

## Adrenoleucodystrophy: A Rare Case Report

B. Zouita<sup>1\*</sup>, M. Ranib<sup>1</sup>, S. Ouassil<sup>1</sup>, D. Basraoui<sup>1</sup>, H. Jalal<sup>1</sup>

<sup>1</sup>Radiology Department, Hospital Mére et enfant, CHU Mohamed VI, Marrakech

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\*Corresponding author: B. Zouita

### Abstract

### Case Report

The X linked adrenoleukodystrophy (X-ALD) is a peroxisomal disease caused by defects of the ABCD1 gene on chromosome Xq28 leading to accumulation of very long chain fatty acids (VLCFA), it is a genetic disorder with diverse clinical phenotypes. Of these phenotypes, the cerebral form usually manifests during early childhood with rapid cognitive and neurological deterioration and is accompanied by extensive white matter involvement. Here we report a case of 4-year-old child with a history of death in the sibling with the same symptomatology.

**Keywords:** Adrenoleukodystrophy, imaging, MRI.

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## INTRODUCTION

X linked adrenoleukodystrophy (X-ALD) is a rare genetic disease with prevalence of 0.5–3.3 in 100 000 men [1], characterized by progressive demyelination within the central and peripheral nervous system, adrenal insufficiency (Addison's disease) and accumulation of very-long-chain fatty acids (VLCFA) in plasma, fibroblasts and tissues. X-ALD is caused by mutations in the ABCD1 gene, located at Xq28, which encodes the ALD protein, which belongs to the subfamily D of ABC transporters (ATP-binding cassette) [2]. Affected male members of the same family may present with different phenotypes: cerebral adrenoleukodystrophy (childhood, juvenile or adult forms), adrenomyeloneuropathy or isolated adrenal insufficiency. The clinical presentation varies depending on the neuropathology, which in turn is influenced by epigenetic, environmental and stochastic factors [1]. Here we report a case of adrenoleukodystrophy diagnosed in a 4-year-old child.

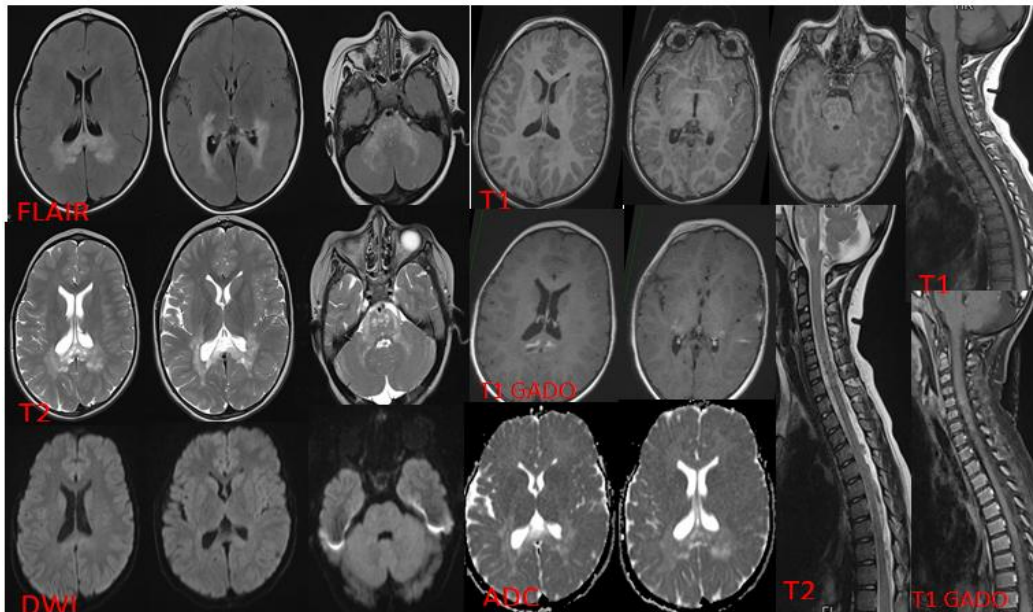
## CASE REPORT

4-year-old child, second born child to the non-consanguineous parents, with a history of death in the sibling with the same symptomatology, presenting for a psychomotor regression evolving for a year (Fig 1), made of functional impotence of the two lower limbs, behavioral disorders and a decreased in visual acuity, a brain MRI was requested to search for an etiology, which showed white matter signal abnormalities, Peri-

ventricular, parieto-occipital posterior and the semi-oval center, bilateral and symmetrical, the knee of the corpus callosum, the brainstem, the two cerebellar hemispheres, intramedullary in the cervical region, range from C4 to D1, in Hyposignal T1, hypersignal T2 and FLAIR, heterogenesly enhanced after injection of Gadolinium (Fig 2), the diagnosis of adrenoleukodystrophy is retained, the genetic study did not show a mutation in the ABCD1 gene but it objectified two mutations never described in this disease (UNC13D and LRP2).



