wjpmr, 2022, 8(6), 203-206

SJIF Impact Factor: 5.922

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Case Report

ISSN 2455-3301

WJPMR

STARGARDT DISEASE: A CASE STUDY

Kalyan Singh Maurya[1], Shitiz Saxena[2], Vineet Kumar[3], Madhulika Sinha[4], Merin Johny[5], Rajat Patel[6], Tanmay Srivastav[7]* and Deepak Mishra[8]

[1,2,3,4,5,6]Junior Resident, Regional Institute Of Ophthalmology, Bhu.
[7]Senior Resident, Regional Institute of Ophthalmology, BHU.
[8]Associate Professor, Regional Institute of Ophthalmology, Bhu.

***Corresponding Author: Tanmay Srivastav**
Senior Resident, Regional Institute of Ophthalmology, BHU.

Article Received on 25/03/2022 **Article Revised on 15/04/2022** **Article Accepted on 05/05/2022**

ABSTRACT

We report a case of Stargardt disease in fifteen year young boy who presented with diminution in vision in both eyes since his childhood. On examination circular lesion was seen at the macula with beaten bronze appearance suggestive of Stargardt disease. Stargardt disease is one of the most common causes of inherited childhood and adulthood visual impairment. Stargardt disease is both phenotypically and genetically highly heterogeneous with significant advances having been made in our ability to identify the disease at the earliest stages.

KEYWORDS: Stargardt disease, Macular dystrophy, Autosomal recessive, Lipofuschin.

INTRODUCTION

Stargardt disease is a form of juvenile inherited dystrophy of macula characterized by deposition of discrete yellowish round or pisciform flecks around posterior pole.[1] These deposits occur usually at the level of retinal pigment epithelium (RPE). It is the most common type of hereditary macular dystrophy. Although incidence of disease is not much known, approximate estimate report the prevalence rate between 1 in 8000–10000.[1–7] The inheritance mode of disease is usually autosomal recessive and mutations in the ABCA4 gene has been reported to be associated with this disease.[8–11] There is no any gender or racial predilection and is heterogeneous both in terms of clinical appearance and on genetic basis.[12–17]

Patients usually presents in first or second decade with complaint of bilateral decreased visual acuity. Late onset is associated with better prognosis.[18] A positive central scotoma and altered color perception may also be present. Visual acuity diminishes gradually to 6/60. Fundus examination reveals presence of some yellowish flecks and snail's slime aspect at macula in early stages. The disease gradually progresses to appearance of bull's eye maculopathy with atrophy of retinal pigment epithelium or beaten bronze appearance at a late stage. Changes occur mainly at posterior pole but sometimes they may affect peripheral retina as well showing disc pallor, attenuation of vessels and pigmentary disturbances.

The investigation of choice is fundus fluorescein angiography as it evidences "silence choroidien". It is a finding of silent choroid which appears dark in FFA most probably due to lipofuschin accumulation in RPE. The retinal vessels appear clearer against a hypofluorescent choroid. ERG and EOG become subnormal in late stages and visual fields also get diminished. There are other factors like genetic modifiers and environmental factors which may influence phenotype as there exists a lot of varied presentation.[19,20] There is no any proven treatment and low vision aids are usually prescribed.

Here we report a case of a 15 year young student with Stargardt's disease in both eyes.

CASE REPORT

A 15 year young boy presented with chief complaints of diminution in vision in his both eyes since childhood. He also reported gradual and progressive loss in his ability to distinguish between faces and colors and point out fine details of objects. There was no similar history in any of his siblings or first degree relatives. He neither did suffer from any chronic illness nor did he receive any prolonged medical treatment. He abstained himself from all sorts of addiction.

His general and systemic examination was within normal limits. On ocular examination, his visual acuity as per Snellen's chart was 6/36 partial in both eyes. His retinoscopy value revealed +1.00 Dsph in both the meridians in both eyes. His color vision was defective in

both the eyes as he was unable to read plates of Ishihara chart.

