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# X- LINKED ADRENOLEUKODYSTROPHY IN 11 YEAR OLD BOY: A RARE CASE REPORT.

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**ABSTRACT** Adrenoleukodystrophy is an X linked genetic disease, which consists of an alteration of the metabolism leading to accumulation of fatty acids of a very large chain (AGCML) associated to demyelinization of axons and adrenal insufficiency. It may initially manifest with alterations of behavior, hearing, vision, speech, writing, gait, and in the more advanced cases, it results in generalized hypertension, loss of cognitive and motor functions and dysphagia. The diagnosis is confirmed by dosing the AGCML's plasmatic levels, findings of the Magnetic Resonance and karyotype.

**KEYWORDS :**

## INTRODUCTION

X-ALD is a neurometabolic disorder that primarily affects the central nervous system, white matter and the adrenal cortex, which is caused by a defect in the ABCD1 gene encoding the adrenoleukodystrophy protein (ALDP), a transporter present in the peroxisomal membrane. ALDP defects lead to accumulation of saturated VLCFA, such as hexacosanoic acid , in the adrenal glands and nervous system, white matter and other tissues, and in plasma[1]. X-linked adrenoleukodystrophy leads to demyelination of the nervous system, adrenal insufficiency, and accumulation of long-chain fatty acids. Most young patients with X-linked adrenoleukodystrophy develop seizures and progressive neurologic deficits, and die within the first two decades of life. With an estimated birth incidence of 1 in 17,000 newborns (male and female), X-ALD is the most common peroxisomal disorder.

## CASE REPORT

An 11 yr old boy presented to the OPD with complaints of difficulty in walking for the last two months, insidious onset, used to limp in the beginning but has progressed to a current stage where he cannot walk and needs support for routine activities. No history of pain in any limb, fever, localized swelling. He also complained of difficulty in hearing, decreased vision and abnormal speech for the last one month. There was no history of seizures, ear ache or ear discharge or any other constitutional symptoms. On examination, his general physical examination was normal. His hair was abnormal that it would sway to any side. His speech was slurred. He could not follow light and there was no perception of light. Hearing tests pointed towards bilateral sensory neural hearing loss. Muscle tone was increased symmetrically in all four limbs. His deep tendon reflexes were brisk in all four limbs and plantars were upgoing. Ankle clonus and knee clonus could be elicited bilaterally. We could not do a proper sensory system examination as the procedure could not be properly explained to the patient. After examination we narrowed down our differentials to UMN lesions : neurotuberculosis, ICSOL and some neurodegenerative disorder.

After the initial blood investigations, we got brain imaging done. On MRI of brain, there was bilateral symmetric and confluent T2 /FLAIR hyperintensity in deep peri-ventricular white matter of parietal, occipital and temporal regions( posterior predominance), body and splenium of corpus callosum, posterior limbs of internal capsules, posterior aspects of extreme capsule and thalami brain stem ( descending pyramidal tracts, substantia niagra), cerebellar peduncles and deep cerebellar white matter with linear smooth peripheral enhancement. These findings were highly suggestive of X- linked adrenoleukodystrophy. Patient could not afford to go to a center where biochemical analysis and genetic counselling of the patient's family could be done.

## DISCUSSION

Adrenoleukodystrophy disorder is one of the x-linked genetic disorders caused by the myelin sheath breakdown in the brain around the nerve cells and progressive adrenal insufficiency. It is characterized by cerebral demyelination, adrenomyeloneuropathy and myelopathy. Patients with X-ALD are asymptomatic at birth. Almost all males with X-ALD develop adrenocortical insufficiency during life, about 80 % before adulthood. Cerebral demyelination is estimated to occur in about 40 % of male X-ALD patients before the age of 18 years, but is well documented to occur also in adulthood.

