Adrenoleukodystrophy

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- Safety and efficacy of leriglitazone in childhood cerebral adrenoleukodystrophy (NEXUS): an interim analysis of an open-label, phase 2/3 trial
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- Revisiting the Pathogenesis of X-Linked Adrenoleukodystrophy
- Neurofilament light chain as a biomarker to indicate early activation of cerebral disease in boys with adrenoleukodystrophy
- Nervonic acid, a long chain monounsaturated fatty acid, improves mitochondrial function in adrenomyeloneuropathy fibroblasts
- Unraveling X-linked adrenoleukodystrophy in women: a rare case of central nervous system manifestations and implications for screening
- Seizures in childhood cerebral adrenoleukodystrophy: New insights and remaining knowledge gaps

Adrenoleukodystrophy (ALD) is a rare, genetic disorder that primarily affects the nervous system and the adrenal glands. It belongs to a group of disorders known as leukodystrophies, which are characterized by the degeneration of the myelin sheath in the nervous system.

Here are key features of Adrenoleukodystrophy:

Genetics: ALD is caused by mutations in the ABCD1 gene, which is located on the X chromosome. As it is an X-linked disorder, it mainly affects males. Females can be carriers of the gene mutation but are usually asymptomatic.

Biochemical Basis: The ABCD1 gene encodes a protein involved in the transport of very-long-chain fatty acids (VLCFAs) into the peroxisomes, where they are broken down. Mutations in this gene lead to the accumulation of VLCFAs, particularly in the adrenal glands and the white matter of the nervous system.

Clinical Manifestations: The symptoms of ALD can vary widely, and there are different forms of the disorder. The most severe form is the childhood cerebral form, which typically presents between the ages of 4 and 10. Symptoms include behavioral changes, cognitive decline, loss of muscle control, and visual and hearing problems. Adrenal insufficiency (Addison's disease) may also occur.

Adrenal Gland Involvement: In addition to neurological symptoms, ALD often affects the adrenal glands, leading to adrenal insufficiency. This can result in fatigue, weakness, weight loss, and other symptoms related to hormonal imbalances.

Diagnostic Methods: Diagnosis is often based on clinical symptoms, family history, and biochemical testing for elevated levels of VLCFAs. Genetic testing can confirm the presence of mutations in the ABCD1 gene.

Treatment: Unfortunately, there is no cure for ALD. Treatment may involve managing symptoms and providing supportive care. Hematopoietic stem cell transplantation (HSCT) has been shown to be effective in halting the progression of cerebral ALD if performed at an early stage, before significant neurological damage has occurred.

Adrenoleukodystrophy is a complex disorder that requires a multidisciplinary approach involving neurologists, endocrinologists, and other specialists. Early diagnosis and intervention are crucial for

better outcomes, particularly in cases where stem cell transplantation may be considered as a treatment option.

Case reports

This case report studies a 12-year-old boy with a family history of X-linked adrenal leukodystrophy and his 8-year-old younger brother [1].

A 45-year-old Caucasian woman presented with chronic bilateral, painless, progressive, peripheral vision loss. She was found to have bilateral optic atrophy and non-enhancing multifocal white matter lesions on magnetic resonance imaging of the brain. Cerebrospinal fluid analysis showed elevated myelin basic protein. She was diagnosed as the carrier state of X-linked adrenoleukodystrophy (X-ALD). X-ALD can mimic the clinical and radiographic features of multiple sclerosis in a female carrier. This is the first case report of bilateral optic atrophy in a female X-ALD carrier in the English ophthalmic literature [2].

1)
Ni Y, Liu C, Tan L. Male Carrier of X-Linked Adrenal Leukodystrophy Due to 47, XXY Karyotype. JAMA Neurol. 2024 Mar 4. doi: 10.1001/jamaneurol.2024.0061. Epub ahead of print. PMID: 38436991.
2)
Shamim MM, Vickers A, Lee AG, Costello F. The X Factor. Surv Ophthalmol. 2018 Dec 3. pii: S0039-6257(18)30308-4. doi: 10.1016/j.survophthal.2018.11.003. [Epub ahead of print] PubMed PMID: 30521817.