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CASE REPORT
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BEST1 is a Rare One

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ABSTRACT

MRCS syndrome caused by a BEST1 mutation, which was described in one family, is characterized by microcornea, rod–cone dystrophy, early-onset cataract, and posterior staphyloma. The present case aims to gather data on this rare genetic disorder and help pave the way for therapy in future. MRCS syndrome caused by a BEST1 mutation, which was described in one family, is characterized by microcornea, rod–cone dystrophy, early-onset pulverulent cataract, and posterior staphylomaAt present, no definitive therapies or treatments exist for patients with bestrophinopathies. Investigation of MRCS syndrome in patients will promote better rehabilitation and monitoring of patients. An early treatment could help to avoid the effect of long term desensitization of optic nerve and amblyopia

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Key Words
Mutation
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INTRODUCTION

Mutations in the *BEST1* gene are causally associated with an increasing number of inherited ophthalmic diseases, which have collectively been termed "bestrophinopathies"[1]. MRCS syndrome caused by a BEST1 mutation, which was described in one family, is characterized by microcornea, rod–cone dystrophy, early-onset cataract, and posterior staphyloma[2]. We present a case of a 29 year old male who presented to our OPD with complaints of progressive diminution of vision. The clinical characteristics and ultrasonography help in diagnosis. The present case aims to gather data on this rare genetic disorder and help pave the way for therapy in future.

CASE REPORT

A 29 year old male presented to Ophthalmology outpatient department with complaints of diminished vision in left eye since childhood, which is more at night. It was gradually progressive and painless. In the right eye, he gave a history of ocular trauma in childhood which led to loss of vision. The patient gave a history of similar complaints in the eye of his sister in a with other four siblings having normal sight. He also has two kids with the male child having similar eyes. There is no history of use of spectacles. Rotatory nystagmus was observed.

UCVA in the left eye was 1/60 finger counting. Near vision by Jaeghar's chart was defective. By ishihara chart, the patient could not read the first plate.

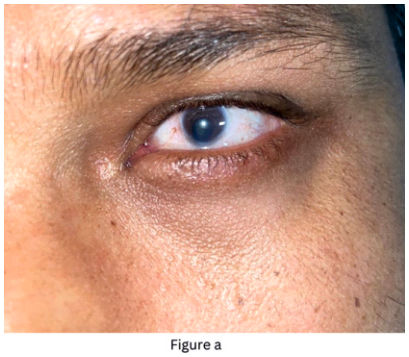

Figure a

Slit lamp examination of the left eye showed ocular appendages to be within normal limits. Sclera and conjunctiva were normal. Cornea was round with a diameter of 6 mm. Anterior chamber was shallow with a von-herrick grading of 2. Iris coloboma was present inferno-nasally. The pupil was keyhole shaped and reactive (Figure a). Upon pharmacological mydriasis, lenticular opacity was present inferiorly in the lens

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(Figure b). Indirect ophthalmoscopy revealed hyperpigmentation patches at the macula. Posterior staphyloma at the disc was observed. Retino-choroidal coloboma of type 6 by Lingam Gopal classification was observed. Retinal blood vessels were attenuated and peripheral retina had pigmentations. B-scan of the left eye showed increased axial length (28.7 mm) with posterior staphyloma at disc, calcification at the medial chorio-retinal junction with few thin echogenic membrane seen in posterior chamber which move on oculokinetic movement and calcification foci in the lens suggestive of cataractous changes (Figure c). Intraocular pressure by applanation was 20mm Hg.OCT imaging showed RPE mottling temporal to the coloboma (Figure d). Slit lamp examination of the right eye showed normal ocular appendages, sclera and conjunctiva. Leucomatous corneal opacity was present all over the cornea.

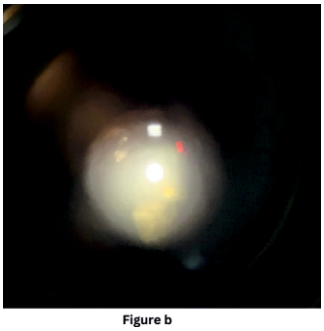

Figure b

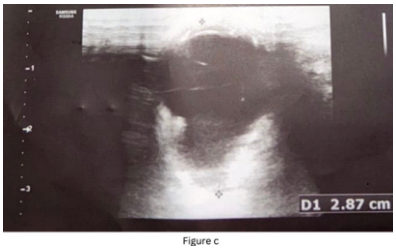

Figure c

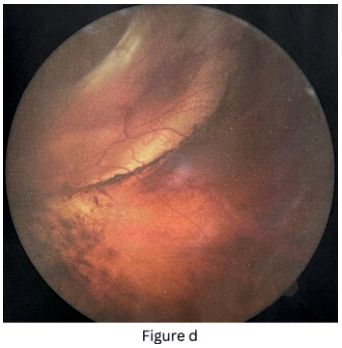

Figure d

BCVA in the left eye by +10D lens was 3/60 finger counting. Cataract surgery was postponed, as amblyopia was suspected, until further visit as the benefits outweighed the harm.

