Phenotypic variability in a Tunisian family with X-linked adrenoleukodystrophy caused by the p.Gln316Pro novel mutation

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Background
X-linked adrenoleukodystrophy (X-ALD; MIM #300100) is a neurodegenerative recessive disorder that affects the brain white matter and associated with adrenal insufficiency. It is characterized by an abnormal function of the peroxisomes, which leads to an accumulation of the very long chain fatty acids in plasma and tissues. Mutations in the ABCD1 gene affect the function of the encoded protein ALDP.

Aims
The present study reports the molecular investigation and the phenotypic variability in a Tunisian family with childhood cerebral adrenoleukodystrophy.

Methods
Two affected boys belonging to a Tunisian family with X-ALD were evaluated for sequence variations. Blood samples were collected and isolated DNA derived from subjects was amplified. The entire sequence of the ABCD1 gene was analyzed by PCR and direct sequencing. Using Bioinformatic tools, the variation was analyzed by PolyPhen and SIFT prediction softwares.

Results
The ABCD1 gene sequencing indicated a novel hemizygous mutation c.947A>C (p.Gln316Pro) in the exon 2. The new mutation abolished a restriction site for DdeI enzyme. This missense variation was predicted to be possibly damaging by the PolyPhen and SIFT prediction software. Based on the disease’s progress, the clinical signs and biochemical aspects between the two siblings, we demonstrate that there is a phenotypic variability between the two siblings.

Conclusions
This study reports a new mutation in the ABCD1 gene in a Tunisian family with X-ALD leading to a phenotypic variability between two siblings. This finding demonstrates that there is no phenotype-genotype correlation and the involvement of others factors in X-ALD disease.

Disclosure of interest
The authors have not supplied their declaration of conflict of interest.

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