The clinical polymorphism and variability of X-linked adrenoleukodystrophy in one Russian family

Yuliya Sidorova, Leila Sozaeva, Maria Kareva, Valentina Peterkova
Endocrinology Research Centre, Moscow, Russia

Introduction

Adrenoleukodystrophy is an X-linked, inherited metabolic disorder. Here, we present 3 clinical cases of different phenotypes with one mutation in ABCD1 gene in one family.

Patient 1

At the age of 9 years, manifestation of neurological symptoms was observed, skin color changed, these symptoms progressed monthly.

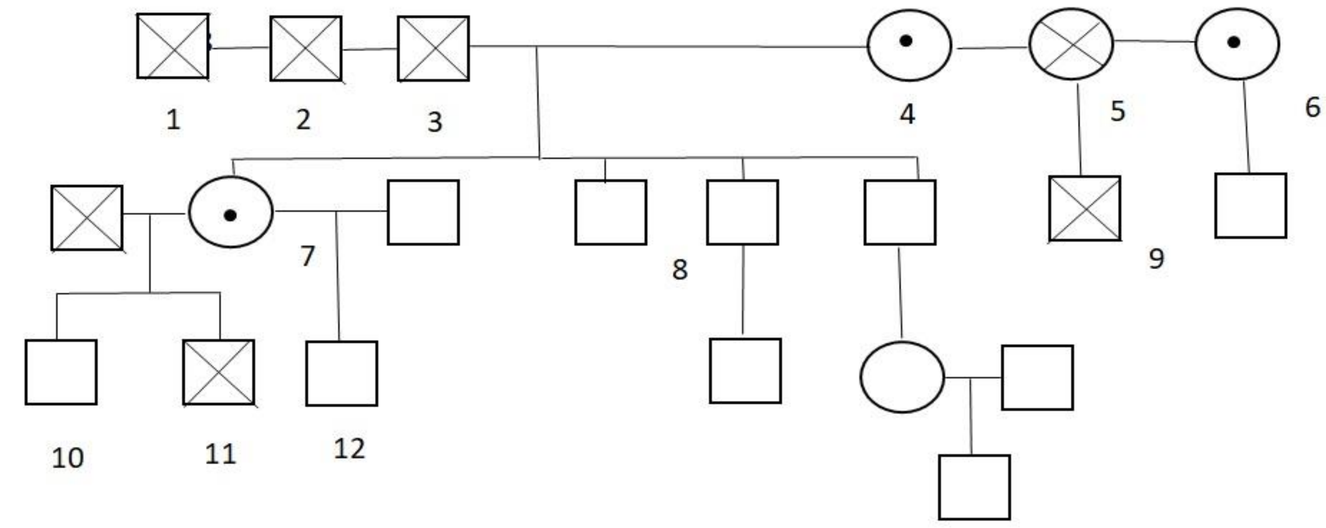
MRI of the brain: 13 points on Loes scale.

X-linked adrenoleukodystrophy was confirmed by biochemical (elevation of very long chain fatty acids - VLCFA) and molecular genetic studies (a mutation in exon 1 of the gene *ABCD1* (c.871G>A **(p.Glu291Lys**) in the hemizygous state).

The child was diagnosed with X- linked adrenoleukodystrophy, childhood cerebral form, primary adrenal insufficiency, and hormone replacement therapy was prescribed.

Six months after the manifestation of the disease the child died.

Pedigree



1, 2 – death at the age of 20-25 from epistatus

3, 5 – death in eldery age

4 – age 75, maybe carrier (no genetic test, and have symptoms - neurological signs, such as scatacratia, urinary problems. These symptoms appear after car accident and may be the result of this.

6 - age 82, maybe carrier (scatacratia, urinary problems)

7 – age 37, maybe carrier: stiffness, weakness of the lower limbs, numbness. But mother have B12 anemia, and these neurological symptoms may be the result of this.

8 – age 42, infertility?

9 – newborn death, reasons unknown

10 - patient 3

11 – paient 1

12 – patient 2

Patient 2

At the age of 1 year 4 months the boy stopped sitting down, was constantly sleeping, was sluggish.

Molecular genetic study: an identical mutation in the *ABCD1* gene was detected.

During the examination, primary adrenal insufficiency was diagnosed, hormone replacement therapy was prescribed.

Up to 4 years of age during dynamic observation there were no changes in the nervous system, according to MRI of the brain, there were no pathologies. Currently, the boy has X-linked adrenoleukodystrophy: Addison`s disease only.

Patient 3

14 years: At the time of the examination, there were no complaints. There have never been clinical signs of adrenal insufficiency and neurological symptoms.

The diagnosis of X-linked adrenoleukodystrophy was confirmed by elevation of VLCFA and the presence of a mutation in the *ABCD1* gene, as in younger brothers.

During ACTH stimulation test (with cosyntropin), cortisol was increased up to 1173 nmol/l.

Sex hormones correspond to puberty stage (Tanner 3).

The boy may have an asymptomatic X-ALD phenotype.

Conclusions

There is no correlation between the genotype and the phenotype. In this family, the presence of 3 forms of the disease is noted: childhood cerebral form, Addison`s disease only and asymptomatic phenotype. However, progression of the disease is possible; patients require medical follow-up. Factors affecting the development of one form or another are currently unknown.