Atypical X-linked adult adrenoleukodystrophy with cerebellar and brainstem involvement – a case report

Elena Lazar[1], Mirela Ilie[1], Radu Tanasescu[2,3], Bogdan O. Popescu[2,3], Corin Badiu[1,3]

1. "C.I.Parhon" National institute of Endocrinology, Bucharest, Romania
2. „Clinical Hospital Colentina – Department of Neurology II"
3. "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

Introduction[4]:

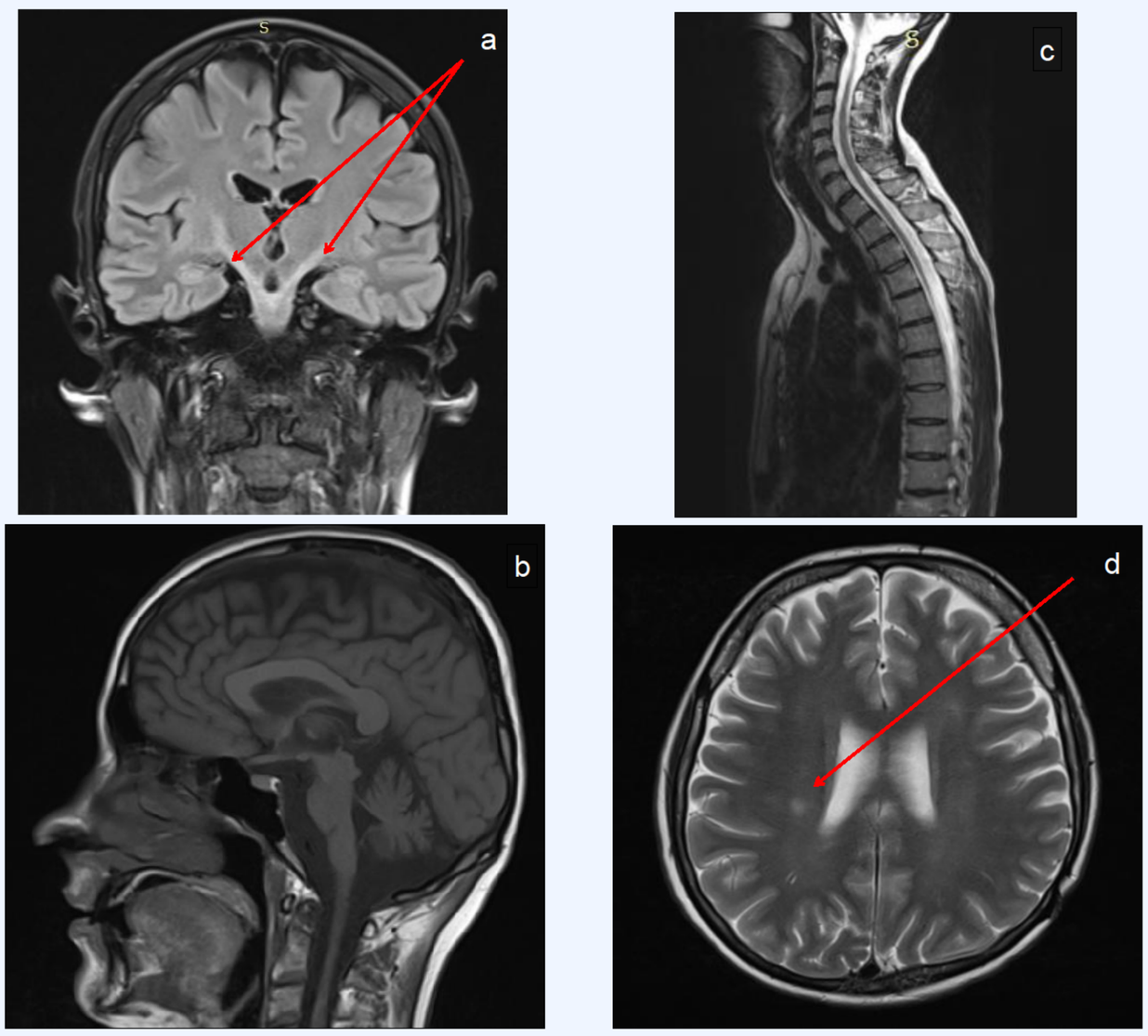
► X-linked adrenoleukodystrophy (ALD) is a peroxisomal disorder of beta-oxidation that results in accumulation of very long chain fatty acids (VLCFAs) in various tissues.

► The clinical phenotype of X-ALD in adults is variable and involves dysfunction of the **adrenal cortex**, of the **Leydig cells** and of the **nervous system** (including adrenomyeloneuropathy [AMN]). Clinical phenotypes, age and severity of clinical presentation vary and therefore it can be overlooked.

