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Case Report

Diagnosed with primary adrenal insufficiency? search adrenoleukodystrophy-two brothers presented with similar phenotype

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ABSTRACT

X-linked adrenoleukodystrophy (X-ALD) is a genetic disease with a variety of phenotypic expression. This is the first case report of X-AMN/ALD in two brothers in Bangladesh confirmed by raised VLCFA. Our index patient of 19 years presented on 2014 with adrenal insufficiency, after one year developed progressive spastic paraparesis along with cognitive declination and behavioral abnormality. His only brother was clinically asymptomatic at presentation with Addison's disease and extensor planter reflexes. After three years of follow up, index patient became bed bound with slurred speech, urinary urge incontinence and his brother developed spastic paraparesis with cognitive impairment. None had gonadal impairment. Follow up MRI after three years revealed lesion in brainstem in both along with atrophy of thoracic segment of spinal cord in index patient and cerebellum, internal capsule involvement in his brother. Both were of pure AMN variety but due to presence of cognitive impairment and behavioral abnormality they can be categorized as cerebral variety of AMN. On 2023, our index patient is still surviving with major functional disability and his brother died on 2019, 5 years of initial diagnosis.

Keywords: Addison's disease, Primary adrenal insufficiency, ALD

INTRODUCTION

X-linked adrenoleukodystrophy (X-ALD) was first described in 1923.[1,2] The adult form was named adrenoleukodystrophy (AMN) by Griffin et al in 1977.[3] It is caused due to inborn mutations in the ABCD[1] gene located on the X chromosome.[4] Mutation in this gene causes absence or dysfunction of ALD protein (ALDP), a peroxisomal transmembrane protein that transports VLCF acyl-Coenzyme A esters from the cytosole into the peroxisome resulting in impaired peroxisomal beta-oxidation of very long chain fatty acids (VLCFA: ≥C22) and it's accumulation in plasma and all tissue primarily white matter of CNS, adrenal cortex and Leydig cells in the testis.[5,6] The overall birth prevalence is 1:15,000 (male patients and female patients).[7] It has a wide range of phenotypic expression. Patients are asymptomatic at birth, affected males have three main phenotypes- rapidly progressive leukodystrophy (cerebral ALD), a slowly progressive myeloneuropathy (adrenomyeloneuropathy) and Addison disease.[8-11] It is X-linked disorder at least half of the women who are heterozygous for X-ALD develop an adrenomyeloneuropathy-like syndrome in middle or later age.[9,12-14] Cerebral ALD and primary adrenal insufficiency are extremely rare in women.[15]

One report from Bangladesh was not confirmed with VLCFA. We present X-AMN/ALD in two brothers in Bangladesh which was confirmed by raised VLCFA.[16]

Currently, it is not possible to predict the individual disease course.[17] Only supportive treatment is available for myeloneuropathy, hormone replacement for adrenal insufficiency, but hematopoietic stem cell transplant (HSCT) is the treatment of choice for patients with early ALD although it does not reverse neurological changes or prevent adrenal involvement or myeloneuropathy.[8,17,18]

ALD screening is added to the recommended uniform screening panel of newborn in the USA since 2016 and now Netherland, Spain, Israel, Slovenia, and Ireland approved pilot projects or regional screening.[19,20]

As it is a rare disease, devastating disease and frequently there is delay in diagnosis, it is essential for all clinicians to be aware of this disease, particularly in patients presenting with adrenal insufficiency in combination with neurological manifestations with or without hypogonadism and those with positive family history. As no effective therapy is available, awareness of X-ALD is needed for early diagnosis, family screening and genetic counseling for preventing this distressing disease.

CASE REPORT

Our index patient of 19 years, a student, nonsmoker, non-alcoholic from Savar, a rural area around 50 km from the capital city, Dhaka, presented on July 2014 with anorexia, weakness, vomiting for 3 years without history of other bowel symptoms, jaundice, fever, cough, haemoptysis, contact with patients with known tuberculosis. He lost 3 kg weight over last 3 years. His school performance was more than average at the primary level but gradually declining for 3 years. He discontinued his study because of poverty and illness.

