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## A RARE CASE OF SIMPLE HEREDITARY RECESSIVE OPTIC ATROPHY

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**ABSTRACT**

Simple Autosomal Recessive Optic Atrophy (AROA) is a rare hereditary disorder that belongs to a group of disorders called Hereditary Optic Atrophy. Patients diagnosed with simple AROA have complete blindness since birth or from first few months of life. This blindness does not improve with age. However, no other organ or system is affected in this disorder. There is no known cause or gene mutation associated with it. Here we report a case of a two year old child diagnosed with simple AROA. Family history of the patient revealed that an older deceased relative also suffered from similar symptoms. Identification of this and similar cases of the simple AROA can help us better understand this disorder and hopefully one day help us develop a treatment for it.

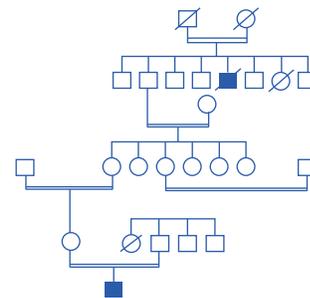
**INTRODUCTION**

Hereditary optic atrophy (HOA) are a group of disorders that present with optic atrophy as an isolated symptom or along with complex multi-systemic disorders<sup>(1, 2)</sup>. HOA includes: 1) simple Autosomal Recessive Optic Atrophy (AROA), 2) Autosomal Dominant Optic Atrophy, 3) Behr's syndrome and 4) Leber's hereditary optic neuropathy. Optic atrophy is also a symptom of other disorders for example Friedreich's ataxia and Wolfram syndrome etc<sup>(1)</sup>. The most frequent and well-known HOA disorders are the autosomal-dominant optic atrophy and Leber's hereditary optic neuropathy<sup>(3)</sup>. In a typical case of simple AROA, blindness is present at birth, with associated pale optic disk and cupping, proliferation of astrocytes, decreased retinal vasculature and occasionally pendular nystagmus<sup>(2, 4)</sup>. One study mapped the disease-causing gene to chromosome 8q21-q22; however no particular gene or mutation could be associated with disorder<sup>(5)</sup>. In another study, mutation in the TMEM126A gene was associated with AROA<sup>(6, 7)</sup>. Although severe visual loss manifest in early childhood in these patients, sensory-motor axonal neuropathy and sensorineural hearing defects also occurred in some cases, making the findings of this study possibly not relevant to simple AROA<sup>(6)</sup>. Here we report a rare case of simple AROA, who has clinical features and family history suggestive of simple AROA.

**CASE REPORT**

A two year old patient presented in Pediatric Neurology clinic of Aga Khan University Hospital in September

2014, with complaint of congenital blindness. The parents first noticed the symptoms when the child was three to four months old. The child did not follow the finger or blinked when exposed to light. Hearing and speech development was normal. The child's interaction with other children and family members was normal, indicating normal intellectual development. The child resulted from a normal conception. Normal delivery occurred after nine months of uneventful-pregnancy. The child did not have any major trauma during development.



**Figure 1.** A detailed pedigree of a child diagnosed with autosomal recessive optic atrophy. The great grand-uncle of the affected child was the only other individual diagnosed with simple AROA.

There was also no history of seizures, meningitis, encephalitis or any other neuro-developmental disorders. A detailed family history revealed that the child's parents have a consanguineous marriage. The child's great grand-uncle also had congenital blindness, similar to this child. The great grand-uncle was also normal in every other way and died at the age of 50 years.

**Figure 2.** MRI of the transverse section of the brain. The thickness of both right and left optic nerve was 0.9mm, while the optic chiasm measures 2.4mm. These values are significantly less than those observed in normally developing children of this age.



A detailed pedigree of this child is shown in figure 1. At the time of presentation in clinic the child's general and detailed neurological examination were unremarkable, except for complete visual loss. A detailed ophthalmological exam revealed bilateral pale optic disk with indications of cupping and severe thinning of retinal vasculature. Magnetic Resonance Imaging of the child's brain showed significant thinning of the optic nerves and chiasm (figure 2). After careful consideration of all the clinical, radiological and laboratory parameters the patient was diagnosed as a case of simple AROA.

## DISCUSSION

Compared to Autosomal Dominant Optic Atrophy, Behr's syndrome and Leber's hereditary optic neuropathy, the simple AROA is a very rare disorder with no known cause or treatment options. In a study published over a decade ago, the mutation for simple AROA was mapped to chromosome 8q<sup>(5)</sup>. Another study found an association between mutation in TMEM126A gene and simple AROA<sup>(7)</sup>. However, some of the patients carrying mutation in TMEM126A gene were also reported to have sensory-motor axonal neuropathy and sensorineural hearing defects, making the diagnosis of simple AROA unlikely<sup>(6)</sup>. Therefore, it is fair to conclude that the mutation for simple AROA remains undiscovered. Here we report a case of a two year old child diagnosed with simple AROA independently by a neurologist and an

ophthalmologist. The identification of more such cases can be very helpful in improving our understanding of this disease and help us develop better diagnostic techniques and treatment strategies.

## CONCLUSION

We have reported a rare case of simple AROA diagnosed in a two year old child with a family history also suggestive of this diagnosis. Identification of similar cases can help us develop a better understanding of this disease and possibly help in developing a treatment strategy.

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**Author's contribution:**

**Fazal M Arain:** Study concept and design, data collection, data analysis, manuscript writing, manuscript review

**Prem Chand:** Study concept and design, data collection, data analysis, manuscript review

**Tanveer A Choudary:** Data analysis, manuscript writing, manuscript review