© Wydawnictwo UR 2019
ISSN 2544-1361 (online); ISSN 2544-2406
doi: 10.15584/ejcem.2019.3.13

http://www.ejcem.ur.edu.pl/en/
European Journal of Clinical and Experimental Medicine
Eur J Clin Exp Med 2019; 17 (3): 274–276

CASUISTIC PAPER

Natalia Leksa [1,2(ABCDGF)], David Aebisher [3(DFG)], Sabina Galiniak [4(DFG)], Dominika Uberman-Kluz [2,5(DFG)], Serweryn Bartosz [2(DFG)], Dorota Bartusik-Aebisher [4(ABDFG)]

Adrenomyeloneuropathy – a case report

[1] Department of Anatomy, Faculty of Medicine, University of Rzeszów, Rzeszów, Poland
[2] Department of Neurology, MSWiA Hospital, Rzeszów, Poland
[3] Department of Photomedicine and Physical Chemistry, Faculty of Medicine, University of Rzeszów, Rzeszów, Poland
[4] Department of Family Pedagogy, Faculty of Pedagogy, University of Rzeszów, Rzeszów, Poland
[5] Department of Biochemistry and General Chemistry, Faculty of Medicine, University of Rzeszów, Rzeszów, Poland

ABSTRACT

Introduction. Adrenoleukodystrophy is a genetic disorder linked to the X chromosome, in which the peroxisomal beta-oxidation process is disturbed. It is a metabolic disease that results in the accumulation of very long chain fatty acids (VLCFAs - very long chain fatty acids) responsible for the symptoms of damage to the adrenal cortex, gonads and the brain.

Aim. A clinical case is reported.

Description of case. This article describes the case of a 64-year-old woman who had neurological symptoms for many years, gradually increasing without significant improvement after the treatment (periodic steroid therapy).

Conclusion. Based on tests (including the determination of the ABCD1 gene and very long chain fatty acids - VLCFA), adrenoleukodystrophy was suspected.

Keywords. adrenoleukodystrophy, fatty acids, steroid therapy

Introduction

Adrenoleukodystrophy is caused by the mutation of the ABCD1 gene on the Xq28 chromosome.[1-4] This recessive mutation causes a defect of peroxisomal beta oxidation and the storage of saturated very long-chain fatty acids in all tissues of the body. It is most manifested in the adrenal cortex, myelin of the central nervous system and in Leydig cells in the testes.[4-7] The ABCD1 gene is responsible for proper functioning of the protein ALD, which belongs to transport proteins with an ATP binding cassette.[8-10] In 1997, Moser et al. distinguished seven phenotypes:[1]

Brain children's figure
1. Brain juvenile
2. Brain form of adults
3. Adrenomyeloneuropathy

Corresponding author: Natalia Leksa, e-mail: leksanatalia@gmail.com

Participation of co-authors: A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 4.05.2019 | Accepted: 15.08.2019
Publication date: September 2019

Leksa N, Aebisher D, Galiniak S et al. *Adrenomyeloneuropathy – a case report.* Eur J Clin Exp Med. 2019;17(3):274–276. doi: 10.15584/ejcem.2019.3.13

4. Adrenal insufficiency without neurological symptoms
5. Asymptomatic form
6. Heterozygotes

The most common phenotype is a childlike brain form that occurs in boys with normal early development. It was described by Siemerling and Creutzfeld in 1923.[3] There is a rapidly progressing demyelination of the white matter of the brain. The boys are asymptomatic, the mean duration of symptoms is 7 years. Initially, the disease is manifested by lack of concentration, hyperactivity, emotional lability.[8-12] Then, ophthalmologic symptoms (atrophy of the optic nerve), auditory (deafness), and coordination problems are added. The progress of symptoms is very fast, which results in a quick transition to the vegetative state - on average, 1-2 years. The basic diagnostic method is magnetic resonance imaging, which shows damage to the white matter of the posterior parietal and occipital areas as well as frontal areas.[12-18] Occasionally, there is also a juvenile figure, similar in its symptoms to the childish form, whose beginning falls on adolescence.