He was Ill-looking, lethargic with increased pigmentation in perioral skin, lips, tongue, mucus membrane, palmar creases, knuckles (Figure 1). His blood pressure was 90/60 (lying), 80/50 (standing) mm of Hg, BMI was 14 kg/m^2.

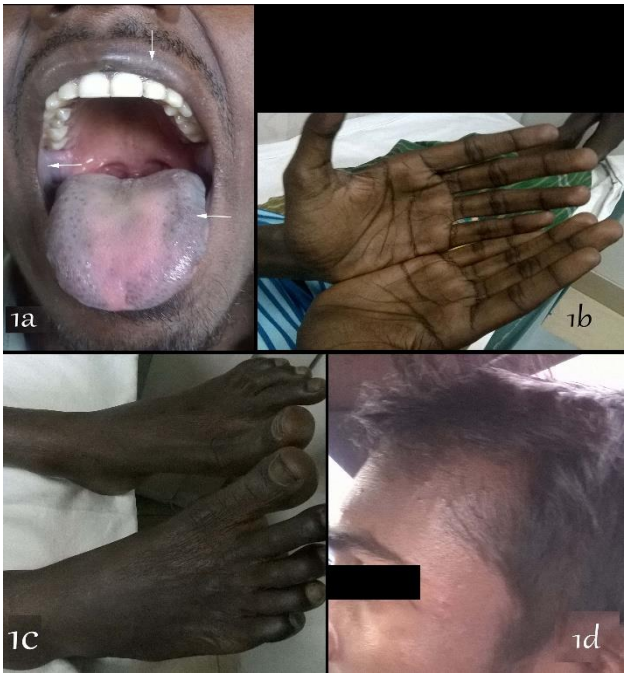

Figure 1 (A-D): Index patient: increased pigmentation in tongue, lips, mucus membrane, palmar crease leg and reduced scalp hair.

Serum electrolytes were normal, basal cortisol at 9.00 am was 3.79 microgram/dl (normal 5-25), ACTH >1250 pg/ml (normal <46). He was diagnosed with Addison's disease, tablet hydrocortisone, 15 mg at morning, 5 mg at afternoon was started and a steroid card was given.

His appetite increased, vomiting subsided but after one year he presented with abnormal irrelevant talking, irritability, loss of concentration, weakness and difficulty in walking without any history of headache, visual disturbance, sensory symptoms, sphincter incontinence.

He had reduced scalp hair. Neurological examination revealed euphoric mood with normal speech, intact cranial nerves, absent jaw jerk. In both upper and lower limbs bulk, tone of the muscles were normal with power 5/5, all jerks were exaggerated with bilateral planter extensor reflexes, Hoffmann sign was positive. Touch, pressure, pain and temperature sensations were intact. Vibration sensation was impaired but position sensation was intact in both lower limbs. Cerebellar functions were normal. He had spastic gait but could stand from a squatting position. Examination of spine and other systems were normal.

For further evaluation he got admitted in Bangabandhu Sheikh Mujib Medical University. Considering adrenal insufficiency with neurological involvement, ALD was strongly suspected. His elder brother (22 years) was asymptomatic with increased pigmentation on tongue, palmar crease with scanty scalp hair (Figure 2).