► AMN typically presents in adult males between 20 and 40 years of age (average 28 years) and comprises approximately 40 to 45 percent of ALD/AMN complex. The primary manifestation is spinal cord dysfunction with progressive stiffness and weakness of the legs (spastic paraparesis), abnormal sphincter control, and sexual dysfunction.

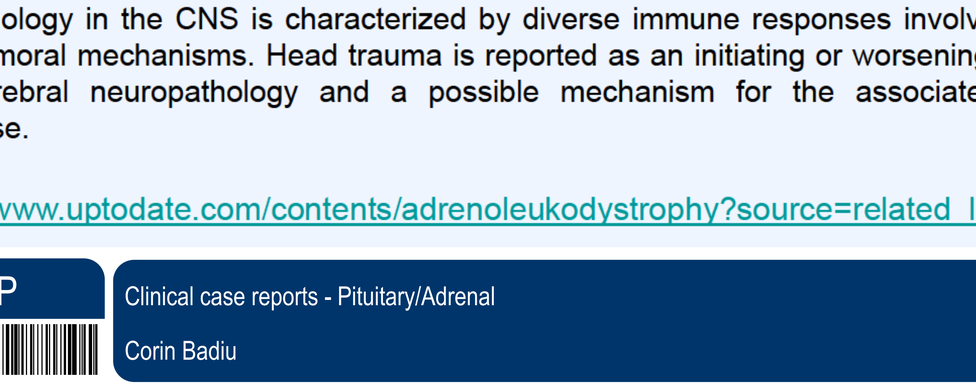
Aim: To report a case of a rare adult-onset cerebello-brainstem presentation of a sporadic ALD with sparing of the occipito-parietal lobes and autonomic dysfunction, which resembles multi-system atrophy

MRI evaluation: marked cerebellar and midbrain atrophy with bilateral demyelination of the long tracts and hypotrophy of dorsal columns of the spinal cord



a. Band hyperintense FLAIR signal of the internal capsules; b. Cerebellar atrophy;
c. Hypotrophy of dorsal columns of the spinal cord; d. SM-like cerebral lesions

Pathogenesis[4]:



► **ALD** is caused by mutations in the ATP-Binding Cassette (ABC), Subfamily D, Member 1 gene (ABCD1 gene), located at Xq28, that encodes an ABC transporter.
ABCD1 mutations may prevent normal transport of **very long chain fatty acids (VLCFAs)** into peroxisomes, thereby preventing beta-oxidation and breakdown of VLCFAs. **Accumulation of abnormal VLCFAs in affected organs is presumed to underlie the pathologic process of the adrenoleukodystrophies (ALD).**

► In the adrenal gland, abnormal VLCFAs may directly alter cellular function by inhibiting the effects of ACTH on the adrenocortical cells, or indirectly by initiating an autoimmune response.

► Pathology in the CNS is characterized by diverse immune responses involving cellular and humoral mechanisms. Head trauma is reported as an initiating or worsening feature in the cerebral neuropathology and a possible mechanism for the associated immune response.

Case report:

► We report the case of a 33 year old man with Addison's disease since his early twenties and a 2-year history of progressive neurological deterioration preceded by a psychiatric bout with mania and psychosis. The disturbances started as a slowly progressive gait ataxia, unsteadiness and the need for walking support.

At admission:

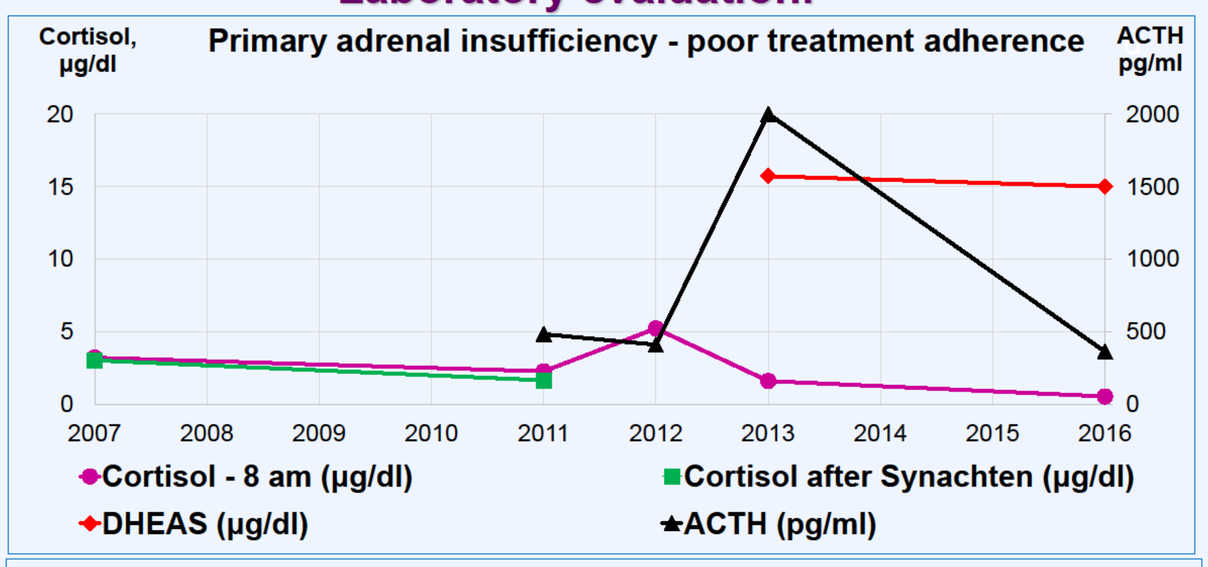
►Neurologic examination reveals generalized ataxia was accompanied by atypical parkinsonism, urinary disturbances and spastic para-paresis with inability to walk.