The adult brain form described in 1976 is mainly characterized by spastic paraplegia. There is no brain demyelination here either clinically or pathomorphologically. Additional ailments include cerebellar dysfunction or olive-bridge-cerebellar atrophy. There may be disturbances in the functioning of the adrenal cortex, progressive disturbances of hearing, vision, and headaches.[4]

In 1977, adrenomyeloneuropathy was described, in which hypogonadism, adrenal insufficiency - beginning in childhood, and paraparesis in the third decade of life were described. Additional symptoms associated with the above ailments include neuropathy, impotence, and sphincter disorders.[5]

The diagnosis of adrenoleukodystrophy includes:

1. Family history allows to determine the diagnosis in 95% of cases
2. Determination of serum VLCFA level - the level of hexacosic acid (C26: 0) and its ratio to docosan (C22: 0), rarely tetrakosan (C24: 0) is determined
3. 3) VLCFA determination in skin fibroblasts and red blood cell cultures
4. Genetic examination - analysis of the ABCD1 gene mutation
5. Prenatal tests - determination of VLCFA level or DNA test from cells obtained from chorionic tube or amniotic fluid
6. Screening test - determination of the level of lysophosphatidylcholine C26: 0 in a dry drop of blood
7. MR examination - abnormalities in the MR picture are usually better than clinical symptoms
8. Endocrine examination - may show a decrease in the level of some hormones (ACTH, testosterone, DHEA)
9. In cerebrospinal fluid an elevated level of protein with intratekinal IgG synthesis, pleocytosis
10. Extended visual evoked and auditory evoked potentials from the brainstem

Description of the case

A 64-year-old female patient was admitted to the Department of Neurology due to the worsening of the lower limbs, dizziness, and disturbances of the balance, which had been increasing for 2 months. In addition, she reported recurrent headaches in the temporo-parietal region of a stabbing nature, usually on the right side, short-term memory disturbances, difficulty in finding words, and incontinence. The above-mentioned complaints have been occurring for about 39 years and have been intensified periodically. The patient was repeatedly hospitalized and diagnosed in the direction of multiple sclerosis, despite the absence of demyelinating lesions in imaging studies. Family history showed similar symptoms in the patient's daughter - the family underwent genetic testing, which revealed a mutation in the ABCD1 gene. In the neurological examination on the day of admission to the ward: conscious patient, logical contact, auto and allopsychic, psychomotor slowing, negative meningeal symptoms, nystagmus absent, bilateral temporal temporal vision limitation with greater severity on the left side, in the range of the remaining cranial nerves pathology, discrete paresis of the pyramidal type of lower limbs, increased muscular tension of the lower limbs spastic type with greater severity on the left side, knee and step reflex increased with greater severity on the right side, Babinski's symptom is present on both sides, Openheim's symptom on the right, left side +/-, deformation of the lower limbs, feet hollowed with greater severity on the left side, dysmetria in the upper limbs with greater severity on the right side, Romberg's test lability without direction, skin reflexes absent, and symptoms of absent deliberation.

During the hospitalization, the department performed basic laboratory tests that showed hypercholesterolemia (statins were included in the treatment). The level of folic acid and vitamin B12 is correct. ACTH concentration and diurnal cortisol profile in the norm. The corticotropin stimulation test was not performed due to lack of preparation (Synacthen). In the magnetic resonance imaging of the head, single focal lesions of a vasogenic / demyelinating character were imaged in the white matter of both brain hemispheres, and in the deep left brain hemispheres, focal lesions of 15/13/8 mm with the presence of hemosiderin deposits - after hemorrhage into the cavernous haemangioma. The diagnosis was supplemented by an electroneurographic study that revealed sub-acute sensory-motor neuropathy of the axonal type. Based on the clinical picture, family history and additional tests (including the de-

termination of the ABCD1 gene and very long chain fatty acids - VLCFA), suspicion of adrenoleukodystrophy was suspected.

Discussion

In the patient for many years, it was suspected that these symptoms are indicative of multiple sclerosis despite the lack of previous demyelization typical for this disease entity. Therefore, multiple sclerosis should always be included in the differential diagnosis of adrenoleukodystrophy. In addition, in any person with Addison's disease, adrenoleukodystrophy should also be considered because of the typical symptoms resulting from damage to the adrenal cortex. It is noteworthy that in the family members of the patient, genetic tests for the mutation of the ABCD1 gene were positive. In adults, the course of the disease is significantly slower compared to children, hence the complaints accompanied the patient for many years. Although the disease due to the method of inheritance should affect only men, the patients may be in mild or moderate form, as in the presented patient. There is no specific treatment for the abovementioned unit. The very avoidance of VLCFA in the diet does not lead to biochemical changes due to their endogenous synthesis.

