AN ADOLESCENT CASE WITH ADRENOLEUKODYSTROPYH DIAGNOSED AFTER DETECTION OF LEYDIG CELL DYSFUNCTION

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INTRODUCTION

X-linked adrenoleukodystrophy (X-ALD) is an inherited peroxisomal disease characterized by beta oxidation disorder that causes the accumulation of very long chain fatty acids (VLCFA) in all tissues. It presents with clinical signs due to accumulation of VLCFA in brain white matter, testes, adrenal cortex and skin fibroblasts (1).

AIM

The process leading to the diagnosis of X-ALD at presentation with nonprogressive puberty, adrenal insufficiency and Leydig cell dysfunction will be discussed

METHOD

Case presentation:

- A 16-years and 4-months-old male patient applied to the outpatient clinic due to not entering puberty and the lack of deepening in his voice
- On physical examination, his height (173.3 cm; SDS: -0.06), body weight (53 kg; SDS: -1.55), body mass index (16.7 kg/m^2; SDS: -1.9), testicular volüme (25/25 ml), and stretched penile length (9.5 cm) were measured. His pubic hair growth was in stage-II
- Remarkable laboratory test results were as follows:

  FSH: 3.34 mIU/mL (0.61-7.9),
  LH: 16.12 mIU/mL (0.5-8),
  Total testosterone: 31 ng/dL (300-1200)

RESULTS

In laboratory tests on the inconsistency of the testosterone level with the testicular volume and the retardation of the pubic hair stage,

- ACTH was found 1014 pg/mL (223.3 pmol/L),
- cortisol: 3.5 µg/dL (96.5 nmol/L),
- DHEA-SO4: 10 µg/dL (0.27 µmol/L) ,and
- 1,4-Δandrostenedione: 0.12 ng/ml (0.41 nmol/L)

In the VLCFA panel,

- C24: 118.07 µmol/L (37.14-79.4),
- C26: 4.25 µmol/L (0.6-1.3),

- C24/C22: 1.97 (0.689-1.008),
- C26/C22: 0.07 (0.011-0.026) were higher.

6th month follow-up

VLCFA:
Pristanic acid analysis(GC/MS) - 0,79 µmol/L
Phytanic acid analizi (GC/MS) - 1,42 µmol/L
C22:0: 47,62 µmol/L
C24:0: 74,57 µmol/L (37,14 – 79,4)
C26: 0,67 µmol/L (0,6 – 1,3)
C24:0/C22:0: 1,57 (0,689 – 1,008)
C26:0/C22:0: 0,01 (0,011 – 0,026)

No worsening of neurological findings

Cranial MR: No progression in pathological findingf
LOES Score: 4

Spinal MR: No spinal involvement

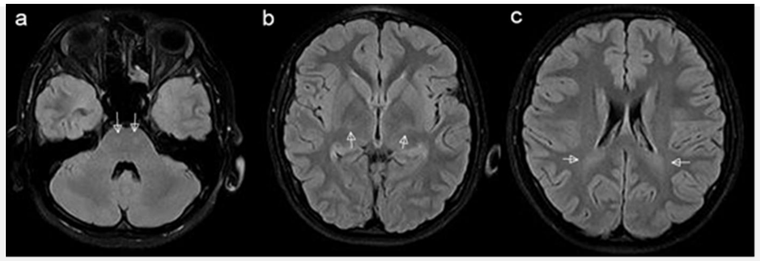
12th month follow-up

VLCFA:
Pristanic acid analysis(GC/MS) – 0.03 µmol/L
Phytanic acid analizi (GC/MS) – 0.54 µmol/L
C22:0: 47,6 µmol/L
C24:0: 39.65 µmol/L (37,14 – 79,4)
C26: 1.26 µmol/L (0,6 – 1,3)
C24:0/C22:0: 0.84 (0,689 – 1,008)
C26:0/C22:0: **0,026** (0,011 – 0,026)

No worsening of neurological findings

Cranial MR: No progression in pathological findingf
LOES Score: 4

Spinal MR: No spinal involvement



In brain magnetic resonance imaging, hyperintense signal changes in the bilateral thalamus, Posterior pons (a), posterior leg of the internal capsule (b), bilateral parieto-occipital white matter (c) and corpus callosum splenium were observed in consistent with X-ALD.
LOES score is 4.

ABCD1 gene
c.652C>A (p.P218T) (p.Pro218Thr) (hemizygous) ACMG: Pathogenic

c.698C>T (p.A233V) (p.Ala233Val) (Hemizygous) (CIS-Position) ACMG: Highly pathogenic

In his neurological examination, there was only slight inability in heel walking

- In brain magnetic resonance imaging, hyperintense signal changes in the bilateral thalamus, posterior leg of the internal capsule, posterior pons, bilateral parieto-occipital white matter and corpus callosum splenium were observed in consistent with X-ALD LOES score reported as 4
- No spinal involvement in spinal MR

- Hydrocortisone and Lorenzo's oil treatments were initiated
- The combined heterozygous mutation of the ABCD1 gene c.652C>A (p.P218T) (p.Pro218Thr)/c.698C>T (p.A233V) (p.Ala233Val) was detected
- Childhood cerebral adrenoleukodystrophy or slowly progressive adrenomyeloneuropathy with cerebral involvement was considered, if necessary bone marrow transplantation was planned according to the clinical course of the patient

CONCLUSIONS

In adolescents presenting with Leydig cell dysfunction, primary adrenal insufficiency should be screened and if primary adrenal insufficiency is detected, adrenoleukodystrophy should be investigated

REFERENCES

1. Moser HW, et al. Adrenoleukodystrophy: new approaches to a neurodegenerative disease. *JAMA 2005; 294:3131-3134.*

CONTACT INFORMATION

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