**Fig 1: Photographs showing the child before (A) and a year after the beginning of his disease (B)**



**Fig 1: Cerebral MRI: white matter signal abnormalities, Peri-ventricular, parieto-occipital posterior, the semi-oval center, bilateral and symmetrical, the knee of the corpus callosum, the brainstem, the two cerebellar hemispheres, intramedullary in the cervical region, range from C4 to D1, in Hyposignal T1, hypersignal T2 and FLAIR, heterogenously enhanced after injection of PDC, the diagnosis of adrenoleukodystrophy is retained**

## DISCUSSION

X-linked adrenoleukodystrophy (ALD) is a peroxisome fatty acid beta-oxidation disorder that results in the accumulation of very long-chain fatty acids (VLCFAs) in tissues throughout the body; the highest levels of accumulation occur in myelin in the central nervous system, the adrenal cortex, and Leydig cells [3].

The genetic defect responsible for X-linked ALD is located in Xq28, the terminal segment of the long arm of the X chromosome. This gene normally encodes for a peroxisomal membrane protein called ALD-P [4].

Based on clinical onset and manifestations, X-linked ALD can be classified into several phenotypes (childhood, adolescent, and adult cerebral X-linked ALD; adrenomyeloneuropathy [AMN]; Addison disease– only type; asymptomatic type), each type having its own clinical features and prognosis. Childhood cerebral X-linked ALD is, clinically speaking, the most severe type. Patients with childhood cerebral X linked ALD usually show normal development until they reach 4–10 years of age, at which time behavioral changes including memory impairment and emotional instability manifest to varying degrees, followed by progressive deterioration of the vision, hearing, and motor function. In addition to CNS symptoms, adrenal dysfunction or gonadal insufficiency may be seen [5, 6].

Computed tomography (CT) scanning was used initially to diagnose demyelinating lesions of

ALD, but only at an advanced stage. Nowadays, MRI has supplanted CT [7].

MRI has proven crucial in the diagnostic workup of patients with leukoencephalopathies. MRI pattern recognition is a way of systematically analyzing many details on MR images and integrating these into patterns by disease [8].

MRI can also demonstrate the three zones recognized histologically in ALD. The external zone exhibits active destruction of myelin without inflammation, high signal on T2 and low-to-intermediate signal on T1. The intermediate zone shows signs of active inflammation while MRI shows contrast enhancement on T1. The internal zone is completely demyelinated and exhausted. It can display cavitation and calcifications best visualized on CT. The white matter involvement often appears symmetrical and bilateral, however, not always after careful evaluation. Unlike deep white matter, U fibers and cortex are spared, being most visible on T1-weighted MR [9].

Loes *et al.*, [10] described five different MRI patterns of adrenoleukodystrophy based on the involved anatomic locations and MR patterns of progression:

- Deep white matter in the parieto-occipital lobes and splenium of the corpus callosum (66% of cases, chiefly in children)
- Frontal lobe or genu of the corpus callosum (15.5%, mostly in adolescents)
- Fronto-pontine or corticospinal projection fibers (12%, mostly in adults)
- Cerebellar white matter (1%, mostly in adolescents)

- Combined parieto-occipital and frontal white matter (2.5%, mostly children)
- Spinal cord involvement is pronounced in the adrenomyeloneuropathy form of the disease.

MRI can be used not only to diagnose but also to predict disease progression among patients with X-linked ALD because the severity of the inflammatory process has been correlated with rapidity of disease progression and contrast-enhanced T1-weighted spin-echo. The enhancement is attributed to a breakdown of the blood-brain barrier resulting from an autoimmune or cytokine-mediated inflammatory process. A lack of enhancement is associated with stable disease in 85-90% of patients [11].

Although new MRI techniques such as diffusion weighted imaging and MR spectroscopy have been shown to be clinically useful in patients with childhood cerebral X-linked ALD, conventional brain MRI, with T1- and T2-weighted, and fluid-attenuated inversion recovery (FLAIR) sequences, is widely available and remains a valuable tool for assessing this disease [9, 11].

