right eye (A) and left eye (B) show numerous yellow sub-retinal flecks in the fovea (white arrows), and Macular optical coherence tomography reveal outer retinal atrophy, fovea thinning, and hyperreflective deposits (red arrows) at the level of the retinal pigment epithelium

Corneal imaging including pentacam was normal. Also, OCT of macula revealed bilateral outer retinal atrophy and decreased thickness of fovea **(Figure 1)**. In the next step, FA was done and a presence of dark choroid was seen **(Figure 2)**. Genetic testing by target enrichment was performed and showed a pathogenic variant in the ABCA4 gene confirming the diagnosis of SD.



a)



b)

Figure 2. Fluorescein angiography of right eye (A) and left eye (B) show typical dark choroid pattern (white arrows)

Results and Discussion

SD is an inherited clinical condition that may misdiagnose due to wide clinical presentations and can masquerade other macular dystrophies. Although SD is the most common juvenile macular dystrophy, it remains a challenging cause of VA loss in children and young adults. Absence of fundus lesions at the time of presentation, lack of clinicians' experience in the detection of subtle fundus abnormalities, low capabilities for expression of vision loss, and VA fluctuation are the most common reasons for the delay in diagnosis and misdiagnosis of SD [6-11]. SD patients may present without fundus abnormalities [5, 6]. The absence of fundus abnormalities in SD may lead to unnecessary evaluations [6, 7]. In a cohort study, 31 cases (11.1%) of 280 SD patients, had no fundus abnormalities at the first ophthalmic consultation [6]. In another study, of 40 patients with SD, 14 (35%) had been misdiagnosed [5]. The primary presentation of SD is progressive vision loss, but the hallmark in diagnosis is the emergence of several atrophic lesions in the macula. Also, VA impairment may fluctuate in SD. Bax *et al*. reported VA fluctuation in 10/31 of SD patients [6]. The presentation of the disease as the most prevalent form of juvenile-onset macular dystrophy usually begins within the first or second decade of the life; however, some cases such as our case have been diagnosed at older ages [5, 6, 8-10, 12].

The diagnosis is mostly dependent on the use of instruments instead of clinical assessments. Diverse modalities have been applied to distinguish SD [5]. In FAF, typical hyperfluorescent lesions in the area of flecks and hypofluorescent in the area of macular atrophy are seen may present before typical fundus lesions. Loss of RPE and thining of outer retina were the findings in the present patient by OCT performance. This modality is another means administered to diagnose SD [6]. FA is the other administered instrument by which our diagnosis was confirmed. We found a dark choroid pattern that is a hallmark of the SD diagnosis. The dark choroid is the hallmark for the diagnosis of SD as it is presented in up to 80% of the patients. Nevertheless, it is less favored due to being invasive, and less helpful in those without fundus abnormalities as the choroid may be relatively less dark [7].

Conclusion

In conclusion, here we presented a case of late-onset SD that was misdiagnosed due to the absence of fundus abnormalities. However, this may have occurred because of the rarity of incidence and lack of experience in the detection of subtle retinal lesions. In children and young adults with visual disturbances, and VA fluctuations, even in the absence of retinal lesions, macular dystrophies should be ruled out.

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Conflict of interest: None

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Ethics statement: The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initial will not be published.

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