

A case report of children of the same family presenting with congenital cataract- as part of a rare genetic disorder—Sengers Syndrome

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Sengers syndrome is a rare autosomal recessive mitochondrial disorder characterized by congenital cataract, hypertrophic cardiomyopathy, and mitochondrial myopathy. We report two siblings with known mutation for Sengers Syndrome (AGK gene mutation) who presented to us with cataract and hypertrophic cardiomyopathy. They have a deceased elder sibling who was operated for cataract earlier.

Key words: AGK gene, congenital cataract, hypertrophic cardiomyopathy


Sengers syndrome, first described by Sengers in 1975, is a rare autosomal recessive mitochondrial disease characterized by congenital cataract, hypertrophic cardiomyopathy, and mitochondrial myopathy (muscle weakness and lactic acidosis after exercise).^[1] To this date, approximately 40 cases have been described worldwide.^[2,3] Genetically, Senger syndrome is classified as a DNA depletion syndrome (DDS type 10).^[4] The mutation of the AGK gene (acylglycerol kinase) has been identified in Sengers syndrome. The clinical spectrum varies,

ranging from a benign slowly progressive form with survival up to the 4th decade (AGK splice site variant) to a lethal form where there is death at infancy (homozygous AGK nonsense mutation).^[3] AGK is responsible for converting diacylglycerol (DAG) and monoacylglycerol (MAG) to phosphatidic acid and lysophosphatidic acid. AGK mutation leads to the accumulation of DAG and MAG that form reactive oxygen species that damage organs containing mitochondria.^[5] The lipid composition of inner mitochondrial membrane changes affecting respiratory chain complexes, adenine nucleotide translocator, and protein import.^[3,6] The mutation presents with a wide spectrum of phenotypes that may include central nervous system involvement,^[6,7] growth retardation,^[8] nystagmus, and strabismus.^[9]

Case Report

A family presented to us with complaints of vision defects and heart defects among their children. The parents were third-degree consanguineous [Fig. 1]. The genomic study of their children was done. A total of 98 genes known to be associated with Sengers Syndrome have been analyzed and two of the siblings showed a homozygous AGK gene mutation (chromosome 7) known to be pathogenic for Sengers syndrome.

Our index case was their youngest child who was five months old. The parents complained that the child did not fix at mother or other objects since birth and they had noticed a white reflex since two months of age. The child was born at term by LSCS with a birth weight of 2.7 Kg (5.95 lbs) and normal Apgar score. The child had attained other milestones appropriate for the age. The family pedigree revealed an elder sibling who was operated for cataract at the age of 2 years and died at the age of 8 years following short febrile illness and respiratory difficulty. Another surviving sibling with similar complains was diagnosed to have cataract in both her eyes at the age of 2 years. Upon examination of our index case, the child could not fix and

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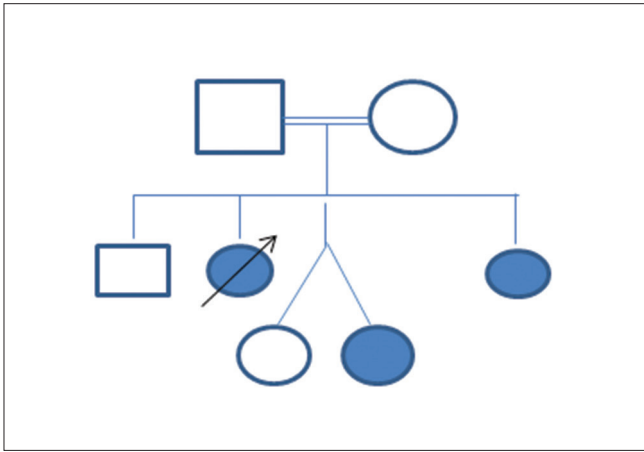


Figure 1: Pedigree chart showing affected children in the same family

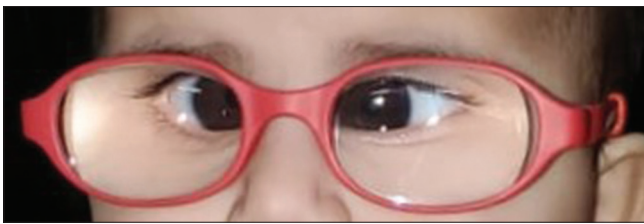


Figure 3: Postoperative photo of the index case showing good fixation with aphakic glasses

follow light. A horizontal pendular nystagmus was noted in both eyes. The lens appeared to be opacified suggestive of total cataract in both eyes [Fig. 2]. Fundus could not be visualized owing to an opaque media. B scan ultrasonography revealed a cataractous lens and a normal fundus. The examination by a cardiologist and an echocardiography revealed mild concentric hypertrophy of the left ventricle. Cataract surgery was done for one eye followed by other within 2 weeks under moderate risk for anesthesia. Considering the fact that the patient is a risk for general anesthesia and the age of the child, both the eyes were left aphakic. Following surgery, the patient was seen to fix and follow light and nystagmus had improved. Aphakic glasses were given to the child [Fig. 3].