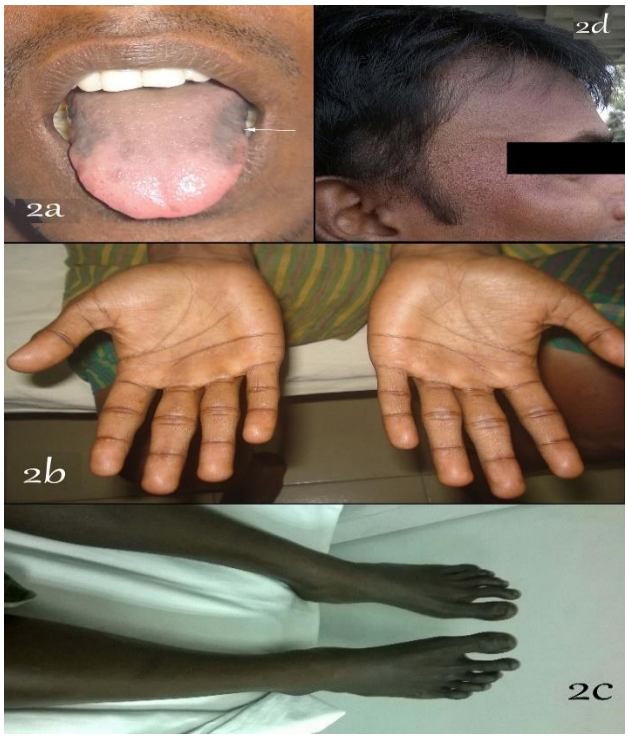

Figure 2 (A-D): Brother: increased pigmentation in tongue, palmar crease, leg and frontal scalp baldness.

His blood pressure on lying was 110/70 mm of Hg without any postural hypotension. Neurological examination revealed euphoric mood with normal speech, intact cranial nerves, absent jaw jerk. Bulk and tone of the muscles of all limbs were normal, power was 5/5, all jerks of both upper and lower limbs were exaggerated with bilateral planter extensor reflexes, Hoffmann sign was positive. Touch, pressure, pain, temperature, position and vibration sensations were normal, cerebellar examination, gait, examination of spine, other systems revealed normal.

His ACTH was high (>1250 pg/ml), basal cortisol at 9 am was 196.70 nmol/L. He was started with tablet hydrocortisone 15 mg in morning, 5 mg at evening.

As this young patient with Addison's disease developed neurological symptoms and his only brother was also found to have Addison's disease with neurological involvement, our clinical diagnosis was X-ALD.

Investigations

MRI of brain

T2 and FLAIR images showed bilateral hyperintense basal ganglia which occurs in metabolic disorder/demyelinating disease (Figure 3).

Electophysiologic study revealed somatosensory evoked potentials (SEPs) were normal. Visual evoked potentials (VEPs) and brainstem auditory evoked potentials (BAEPs) did not demonstrate any definite abnormal findings. Nerve conduction studies (NCS), needle electromyographic (EMG) examinations were within normal range.

Plasma VLCFA analysis is recommended in all male patients with Addison's disease or progressive spastic paraparesis of unknown cause and is the most frequently used diagnostic test for X-ALD. Three parameters analyzed are the concentration of C26:0, the ratio of C24:0/C22:0 and C26:0/C22:0. Blood sample was sent in National University Hospital (NUH), Singapore. In index patient C26:0 was significantly high, the C24/C22 and C26/C22 ratios were abnormal (Table 1).

LH, FSH, Testosterone level were within normal limit.

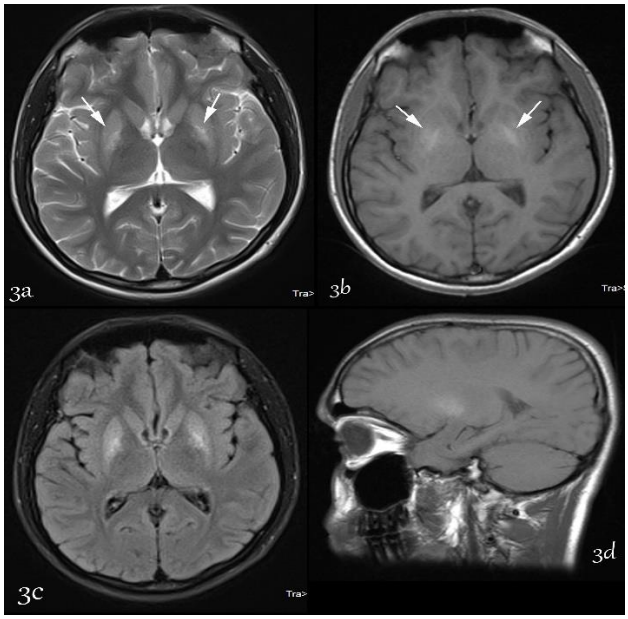

Figure 3: Initial MRI of brain in Index patient showing symmetrical increased signal intensity in basal ganglia (globus pallidus) region in T2 and flair.