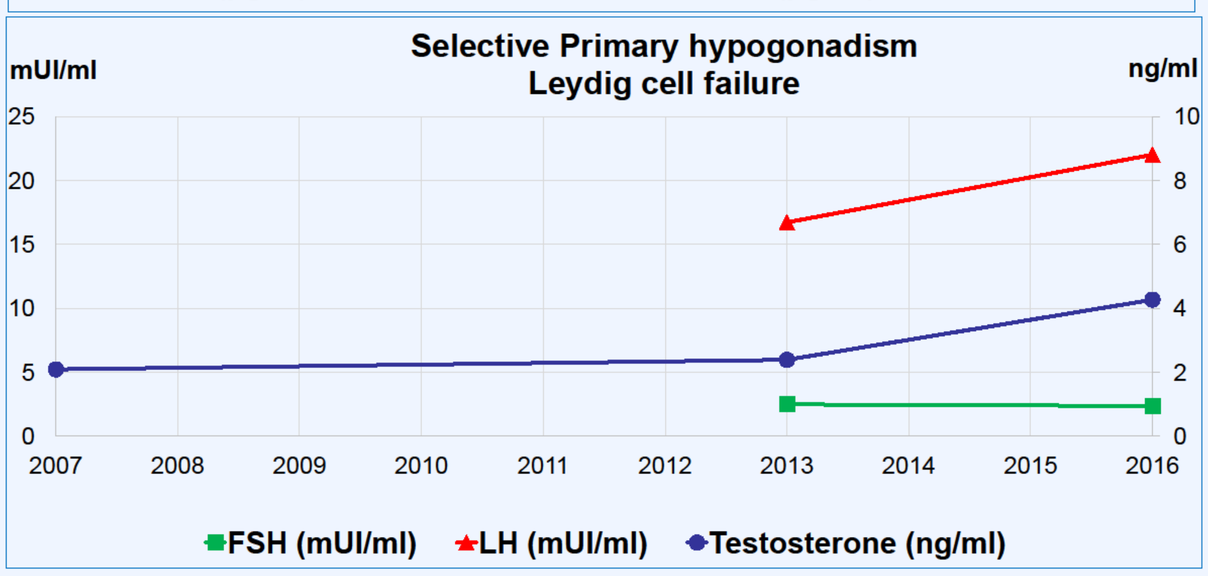
► General examination also shows hyperpigmentation, systolic BP ~ 90mmHg but also hip pain and we noticed a short right leg – radiographic findings – femoral neck fracture with osteoarthritis.

► He mentions that he suffered a head injury by falling from own height, 6 months ago which was followed by a rapid neurological deterioration.

► He received gluco- and mineralo-corticoid replacement therapy.

Laboratory evaluation:





Elevated plasma concentration of VLCFA: C22.0:15.9 mg/L (10.5- 51 mg/L); C24:26.3 mg/L (8.5-35.7 mg/L)
C26:1.01, mg/L (0.1-0.6 mg/L); C26/C22:0.06 (<0.04), C24/C22: 1.65 (<1.16)

Conclusion:

Up to 60% of adolescent and young adult men with ADL/AMN have no or few neurologic abnormalities at the time of diagnosis of adrenal insufficiency. The cerebellum-brainstem form of AMN can be a rare presentation of ALD. ADL/AMN should be considered in any boy or young man with adrenal insufficiency and neurological signs, albeit atypical.

Management:

► **Control of adrenal insufficiency**

► Physical therapy program was initiated to address the progressive loss of balance and fine motor control

► Hip replacement surgery for hip fracture is still under discussion with patient and his family

► Still investigate availability of genetic testing

► Hematopoietic cell transplantation is emerging as the treatment of choice for individuals with early stages of cerebral involvement

4. http://www.uptodate.com/contents/adrenoleukodystrophy?source=related_link access May 2016

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Corin Badiu
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