

# A First Case of Adrenomyeloneuropathy with Mutation R152C: A Case Report with Literature Review

Malek Mansour, Rania Ben Aoun, Maroua Melliti\*, Amel Kacem, Meriem Mselmani, Ridha Mrissa and Jamel Zaouali

Department of Medicine, Military Hospital of Instruction of Tunis, Tunisia

## Abstract

X-linked Adrenoleukodystrophy (X-ALD) is a rare genetic disorder responsible of accumulation of Very Long Chain Fatty Acids (VLCFAs) which accumulate in the central nervous system, adrenal cortex and testes. Various mutations have been identified, the X-ALD mutation database catalogs 2707 (last updated on 04-03-2019) with 61% of missense mutations. This paper reports on a first case of AMN with R152C mutation in ABCD1 gene.

**Keywords:** Adrenoleukodystrophy • Adrenomyeloneuropathy • ABCD1

## Introduction

X-linked adrenoleukodystrophy (X-ALD) is a complex and perplexing neurodegenerative disorder. The metabolic abnormality, elevated levels of very long-chain fatty acids in tissues and plasma, and the biochemical defect, reduced peroxisomal very long-chain acyl-CoA synthetase (VLCSS) activity, are ubiquitous features of the disease. However, clinical manifestations are highly variable with regard to time of onset, site of initial pathology and rate of progression.

## Case Report

A 20-year-old Tunisian boy was born to non-consanguineous parents, with familiar history of gait abnormalities, fallen arches in both genders, cognitive impairment in a 16-year-old brother (Figure 1) and no significant personal history. At the age of 17, he presented with a progressive gait difficulties caused by rigidity and weakness in both legs, associated with both urinary and faecal incontinence. He had a normal psychomotor development.

Neurological examination revealed pyramidal syndrome in both limbs with spastic paraparesis. Neuropsychological evaluation was normal. Brain Magnetic Resonance Imaging (MRI) was normal and the spinal MRI showed thoraco-lumbar spinal cord atrophy. Electromyography (EMG) showed an asymmetrical generalized sensory neuropathy with axonal degeneration. Etiological investigation of spastic paraparesis was negative. VLCFA plasma levels were increased (C24: 0=1.67 with normal values (0.5-0.98)/C22: 0=0.17 with normal values (0.002-0.018) and an increased C24/C22 ratio). Genetic analysis showed the Homozygous missense mutation at codon 152 in exon 1 (454C>T) in R152C locus coding for the ABCD1 gene. The Diagnosis of Adrenomyeloneuropathy (AMN) was established. He was put under symptomatic treatment.

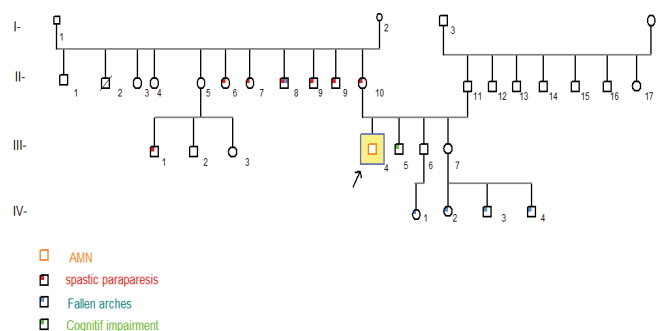
## Discussion

The AMN phenotype has an approximate incidence of 1: 42,000 [1-4] and a frequency of 40-46% in individuals with X-ALD. Clinical symptoms

\*Address for Correspondence: Melliti M, Department of Medicine, Military Hospital of Instruction of Tunis, Tunisia, E-mail: mellitimaroua2602@gmail.com

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**Figure 1.** Family Tree; the presented case is marked with an arrow. Subject II, 6; II, 7; II, 8; II, 9; II, 10 and III, 1 have spastic paraparesis. Subject II, 8; IV, 1; VI, 2; VI, 3 and VI, 4 have fallen arches and subject III, 5 have cognitive impairment. AMN: Adrenomyeloneuropathy.

begin around the third decade (earliest in the second decade and latest in the fifth) [5] same as our patient who began gait difficulties at the age of 17. It usually involves thoracic and lumbosacral regions [2]. In this article we report the third case with missense R152C mutation in ABCD1 gene [3,5] as well as the first AMN case with R152C mutation. The first reported patient presented at the age of 8 a cerebral form of adrenoleukodystrophy, further details were not mentioned [5]. The second reported patient had at the age of 4 an adrenocortical insufficiency with elevated VLCFA plasma levels, he presented at the age of 36 a progressive front temporal type of dementia, with Brain MRI (T2-weighted) showing extensive confluent high signal intensity in the frontal white matter compatible with a cerebral X-ALD [3]. Our patient had a different phenotype (AMN) with a slowly progressive weakness and rigidity in both limbs, thoraco-lumbar spinal cord atrophy on MRI and axonopathy on EMG. This is the first different phenotype described in R152C mutation for the ABCD1 gene. There are no other Tunisian Cases reported with this mutation [4]. In Conclusion, the clinical manifestation of X-ALD is highly variable; there is no correlation between clinical phenotype and genotypes as we can see in our case.

## Conclusion

The treatment options for X-ALD are still narrow. The Hematopoietic Stem Cell Transplantation (HSCT) stands as the only probed treatment for early detected cerebral X-ALD. The treatment of patients with AMN is mainly symptomatic but careful follow-up is also necessary as this phenotype can evolve towards cerebral X-ALD. Although the R152C mutation has been reported, this is the first study to our knowledge to have report the association of this mutation to AMN.

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## References

1. Matteo Foschi, Veria Vacchiano, Patrizia Avoni and Alex Incensi, et al. "Broadening the Spectrum of Adulthood X-Linked Adrenoleukodystrophy: A Report of Two Atypical Cases." *Front Neurol* 10 (2019): 70.
2. Vincenzo Donadio, Alex Incensi, Veria Vacchiano and Rossella Infante, et al. "The autonomic innervation of hairy skin in humans: An *in vivo* confocal study." *Sci Rep* 9 (2019): 01.
3. Larner, James. "Adult-Onset Dementia with Prominent Frontal Lobe Dysfunction in X Linked Adrenoleukodystrophy with R152C Mutation in ABCD1 Gene." *J Neurol* 250 (2003): 1253-1254.
4. Fakhri Kallabi, Ikhlass Hadj Salem, Ghada Ben Salah and Hadhami Ben Turkia, et al. "Molecular Characterization of X-Linked Adrenoleukodystrophy in a Tunisian Family: Identification of a Novel Missense Mutation in the ABCD1 Gene." *Neurodegener Dis* 12 (2013): 207-211.
5. Moser, Hugo. "Clinical and Therapeutic Aspects of Adrenoleukodystrophy and Adrenomyeloneuropathy." *J Neuropathol Exp Neurol* 54 (1995): 740-745.

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