Table 1: Plasma VLCFA analysis in index patient, his brother and mother.

Plasma VLCFA	Index patient	Brother	Mother	Reference range (µmol/L)
Docosanoic acid (C22)	34	51.7	42.2	30-112
Tetracosanoic acid (C24)	62	73.4	46.3	14-80
Hexacosanoic acid (C26)	4.21 H	3.33 H	1.08	0.33-1.5
C24:C22 ratio	1.82 H	1.42 H	1.01	0.44-1.05
C26:C22 ratio	0.125 H	0.064 H	0.026	0.005-0.030
Phytanic acid	0.56	3.42	4.98	0.20-19.30
Pristanic acid	0.60	0.38	0.39	0.00-2.00

In his brother, initial MRI of brain, electrophysiological study of nerves, serum LH, FSH, testosterone level revealed normal. VLCFA analysis showed high C26:0 with abnormal ratio of C24:0/C22:0 and C26:0 / C22:0 (Table 1). This finding is indicative of hemizygosity for X-ALD /AMN. VLCFA analysis of mother revealed normal (Table 1).

Outcome and follow-up

After three years, our index patient had no more vomiting as well as his general wellbeing, blood pressure, pigmentation improved significantly but neurological symptoms deteriorated. He became bedbound and could stand only with assistance, had slurred speech, urinary urge incontinence. Follow up MRI of brain and spinal cord revealed symmetrical hyperintensity involving brainstem in T2 and FLAIR images and atrophy in the thoracic segment of spinal cord (Figure 4). On 2023, he is still surviving but completely bedbound.

His asymptomatic elderly brother developed gradual cognitive impairment with spastic gait without any sensory impairment and still could do his daily activities

by himself. His MRI of brain revealed symmetrical hyperintensity involving brainstem and cerebellum (dentate nucleus), basal ganglia, posterior limb of internal capsule in T2 and FLAIR images (Figure 5). His condition deteriorated rapidly and he died on 2019, 5 years of initial diagnosis.

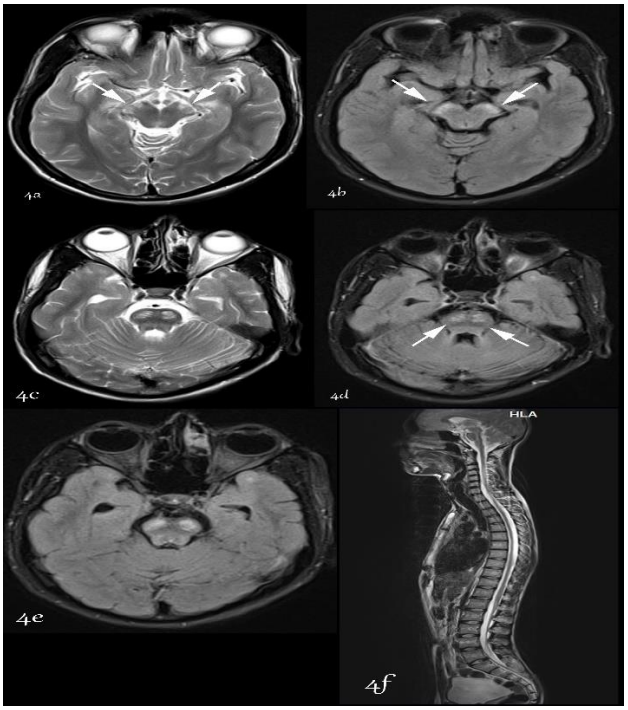

Figure 4: Follow up MRI of brain and spinal cord in index patient showing symmetrical signal hyperintensity involving cerebral peduncle of mid brain (a, b), pons (c, d, e) in T2 and flair and atrophy of thoracic segment of spinal cord (f) in T2 image.