Although the prevalence of adrenoleukodystrophy is 1:16,800 live-born, it is the most common peroxisomal disease and the most common inherited disease involving the white matter of the central nervous system, its course may be varied.[12-18] Even within members of the same family, there may be different forms of the disease. Symptoms may appear at various ages and with varying severity and prevalence of neurological or endocrine-related disorders. In the case of the presented patient, symptoms appeared in the adult period, mainly manifesting as ailments of the nervous system.

Conclusion

Only the combination of a restrictive diet low in VLCFA and the use of glycerol oil or Lorenzo oil results in a reduction in the concentration of VLCFA, but biochemical changes are not accompanied by clinical improvement. The sense of using this type of treatment is effective only in boys with a pre-symptomatic period. Despite the lack of effective treatment, the most important in this case is diagnostics especially in people with a history of genetic diseases.

References

1. Moser HW, Raymond GV, Dubey P. Adrenoleukodystrophy: new approaches to a neurodegenerative disease. *JAMA*. 2005;294(24):3131-3134.
2. Moser HW. Adrenoleukodystrophy: phnotype, genetics, pathogenesis and therapy. *Brain.* 1997;120(8):1485-1508.
3. Siemerling E, Creutzfeld HG. Bronzekrankheit und sklerosierende Encephalomyelitis. *Arch. Psych. Nervkrankh.* 1923;68(1),1923:217–244.
4. Budka H, Sluga E, Heiss WD. Spastic paraplegia associated with Addison`s disease: variant of adrenoleukodystrophy. *J. Neurol.* 1976;213(3):237-250.
5. Griffin JW, Goren E, Schaumburg HH, Engel WK, Loriaux L. Adrenomyeloneuropathy: a probable variant of adrenoleukodystrophy. Clinical and endocrinologic aspect. *Neurology*. 1977;27(12):1107-1113.
6. Allgrove J, Clayden GS, Grant DB, Macaulay JC. Familial glucocorticoid deficiency with achalasia of the cardias and deficient tear production. *Lancet. 1978*; 1(8077):1284-1286.
7. Heffungs W, Hameister H, Ropers HH. Addison disease and cerebral sclerosis in an apparently heterozygous girl: evidence for inactivation of the adrenoleukodystrophy locus. *Clin. Genet*. 1980;18:184-188.
8. Igarashi M, Schaumburg HH, Powers J, Kihsimoto Y, Kolodny EH, Suzuki K. Fatty acid abnormality in adrenoleukodystrophy. *J. Neurochem*. 1976;26:851-860.
9. Engelen M, Kemp S, de Visser M, van Geel BM, Wanders RJA, Aubourg P, Poll BT. The X- linked adrenoleukodystrophy (X-ALD): clinical presentation and guidelines for diagnosis, follow- up and management. *Orphanet J Rare Dis*. 2012,7:51.
10. Morski J. Adrenoleukodystrofia sprzężona z chromosomem X. Objawy, diagnostyka i leczenie oraz opis przypadku. *Neur. Dziecięca.* 2012;43.
11. Paláu-Hernández S, Rodriguez-Leyva I, Shiguetomi-Medina JM. Late onset adrenoleukodystrophy: A review related clinical case report. *eNeurologicalSci.* 2019;14:62-67.
12. Crane DI. Revisiting the neuropathogenesis of Zellweger syndrome. *Neurochem Int*. 2014;69:1-8.
13. Engelen M, Barbier M Dijkstra IM. X-linked adrenoleukodystrophy in women: a cross-sectional cohort study. *Brain*. 2014;137:693-706.
14. Engelen M, Kemp S, Poll BT. X-linked adrenoleukodystrophy: pathogenesis and treatment. *Curr Neurol Neurosci Rep*. 2014;14:486-489.
15. Menon GK, Orso E, Aslanidis C. Ultrastructure of skin from Refsum disease with emphasis on epidermal lamellar bodies and stratum corneum barrier lipid organization. *Arch Dermatol Res.* 2014;306:731-737.
16. Turk BR, Moser AB, Fatemi A. Therapeutic strategies in adrenoleukodystrophy. *Wien Med Wochenschr.* 2017;167(9-10):219-226.
17. Theda C, Gibbons K, Defor TE. Newborn screening for X-linked adrenoleukodystrophy: further evidence high throughput screening is feasible. *Mol Genet Metab*. 2014;111:55-57.
18. van Geel BM, Poll-The BT, Verrips A. Hematopoietic cell transplantation does not prevent myelopathy in X-linked adrenoleukodystrophy: a retrospective study. *J Inherit Metab Dis.* 2015;38(2):359-361.