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Segmental Optic Atrophy with Adrenoleukodystrophy ABCD1 Gene Variant

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ABSTRACT

We report a case of Adrenoleukodystrophy ABCD1 gene variant presenting with segmental optic atrophy in a 34-year-old male.

The patient presented to our Neuro-Ophthalmology clinic with complaints of defective vision in both eyes, mild headache and gait disturbances. Ocular examination showed best corrected visual acuity of 6/24 in both eyes and fundus examination revealed temporal pallor of optic disc. Systemic examination revealed spastic paraparesis. Neuroimaging was advised which revealed well defined confluent symmetric bilateral T2/FLAIR hyperintense areas in parietal-occipital deep white matter and in the splenium of the corpus callosum, acoustic and optic radiations bilaterally. Genetic testing was positive for ABCD1 c.1966T>C (p.Ser656Pro) gene variant.

X-linked adrenoleukodystrophy (X-ALD) is a rare neurodegenerative disease characterized by genetic mutation of the ABCD1 gene, primarily affecting males. Our patient presented with defective vision and walking problem due to Adrenoleukodystrophy ABCD1 gene variant. Ocular symptoms often occur after the systemic abnormalities are noted.

KEYWORDS: X-linked adrenoleukodystrophy, ABCD1 gene, segmental optic atrophy

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INTRODUCTION

The most common leukodystrophy is X-linked Adrenoleukodystrophy (X-ALD), a peroxisomal disease with an incidence ranging from 1:15,000–20,000[1,2] to 1:40,000–50,000 males [2,3].

The presentation can be mild impairment in the vibration sensation in lower limbs or when severe can present as progressive quadriparesis. Presentations can also be due to adrenal insufficiency. There can be learning and communication disabilities,vegetative state, and death [4] . ABCD1 gene is the only identified most common association of X-ALD. The exact etiology of this disease is unknown, and no standard treatment is available. Stem cell therapy in early diagnosed cases has shown significant results.

CASE HISTORY

A 34-year-old male, with a known history of Addison's disease presented to our neuroophthalmology clinic with complaints of defective distance and near vision in both eyes which was gradual in onset, progressive in nature for 1 year. Other complaints were headache occasionally (2-3 times a week), back pain, knee pain and difficulty in walking for the past 4 years.

Patient was diagnosed to have Addison's disease 5 years ago and is on treatment with low dose oral steroids for the past 5 years. There was no history of consanguinity in the parents. His elder brother and 2 maternal male cousins had similar history.

On examination, he had hyperpigmentation of skin. Best Corrected Visual Acuity (BCVA) was 6/24 in both eyes. Intraocular Pressure (IOP) were normal in both eyes. He could read only base plate in Ishihara's color plate test in both eyes. Extraocular movements were full in all gazes. Anterior segment examination was normal in both eyes. Both pupils were 3.5mm in size and showed ill sustained reaction to light. Fundus examination revealed temporal pallor of the optic disc in both eyes. Central field test revealed right homonymous hemianopia.

On neurological examination he was found to have spastic paraparesis and Romberg's sign was positive. His MRI brain and orbit with contrast revealed leukodystrophy, bilateral optic atrophy and optic chiasm thinning. Genetic testing utilizing the Next Generation Sequencing was positive for ABCD1 c.1966T>C (p. Ser656Pro) gene variant.

Patient was referred to the neurologist. Multivitamin tablet and Lorenzo's oil were advised to prevent the further

progression of the disease. Low vision aids were advised, and genetic counselling was given.

DISCUSSION

X-ALD is a rare neurodegenerative disease and can present as Addison's disease in the earlier stages. This primary adrenal insufficiency occurs due to accumulation of very long chain fatty acid (VLCFA) in the adrenal gland. It primarily affects males (incidence 1 : 16,800)[5], as reported in our case. Skin hyperpigmentation was seen in our patient. Addison's disease clinically presents with hyperpigmentation, often seen in ALD[6]. Additional presentation involves visual defects, including visual field defects, loss of visual acuity and cortical blindness [7]. In our patient, the ophthalmic assessment showed reduced visual acuity, color vision defect and homonymous hemianopia was found when testing the central fields. The degenerative changes in the brain causes neurological symptoms followed by vision problems, as observed in our patient.

Clinical presentation, VLCFA levels and neuroimaging help in the diagnosis of ALD. In our patient, an MRI brain scan showed well defined confluent symmetric bilateral T2/FLAIR hyperintense areas in parietal-occipital deep white matter, the splenium of the corpus callosum, acoustic and optic radiations bilaterally.

Lorenzo's oil is used prophylactically in asymptomatic patients. It is presumed to normalize the levels of VLCFA (C24:0 and C26:0) in plasma levels of X-ALD. However, no significant effects on the progression are seen in patients with pre-existing neurological symptoms[8].

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