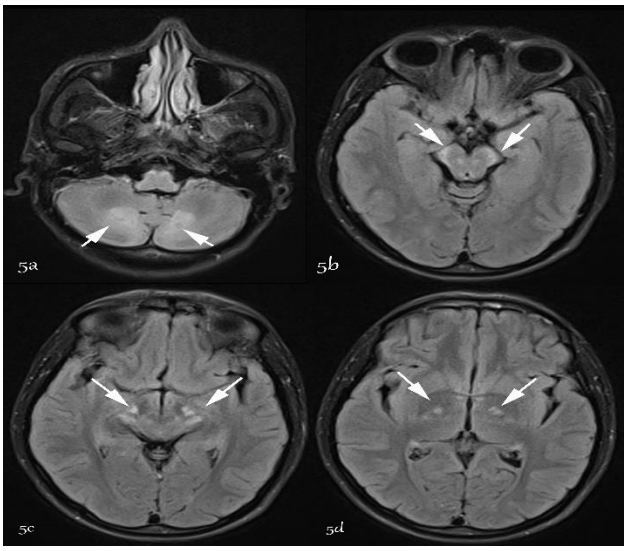

Figure 5 (A-D): Follow up MRI of brain in brother showing symmetrical signal hyperintensity involving cerebellum hemisphere (a), cerebral peduncle of mid brain (b. c), basal ganglia, posterior limb of internal capsule in (d) flair images.

DISCUSSION

X-linked ALD is a rare disease. This patient presented with Addison's disease for which tuberculosis is the commonest cause in underdeveloped countries.[21-23] whereas autoimmune destruction accounts for 75-80% cases in developed countries. Addison's disease in young male should prompt consideration of ALD as the underlying abnormality.[24]

Our index patient presented with symptoms of Addison's disease at the age of 19 which can be the first manifestation of ALD seen in upto 80% of ALD.[17,25-27] His brother (22 years) was clinically asymptomatic at presentation but had adrenal insufficiency with only sign of upper motor neuron lesion indicating that all asymptomatic family members must be screened for adrenal insufficiency and any neurological deficit. Up to 60% of X-ALD have no or few neurologic symptoms at the time of diagnosis of adrenal insufficiency which correlates with his elderly brother.[28] Therefore, preclinical AMN should be considered in patients with adrenal insufficiency. Now it is recommended to obtain morning ACTH and cortisol levels at diagnosis and then monitor these along with renin and electrolytes every 3-6 months.[8,29]

AMN typically presents in adult males at 20-40 years of age and comprises approximately 40-45% of ALD/AMN complex.[8,30-32] The primary manifestation is spastic paraparesis and sexual dysfunction. 70% of AMN have overt or subclinical adrenal insufficiency, can occur before, after or at the same time as the neurological disease but is not correlated with the severity of the neurological disorder.[33,34]

A significant proportion of AMN have associated gonadal dysfunctions.[35] Both of our patients had normal testosterone level. Now its recommended that unless have symptoms, boys and men should not be screened for gonadal insufficiency.[8]

ALD has a variable and unpredictable clinical course.[17] This patient presented with behavioral abnormalities in the form of excessive talking, irritability, inattention and with cognitive decline like learning difficulty and poor academic performance. His brother also developed similar behavioral abnormalities after 3 years of disease progression. Cerebral involvement at the time of diagnosis of AMN is rare (only 6%).[36] In long-term follow-up studies, 27-63% of AMN developed symptoms of cerebral involvement (e.g., cognitive decline, behavioral abnormalities, visual loss, impaired auditory discrimination or seizures).[37] Cerebral ALD is rare after 15 years of age and rapid progression is common leading to death within 5 to 10 years of diagnosis.[38] On 2023 index patient is still alive with total disability but his asymptomatic brother died on 2019 after 5 years of initial diagnosis.

The pathological basis of AMN is a noninflammatory distal axonopathy that involves the long tracts of the spinal cord and to a lesser extent, the peripheral nerves.[39] Brain MRI is normal or may show subtle abnormalities like moderately increased signal intensities of the pyramidal tracts in brainstem and internal capsules on FLAIR and T2 sequences that reflect likely Wallerian degeneration in patients with longstanding symptoms of AMN. These abnormalities are not considered manifestations of cerebral ALD. If the increased signal of the pyramidal tracts becomes more intense and extends beyond the internal capsules into the white matter of the centrum semiovale, this is considered a manifestation of cerebral ALD. MRI of the spinal cord eventually shows non-specific atrophy.[40-42]