On distant direct ophthalmoscopy media were normal with normal red fundal glow in both eyes. On direct ophthalmoscopy, optic disc of both eyes was pale with absent foveal reflex in both eyes. Pallor was more in right eye as compared to left eye. Optic discs were normal in shape and size with well defined margins in both the eyes. Vessels arose from centre of disc with dichotomously branching pattern and with normal arteriovenous ratio of 2:3 in both eyes. An ill-defined circular lesion was seen at the macula with beaten bronze appearance which was more obvious in red free fundus photographs. Numerous small whitish flecks were seen in all four quadrants in both the eyes.(Figure 1and 2).

Visual field testing could not be done due to poor fixation of patient. On fundus fluorescein angiography, characteristic silent choroid was observed in initial stages which became more obvious in late stages as dye spread through retinal vasculature.(Figure 3) This was probably due to accumulation of lipofuschin deposits at the level of retinal pigment epithelium. Macular lesion and flecks were hyperfluorescent. Electrophysiological tests were not performed.

Patient was prescribed low vision aids as a part of his visual rehabilitation and was explained in detail about prognosis of his condition.

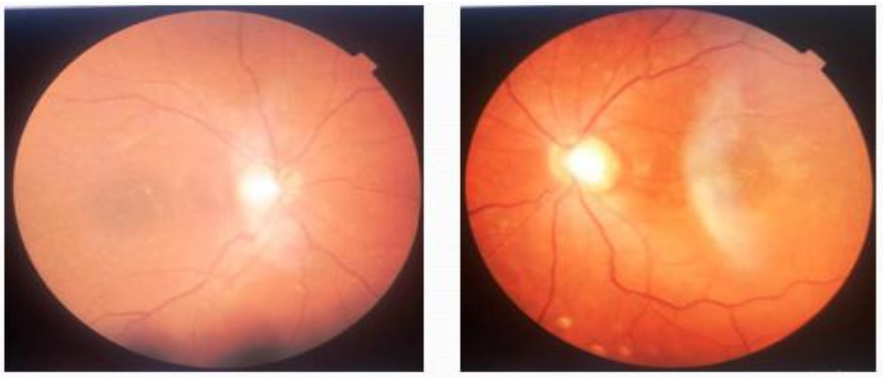

Figure 1: Fundus photographs of right and left eye.

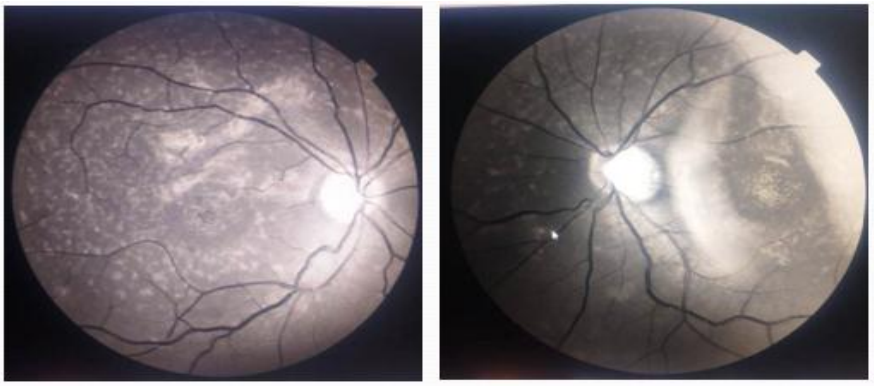

Figure 2: Red free fundus photographs of right and left eye.

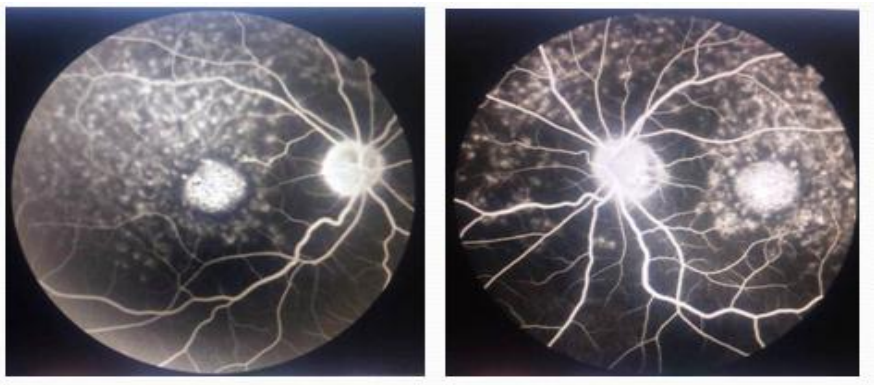

Figure 3: Fundus fluorescein angiography images of right and left eye.