Rapidly progressive cerebral disease is seen in childhood form of ALD. Adrenomyeloneuropathy with or without local CNS demyelination is found in adult form of this disorder. Cerebral ALD in children manifests as cognitive dysfunction (declining school performance) and behavioral problems, in the beginning. Later on, focal neurologic deficits appear, such as visual and auditory agnosia, motor symptoms such as hemiparesis, dysarthria and dysphagia, and sometimes seizures also occur[2]. Symptoms progress rapidly over the course of weeks to months. Severe incapacity and death due to complications such as pneumonia occur within an average of about 2 years. In rare cases, cerebral ALD stabilizes spontaneously, referred to as "arrested" cerebral ALD. In adulthood, presentation is similar, with behavioural changes, especially if the lesions are located in the white matter of the frontal lobe, or psychiatric symptoms[3]. It can reactivate many years later. More than 80 % of women with X-ALD evidence a myelopathy or peripheral neuropathy after the age of 60 years.

The fundamental biochemical defect in X-ALD is impaired degradation of VLCFA by peroxisomal beta-oxidation. It is caused by mutations in the ABCD1 gene, which encodes a peroxisomal transmembrane protein, ALDP[4]. The adrenal cortex, CNS and the leydig cells of testes are the sites of involvement.

Diagnosis is confirmed by imaging and biochemical analysis. On MRI X- ALD is considered if there are white matter changes and especially when there is increased signal intensity on T2-weighed and FLAIR sequences in the parieto-occipital region and the splenium of the corpus callosum. Rim enhancement of demyelinating lesions is usually observed when boys or adult males present with overt neurological symptoms from cerebral ALD. Approximately 20% of males with X-ALD show white matter changes predominantly in the genu of corpus callosum and frontal lobes, or involve the pyramidal tracts

with extension in the white matter of the centrum semiovale. If VLCFA are elevated in plasma it is diagnostic of X-ALD. Also, in women and family screening, the diagnostic test of choice is mutation analysis of the *ABCD1* gene. *ABCD1* mutational analysis can be performed either on a fresh chorionic villus sample at 11–13 weeks of pregnancy or on amniotic cells obtained from amniotic fluid after centrifugation at 15–18 weeks of gestation.

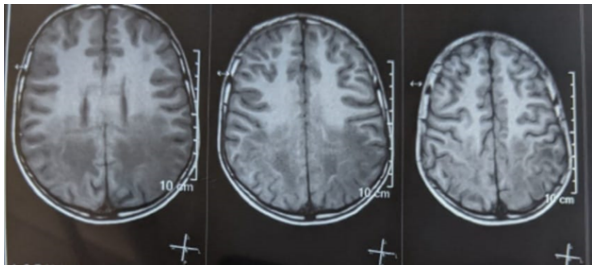

***Figure 1: Axial T1W images showing hypointense lesions in posterior lobe bilaterally involving gray and white matter.***

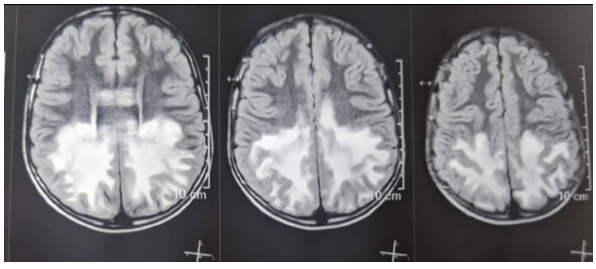

***Figure 2: T2 axial section showing T2 hyperintense lesions in posterior lobe bilaterally involving gray and white matter.***

There is no cure for X- ALD and the management is largely symptomatic. Lorenzo's oil is known to reduce VLCFA levels in blood. Another promising treatment is bone marrow transplantation, but it is effective during the early stage when lesions are present in MRI but symptoms are minimal.

It is likely that all patients with X-ALD if they survive into adulthood eventually develop myelopathy. The severity and progression cannot be predicted for individual patients. This is important when counseling patients: symptoms will occur, but only time will tell how severely affected an individual will be.

## CONCLUSION

Pediatricians, endocrinologists, neurologists and psychiatrists may encounter X-ALD which is a relatively common metabolic disorder in their practice. Recognition of X-ALD is highly important, since in some cases treatment is available, such as allogeneic HCT in the early stage of Cerebral ALD and endocrine replacement therapy for adrenocortical insufficiency. Furthermore, prenatal testing to prevent unnecessary new cases of this devastating disease is available.

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