Disease progression was demonstrated by follow-up MRI. Initially index patient revealed bilateral hyperintense signal change in basal ganglia on T2 and FLAIR images. After 3 years showed additional abnormal signal intensity in the corticospinal tract in the brain stem bilaterally and atrophy of thoracic segment of spinal cord which was difficult to evaluate. His brother who had initial normal MRI of brain, after 3 years revealed bilateral abnormal signal intensity in the brain stem and cerebellum (dentate nucleus) but had no clinical manifestation of cerebellar involvement. In both cases inspite of spastic paraplegia, cognitive and behavioral abnormalities, absence of characteristic diffuse cerebral white matter demyelination was noteworthy. A retrospective study revealed that over a period of 10 years, approximately 20% of AMN patients developed additional cerebral demyelination.[36] and 37-41% adult developed cerebral demyelination on brain MRI.[36,37] Further follow up MRI is needed to demonstrate diffuse cerebral involvement in these cases.

In both cases SEPs, VEPs, BAEPs, NCS and EMG examinations were within normal range which contrast with the findings of axonopathy in majority of ALD.[43]

Both had scanty scalp hair, a striking feature of ALD which is similar to the findings by Konig et al.[44] It was first described in 1955.[45]

If X-ALD is suspected in a male with neurological symptoms (with or without typical brain MRI abnormalities) or Addison's disease, demonstration of elevated plasma VLCFA confirms the diagnosis. As X-linked disease, VLCFA in mother was normal. To confirm heterozygosity, genetic study of mother is recommended.

ALD has a great variability of phenotypic expression - Addison's disease only, cerebral (mild, severe) without AMN, pure AMN, cerebral AMN, cerebellar, asymptomatic, female heterozygous.[46] Its clinical presentation can vary within the same family.[47] Here both brothers presented with similar phenotype-with spastic paraparesis, Addison's disease and absence of diffuse cerebral white matter demyelination on MRI, they can be classified as pure AMN variety. But presence of behavioral abnormality and cognitive declination may categorize them as 'cerebral AMN' phenotypic expression which represent only 15% case of ALD.[46]

It is recommended that all patients who are diagnosed with ALD should be informed about the option of family screening, early diagnosis as HSCT in pre-symptomatic cerebral ALD is a new hope and newborn screening.[8]

CONCLUSION

ALD should be suspected in anyone presented with combination of Addison's disease, neurological feature with or without hypogonadism. In pure AMN variety, presence of cognitive impairment and behavioural abnormality is rare which is present here in both brothers, though characteristic MRI feature of cerebral AMN is absent. Pure AMN can progress to cerebral AMN variety. Steroid replacement has no effects on neurological symptoms. Asymptomatic family members must be screened for ALD.

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REFERENCES

1. Moser HW, Smith KD, Watkins PA, Powers J, Moser AB. X-linked adrenoleukodystrophy. In: Scriver CR, Beaudet AL, Sly WS, Valle D, eds. The Metabolic and Molecular Bases of Inherited Disease. New York, NY: McGraw Hill. 2001;3257-01.
2. Siemerling E, Creutzfeldt HG. Bronzekrankheit und sklerosierende Encephalomyelitis. Arch Psychiatr Nervkrankh. 1923;68:217-44.
3. Griffin JW, Goren E, Schaumburg H, Engel WK, Loriaux L. Adrenomyeloneuropathy: a probable variant of adrenoleukodystrophy.I. Clinical and endocrinologic aspects. Neurology. 1977;27:1107.
4. Mosser J, Douar AM, Sarde CO. Putative X-linked adrenoleukodystrophy gene shares unexpected homology with ABC transporters. Nature. 1993; 361:726-30.
5. Van Roermund CW, Visser WF, Ijlst L. The hu6w@1Q2 man peroxisomal ABC half transporter ALDP functions as a homodimer and accepts acyl-CoA esters. FASEB J. 2008;22:4201-8.
6. Ofman R, Dijkstra IM, van Roermund CW. The role of ELOVL1 in very long-chain fatty acid homeostasis and X-linked adrenoleukodystrophy. EMBO Mol Med. 2010,2:90-7.
7. Moser A, Jones RO, Hubbard WC. Newborn screening for X-linked adrenoleukodystrophy. Int J Neonatal Screen. 2016;2(4):1-5.
8. Engelen M, Van Ballegoij WJC, Mallack EJ. International recommendations for the diagnosis and