DISCUSSION

Stargardt disease is genetic condition caused due to ABCA4 large gene mutations. These mutations prevent 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 collection of lipofuscin in the retina.[21,22] Mutations in ABCA4 can also cause autosomal recessive cone rod dystrophy.[23]

Some ABCR-variant alleles also enhance susceptibility to age-related macular degeneration but further studies are required in this regard.[24]

Glazer and Dryja has proposed three step pathophysiology of Stargardt's disease which states (1) defective Rim protein encoded by ABCA4 gene cause build-up of protonated N-retinyledine-PE in the outer segments of rods (2) A2E a byproduct of N-retinyledine-PE collects in retinal pigment epithelium cells and cause toxicity (3) photoreceptors ultimately atrophy owing to loss of retinal pigment epithelium support function.[25]

In most cases, the parents of people with Stargardt disease each have one damaged ABCA4 gene. A child that inherits a damaged gene from each parent will be affected. This is autosomal recessive inheritance. However the risk of a person with Stargardt disease having an affected child is very low.

There is another condition called Stargardt-like disease. It is due to mutations in the ELOVL4 gene. In this case, even one damaged gene is enough to cause the condition. This is called autosomal dominant inheritance. Stargardt-like disease can be present in multiple generations of a family. Genetic testing and counselling can distinguish between these conditions.

No treatments are currently approved to prevent or slow the vision loss associated with Stargardt disease. Low vision aids are prescribed as no other treatment is currently available.[26] However, it is important to have regular eye exams even if vision is constant in order to avoid serious but treatable complications such as macular edema.

Many researches have been carried out to propose treatments for Stargardt disease. Two types of treatment have already reached the stage of clinical trials.

Gene therapy refers to treatments that aim to place healthy genes into retinal cells, replacing the gene mutation. This might stop or slow the build-up of lipofuscin, preventing further vision loss.

A second set of trials is exploring the transplant of new RPE cells derived from stem cells to help the retina clear the lipofuscin build-up. This might prevent or slow further vision loss. Early trials of this treatment have begun.

CONCLUSION

Stargardt disease is one of the most common causes of inherited childhood and adulthood visual impairment. Stargardt disease is both phenotypically and genetically highly heterogeneous with significant advances having been made in our ability to identify the disease at the earliest stages, characterise clinical features that allow better-informed advice on prognosis, perform accurate rapid molecular genetic testing, and in our understanding of underlying disease mechanisms.

REFERENCES

1. Michaelides M, Hunt DM, Moore AT. The genetics of inherited macular dystrophies. J Med Genet, 2003; 40: 641–50.
2. Fujinami K, Lois N, Davidson AE, et al. A longitudinal study of stargardt disease: clinical and electrophysiologic assessment, progression, and genotype correlations. Am J Ophthalmol, 2013; 155: 1075–88.
3. Fujinami K, Zernant J, Chana RK, et al. Clinical and molecular characteristics of childhood-onset Stargardt disease. Ophthalmology, 2015; 122: 326–34.
4. Molday RS. Insights into the molecular properties of ABCA4 and its role in the visual cycle and stargardt disease. Prog Mol Biol Transl Sci., 2015; 134: 415–31.
5. 5 Strauss RW, Ho A, Munoz B, et al. The natural history of the progression of atrophy secondary to Stargardt disease (ProgStar) studies: design and baseline characteristics: ProgStar Report No. 1. Ophthalmology, 2016; 123: 817–28.
6. Burke TR, Tsang SH. Allelic and phenotypic heterogeneity in ABCA4 mutations. Ophthalmic Genet, 2011; 32: 165–74.
7. Lambertus S, van Huet RA, Bax NM, et al. Early-onset stargardt disease: phenotypic and genotypic characteristics. Ophthalmology, 2015; 122: 335–44.
8. Allikmets R, Singh N, Sun H, et al. A photoreceptor cell-specific ATP-binding transporter gene (ABCR) is mutated in recessive Stargardt macular dystrophy. Nat Genet, 1997; 15: 236–46.
9. Fujinami K, Zernant J, Chana RK, et al. ABCA4 gene screening by next-generation sequencing in a British cohort. Invest Ophthalmol Vis Sci., 2013; 54: 6662–74.
10. Zernant J, Schubert C, Im KM, et al. Analysis of the ABCA4 gene by next-generation sequencing. Invest Ophthalmol Vis Sci., 2011; 52: 8479–87.
11. Haji Abdollahi S, Hirose T. Stargardt-Fundus flavimaculatus: recent advancements and treatment. Semin Ophthalmol, 2013; 28: 372–6.
12. Michaelides M, Chen LL, Brantley MA Jr, et al. ABCA4 mutations and discordant ABCA4 alleles in patients and siblings with bull's-eye maculopathy. Br J Ophthalmol, 2007; 91: 1650–5.
13. Fujinami K, Lois N, Mukherjee R, et al. A longitudinal study of Stargardt disease: quantitative