The other sibling with AGK gene mutation was examined. She was 5 years old, second of a twin birth, and had mild developmental delay compared to her twin sister. The parents complained that she had diminution of vision since early childhood and was diagnosed with cataract in both eyes at 2 years of age. Upon examination, the best corrected visual acuity was 6/36 in both eyes by Snellens testing. Anterior segment examination revealed lamellar cataract in both eyes [Fig. 4]. Fundus examination was normal. Echocardiography by cardiologist revealed severe concentric hypertrophy of left ventricle putting her at high risk for anesthesia. Considering she had a BCVA of 6/36 in both eyes and a lamellar cataract as opposed to her younger sibling with total cataract, cataract surgery was refrained for the time being and regular follow up was advised.

Discussion

Sengers syndrome is a rare autosomal recessive mitochondrial disorder. As seen in this family, the patients variably present

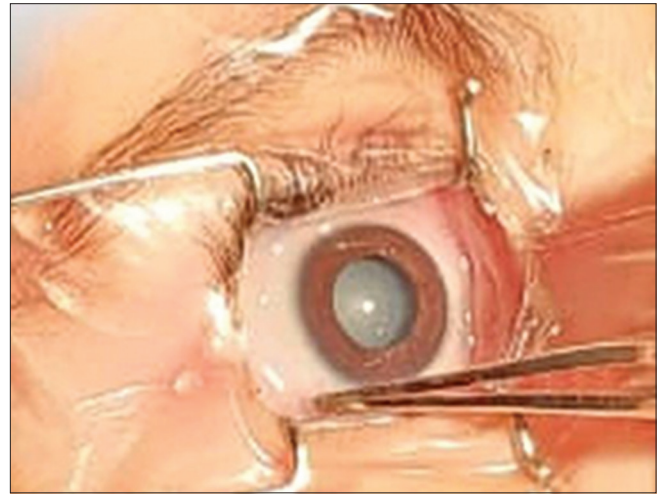


Figure 2: Intraoperative photo of the index child showing total cataract of the right eye

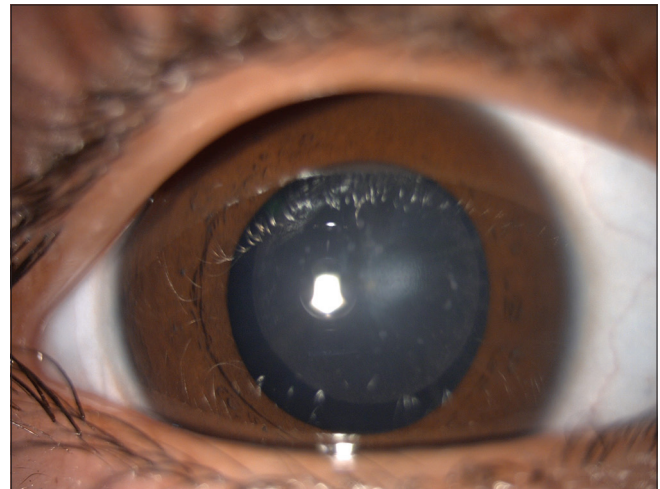


Figure 4: Anterior segment photo of the elder sibling showing lamellar cataract

with cataract, hypertrophic cardiomyopathy, and myopathy. In this case, it was seen that an elder sibling presented with lamellar cataract whereas the younger sibling presented with total cataract, concluding that though cataract is a common entity in Sengers syndrome, the type may vary. It was also seen that mild hypertrophy of the left ventricle was seen in the younger sibling compared to elder sibling who showed severe hypertrophy putting her at a greater risk for general anesthesia. It can be implied that increasing age may increase the severity of hypertrophic cardiomyopathy; hence, an earlier detection can ensure a risk-free cataract surgery.

Sengers syndrome, as it is known, rarely ensures a survival beyond 4th decade and^[3] most succumb to cardiac failure. However, timely cataract surgery can add value to their lives. The standard treatment regimen consists of cataract surgery and medical management of cardiomyopathy.

Genetic counseling becomes very important in these cases. The parents have been counseled about prenatal genetic testing in future pregnancies. The surviving children have

been asked for periodic follow up with cardiologists. The children have not shown any signs of lactic acidosis yet but the parents have been counseled regarding the symptoms of the same.

Conclusion

Though extremely rare, Sengers syndrome may be underdiagnosed due to the lack of genomic testing. This family lost a child to Senger syndrome before the other siblings were diagnosed with same. It is concluded that any child presenting with congenital cataract and hypertrophic cardiomyopathy needs to be evaluated thoroughly including genomic testing whenever possible.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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