management of patients with adrenoleukodystrophy: a consensus-based approach. Neurology. 2022;10.
9. Engelen M, Barbier M, Dijkstra IM. X-linked adrenoleukodystrophy in women: a cross-sectional cohort study. Brain. 2014;137(Pt 3):693-706.
10. Huffffnagel IC, Dijkgraaf MGW, Janssens GE. Disease progression in women with X-linked adrenoleukodystrophy is slow. Orphanet J Rare Dis. 2019;14(1):30.
11. Habekost CT, Schestatsky P, Torres VF. Neurological impairment among heterozygote women for X-linked Adrenoleukodystrophy: a case control study on a clinical, neurophysiological and biochemical characteristics. Orphanet J Rare Dis. 2014;9:6.
12. Dobyns WB, Filauro A, Tomson BN. Inheritance of most X-linked traits is not dominant or recessive, just X-linked. Am J Med Genet. 2004;129A:136-43.
13. Restuccia D, Di Lazzaro V, Valeriani M. Neurophysiological abnormalities in adrenoleukodystrophy carriers. Evidence of different degrees of central nervous system involvement. Brain. 1997;120:1139-48.
14. Horn MA, Nilsen KB, Jorum E, Mellgren SI, Tallaksen CM. Small nerve fifiber involvement is frequent in X-linked adrenoleukodystrophy. Neurology. 2014;82(19):1678-83.
15. Schmidt S, Traber F, Block W. Phenotype assignment in symptomatic female carriers of X-linked adrenoleukodystrophy. J Neurol. 2001;248(1):36-44.
16. Mondol MBA, Siddiqui MMR, Wahab L. Adrenoleukodystrophy: A Rare Case Report. J Bangladesh College of Physicians and Surgeons. 2010;28(3):189-92.
17. Kemp S, Huffffnagel IC, Linthorst GE, Wanders RJ, Engelen M. Adrenoleukodystrophy-neuroendocrine pathogenesis and redefifinition of natural history. Nat Rev Endocrinol. 2016;12(10):606-615.
18. Petryk A, Polgreen LE, Chahla S. No evidence for the reversal of adrenal failure after hematopoietic cell transplantation in X-linked adrenoleukodystrophy. Bone Marrow Transplant. 2012;47:1377-8.
19. Newborn-screening.html. Available at: https://www.aldalliance.org/newbornscreening.html. Accessed on 11 May 2023.
20. Loeber JG, Platis D, Zetterstro¨m RH. Neonatal screening in Europe revisited: an ISNS perspective on the current state and developments since 2010. Int J Neonatal Screen. 2021;7:15.
21. Brooke AM, Monson JP. Addison's disease. Medicine. 2009;37(8):416-9.
22. Bhatia E, Jain SK, Gupta RK, Pandey R. Tuberculous Addison's disease: lack of normalization of adrenocortical function after anti-tuberculous chemotherapy. Clin Endocrinol. (Oxf). 1998;48(3):355-9.
23. Guo YK, Yang ZG, Li Y. Addison's disease due to adrenal tuberculosis: contrast-enhanced features and clinical duration correlation. Eur J Radiol. 2007;62(1):126-31.
24. Laureti S, Casucci G, Santeusanio F, Angeletti G, Aubourg P, Brunetti P. X-linked adrenoleukodystrophy is a frequent cause of idiopathic Addison's disease in young adult male patients. J Clin Endocr Metab. 1996;81:470-74.
25. Burtman E, Regelmann MO. Endocrine dysfunction in X-linked adrenoleukodystrophy. Endocrinol Metab Clin North Am. 2016;45:295-309.
26. Dubey P, Raymond GV, Moser AB. Adrenal insufficiency in asymptomatic adrenoleukodystrophy patients identifified by very long-chain fatty acid screening. J Pediatr. 2005;146:528-32.
27. Regelmann MO, Kamboj MK, Miller BS. Adrenoleukodystrophy: guidance for adrenal surveillance in males identifified by newborn screen. J Clin Endocrinol Metab. 2018;103:4324-31.
28. Sadeghi-Nejad A, Senior B. Adrenomyeloneuropathy presenting as Addison's disease in childhood. N Engl J Med. 1990;322:13-6.
29. Regelmann MO, Kamboj MK, Miller BS. Adrenoleukodystrophy: guidance for adrenal surveillance in males identifified by newborn screen. J Clin Endocrinol Metab. 2018;103:4324-31.
30. Moser HW, Moser AB, Steinberg SJ. X-linked adrenoleukodystrophy. Gene Reviews. www.genetests.org. Accessed on 06 February 2023.
31. Percy AK, Rutledge SL. Adrenoleukodystrophy and related disorders. Ment Retard Dev Disabil Res Rev. 2001;7:179.
32. Turk BR, Theda C, Fatemi A, Moser AB. X-linked adrenoleukodystrophy: Pathology, pathophysiology, diagnostic testing, newborn screening and therapies. Int J Dev Neurosci. 2020; 80:52-72.
33. Moser HW, Moser AB, Naidu S, Bergin A. Clinical aspects of adrenoleukodystrophy and adrenomyeloneuropathy. Dev Neurosci. 1991;13(4-5):254-61.
34. Girard S, Bruckert E, Turpin G. Endocrine disease in adrenoleukodystrophy. Ann Med Interne. 2001;152(1):15-26.
35. Powers JM, Schaumburg HH. The testis in adreno-leukodystrophy. Am J Pathol. 1981;102:90-8.
36. Van Geel BM, Bezman L, Loes DJ, Moser HW, Raymond GV. Evolution of phenotypes in adult male patients with X-linked adrenoleukodystrophy. Ann Neurol. 2001;49:186-94.
37. De Beer M, Engelen M, Van Geel BM. Frequent occurrence of cerebral demyelination in adrenomyeloneuropathy. Neurology. 2014; 83:2227-31.
38. Zhu J, Eichler F, Biffi A. The Changing Face of Adrenoleukodystrophy. Endocr Rev. 2020;41(4):577-93.
39. JM, DeCiero DP, Ito M, Moser AB, Moser HW. Adrenomyeloneuropathy: a neuropathologic review featuring its noninflammatory myelopathy. J Neuropathol Exp Neurol. 2000;59:89-102.