assessment of fundus autofluorescence, progression, and genotype correlations. Invest Ophthalmol Vis Sci., 2013; 54: 8181–90.
14. Fujinami K, Sergouniotis PI, Davidson AE, et al. The clinical effect of homozygous ABCA4 alleles in 18 patients. Ophthalmology, 2013; 120: 2324–31.
15. Fujinami K, Sergouniotis PI, Davidson AE, et al. Clinical and molecular analysis of Stargardt disease with preserved foveal structure and function. Am J Ophthalmol, 2013; 156: 487–501.
16. Westeneng-van Haaften SC, Boon CJ, Cremers FP, et al. Clinical and genetic characteristics of late-onset Stargardt's disease. Ophthalmology, 2012; 119: 1199–210.
17. Lois N, Holder GE, Bunce C, et al. Phenotypic subtypes of Stargardt macular dystrophy-fundus flavimaculatus. Arch Ophthalmol, 2001; 119: 359–69.
18. Rotenstreich Y, Fishman GA, Anderson RJ. Visual acuity loss and clinical observations in a large series of patients with Stargardt disease. Ophthalmology, 2003; 110: 1151–8.
19. Burke TR, Tsang SH, Zernant J, et al. Familial discordance in Stargardt disease. Mol Vis, 2012; 18: 227–33.
20. Singh R, Fujinami K, Chen LL, et al. Longitudinal follow-up of siblings with a discordant Stargardt disease phenotype. Acta Ophthalmol, 2014; 92: e331–2.
21. Cremers FP, Van de Pol DJ, Van Driel M, et al. Autosomal recessive retinitis pigmentosa and cone-rod dystrophy caused by splice site mutations in the Stargardt's disease gene ABCR. Hum Mol Genet, 1998 Mar; 7(3): 355-62.
22. Maugeri A, Klevering BJ, Rohrschneider K, et al. Mutations in the ABCA4 (ABCR) gene are the major cause of autosomal recessive cone-rod dystrophy. Am J Hum Genet, 2000; 67: 960–966.
23. Rudolph G, Kalpadakis P, Haritoglou C, Rivera A, Weber BH. Mutations in the ABCA4 gene in a family with Stargardt's disease and retinitis pigmentosa (STGD1/RP19) Klin Monatsbl Augenheilkd, 2002; 219: 590–596.
24. Bernstein PS Leppert M Singh N Genotype-phenotype analysis of ABCR variants in macular degeneration probands and siblings. *Invest Ophthalmol Vis Sci*., 2002; 43: 466–473.
25. Glazer LC, Dryja TP. Understanding the etiology of Stargardt's disease Ophthalmol Clin North Am, 2002 Mar;15(1): 93-100.
26. Fishman GA, Farber M, Patel BS, et al. Visual acuity loss in patients with Stargardt's macular dystrophy.Ophthalmology, 1987 Jul; 94(7): 809-14.