Elevated VLCFAs are the important biomarkers of X-ALD. Clinically three parameters are analyzed: the amount of hexacosanoic acid (C26:0), the ratio of tetracosanoic acid (C24:0)/docosanoic acid (C22:0), and C26:0/ C22:0. The accumulation of VLCFA (in particular C26:0) is the result of the defective metabolism of peroxisomes and, consequently, exert a cytotoxic effect in neural cells [12].

The prognosis of ALD can be estimated on the basis of age and the severity of the brain MRI abnormality, but there are exceptions to these rules, and some patients may remain stable with no further progression for up to 12 years after the initial neurological symptoms. Although childhood cerebral form, causing a severe disability that leads to death early. On the other hand, the adrenomyeloneuropathy is a milder adult form with involvement of mainly the spinal cord and peripheral nerves, having a slow progression with better prognosis [13].

Treatment is symptomatic, for example, steroid use for adrenal insufficiency and psychotropics for psychiatric symptoms. Statins can reduce VLCFA level, but no influence in neuronal and endocrine functions. Fatty diet should be restricted. Bone marrow transplantation is an option in patient with early neurological features. As ALD is an X-linked recessive disorder, genetic counseling of family members may be advisable. Early diagnosis also brings the possibility of genetic counseling; carrier detection and antenatal diagnosis and thus we can reduce the incidence of this devastating disease [13].

## REFERENCES

1. Meher, R. K., Aghoram, R., & Nair, P. P. (2020). Adrenoleukodystrophy presenting as glue sniffing. *BMJ Case Reports CP*, 13(3), e233036.
2. Nascimento, M., Rodrigues, N., Espada, F., & Fonseca, M. (2012). Adrenoleukodystrophy: a forgotten diagnosis in children with primary Addison's disease. *Case Reports*, 2012, bcr2012006308.
3. Chen, Y., Polara, F., & Pillai, A. (2018). Rare variability in adrenoleukodystrophy: a case report. *Journal of medical case reports*, 12(1), 1-4.
4. Melhem, E. R., Loes, D. J., Georgiades, C. S., Raymond, G. V., & Moser, H. W. (2000). X-linked adrenoleukodystrophy: the role of contrast-enhanced MR imaging in predicting disease progression. *American journal of neuroradiology*, 21(5), 839-844.
5. Moser, H. W. (1997). Adrenoleukodystrophy: phenotype, genetics, pathogenesis and therapy. *Brain: a journal of neurology*, 120(8), 1485-1508.
6. Kim, J. H., & Kim, H. J. (2005). Childhood X-linked adrenoleukodystrophy: clinical-pathologic overview and MR imaging manifestations at initial evaluation and follow-up. *Radiographics*, 25(3), 619-631.
7. Ferrer, I., Aubourg, P., & Pujol, A. (2010). General aspects and neuropathology of X-linked adrenoleukodystrophy. *Brain pathology*, 20(4), 817-830.
8. Galvão, A. C. R., Machado-Porto, G. C. L., Porto, F. H. D. G., Lucato, L. T., & Nitrini, R. (2012). Adult-onset adrenoleukodystrophy presenting as a psychiatric disorder: MRI findings. *Dementia & neuropsychologia*, 6, 290-295.
9. Van der Knaap, M. S., & Valk, J. (2005). *Magnetic Resonance of Myelination and Myelin Disorders*, 3rd ed. Berlin: Springer.
10. Loes, D. J., Fatemi, A., Melhem, E. R., Gupte, N., Bezman, L., Moser, H. W., & Raymond, G. V. (2003). Analysis of MRI patterns aids prediction of progression in X-linked adrenoleukodystrophy. *Neurology*, 61(3), 369-374.
11. Schiffmann, R., & van der Knaap, M. S. (2009). Invited article: an MRI-based approach to the diagnosis of white matter disorders. *Neurology*, 72(8), 750-759.
12. Chen, Y., Polara, F., & Pillai, A. (2018). Rare variability in adrenoleukodystrophy: a case report. *Journal of medical case reports*, 12(1), 1-4.
13. Mondol, M. B. A., Siddiqui, M. M. R., Wahab, L., Hoque, M. A., Khan, S. U., Rahman, K. M., & Mohammad, Q. D. (2010). Adrenoleukodystrophy: a rare case report. *Journal of Bangladesh College of Physicians and Surgeons*, 28(3), 189-192.