40. Dubey P, Fatemi A, Huang H. Diffusion tensor-based imaging reveals occult abnormalities in adrenomyeloneuropathy. Ann Neurol. 2005;58:758-66.
41. Fatemi A, Smith SA, Dubey P. Magnetization transfer MRI demonstrates spinal cord abnormalities in adrenomyeloneuropathy. Neurology. 2005;64:1739-45.
42. Smith SA, Golay X, Fatemi A. Quantitative magnetization transfer characteristics of the human cervical spinal cord in vivo: application to adrenomyeloneuropathy. Magn Reson Med. 2009;61:22-7.
43. Van Geel BM, Koelman JH, Barth PG, Ongerboer de Visser BW. Peripheral nerve abnormalities in adrenomyeloneuropathy: a clinical andelectrodiagnostic study. Neurology. 1996;46:112-8.
44. Konig A, Happle R, Tchitcherina E. An X-linked gene involved in androgenetic alopecia: a lesson to be learned from adrenoleukodystrophy. Dermatology. 2000;200(3):213-8.
45. Harris-Jones JN, Nixon PG. Familial Addison's disease with spastic paraplegia. J Clin Endocrinol Metab.1955;15:739-44.
46. Moser HW, Raymond GV, Dubey P. Adrenoleukodystrophy, New Approaches to a Neurodegenerative Disease JAMA. 2005;294:3131-4.
47. Moser HW, Loes DJ, Melhem ER. X-Linked adrenoleukodystrophy: overview and prognosis as a function of age and brain magnetic resonance imaging abnormality. A study involving 372 patients. Neuropediatrics. 2000;31:227-39.

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