Putting together all these findings, a diagnosis of MRCS syndrome was made. The patient was prescribed refractive correction and was asked to come back for follow-up after 6 months.

DISCUSSION

MRCS syndrome is characterized by[3,4,2]

- Autosomal dominant mode of inheritance,
- Hyperopia,
- Microcornea,
- Early-onset pulverulent cataract,
- Narrow anterior chamber angle,
- Rod-cone dystrophy,
- Posterior staphyloma in eyes with otherwise normal axial lengths;
- Peripheral RPE atrophy and retinal pigmentary abnormalities anterior to the posterior staphyloma in younger patients, which may extend to the posterior pole and staphyloma with advancing age,
- Abnormal EOG,
- Subnormal ERG findings

MRCS syndrome caused by a BEST1 mutation, which was described in one family, is characterized by microcornea, rod–cone dystrophy, early-onset pulverulent cataract, and posterior staphyloma[2]. In the first decades, visual acuity may be fairly good, but beyond the age of 30 years visual acuity often becomes poor (less than 20/100 to absent light perception)[2]. A decrease of visual acuity, presumably due to progressive cataract and possibly photoreceptor dysfunction, may be noted before the age of 30 years, often leading to cataract surgery in the second or third decade[2]. On ophthalmoscopy, peripheral RPE atrophy and retinal pigmentary abnormalities are seen anterior to the posterior staphyloma in younger patients, whereas atrophy and pigmentary changes may extend to the posterior pole and staphyloma with advancing age[2]. Progressive decrease in visual acuity worsens after the age of 30 years, often leading to cataract surgery in the second of third decades; final visual acuity usually ranges from 20/100 to absence of light perception[4] . Although posterior staphyloma in an eye with normal axial length is the most common finding, some patients with a Val239Met BEST1 mutation had nanophthalmos instead of staphyloma, largely overlapping with the ADVIRC phenotype[4] Although the MRCS syndrome is generally more severe than ADVIRC, these conditions overlap and likely form a continuum, as both of these BEST1-related conditions show retinal pigmentary abnormalities, retinal dystrophy, microcornea, and early-onset cataract[2,5].

Differential Diagnosis

Other syndromes of bestrophinopathies must be ruled out when considering a diagnosis of MRCS syndrome. These include Best vitelliform macular dystrophy, adult-onset foveomacular vitelliform dystrophy, Autosomal recessive bestrophinopathy, Autosomal dominant vitreoretinochoroidopathy, Retinitis Pigmentosa and age-related macular degeneration .

TREATMENT

At present, no definitive therapies or treatments exist for patients with bestrophinopathies.

A more practical prophylactic approach, applying YAG laser iridotomies in patients with narrow anterior chamber angles at risk for angle-closure glaucoma, appears a rational and feasible alternative that is at present possible in these cases. Cataract extraction may be successfully performed in patients with disturbing lens opacities.

In vitro studies have found that in ARB mutants with mislocalized Best1 protein and proteasomal degradation, treatment with two proteasome inhibitors, 4-phenylbutyrate and bortezomib, rescued the location of Best1 to the basolateral plasma membrane in MDCK-II cells, and restored chloride conductance[6].

In vitro studies using RPE stem-cells derived from patients with BVMD suggested that valproic acid therapy with or without combined rapamycin could increase the rate of photoreceptor OS degradation[7].

Low Vision Aids:

High-plus spectacles are convex (plus) lenses mounted in a spectacle frame. They provide maximum magnification when objects are positioned at or near the focal distance of the lens, producing parallel rays and the image forming at optical infinity[9,10].

Hand-held magnifiers are convex lens from +4.0D to +40.0D produces an erect, virtual, and magnified image. This is useful for short-time tasks in patients with the field of vision reduced to 10 degrees or more[9].

Stand magnifiers are convex lens which form a virtual, magnified image at a short distance from the lens. The magnifier needs to be held over the reading material and moved across it[10].

Telescope systems for near, or telemicroscopes, are distance telescopes that can be focused from infinity to near range or that can be modified by putting a reading cap over a distance unit[11].

CONCLUSION

Investigation of MRCS syndrome in patients will promote better rehabilitation and monitoring of patients. Consanguinity should be sought in affected individuals. Our case report shows a patient with microcornea and iris coloboma diagnosed to be MRCS syndrome. So, any such patient suspected of having retinal dystrophy must receive complete evaluation and early treatment to avoid the effect of long term desensitization of optic nerve and amblyopia .

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