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Adrenoleukodystrophy: A Rare Case Report

MBA MONDOL[a], MMR SIDDIQUI[b], L WAHAB[c], MA HOQUE[d], SU KHAN[e], KM RAHMAN[f], QD MOHAMMAD[g]

Summary:

A young boy of 18 years was admitted at department of Neurology, Dhaka Medical College Hospital with the complaints of progressive generalized hyper-pigmentation, gradual loss of vision, hearing impairment, abnormal behaviors and one episode of seizure. Examination finding revealed, abnormal behaviors, generalized hyper pigmentation of skin, oral mucosa, gum, tongue and palmer creases. He has diffuse hair loss, bilateral primary optic atrophy, bilateral sensoryneural deafness. All routine investigations revealed normal findings except, CSF protein were elevated, biochemical features (very high ACTH, low basal cortisol) of primary adrenal failure, Magnetic resonance imaging (MRI) of the head showed bilateral symmetrical white matter abnormalities in parieto-occipital regions. The diagnosis of Adreno-leukodystrophy (ALD) was strongly suggested from the medical history, biochemical and radiological (MRI) findings of brain. The purpose of our report is to highlight this very rare nontreatable disease to all. A patient of neuropsychiatric symptoms with Addison's disease we must think about ALD, because it's progression can be delayed with early diagnosis and supportive treatments, it's incidence can be reduced by genetic counseling.

Key words: Adrenoleukodystrophy (ALD), Addison's disease, Very long chain fatty acid (VLCFA).

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Introduction:

Adrenoleukodystrophy (ALD) is a group of genetically determined peroxisomal disorders associated with progressive central demye-lination of brain, primary adrenal cortical insufficiency (Addison's disease) and hypo-gonadism[1]. The more common form of ALD is X-linked with abnormal gene location in Xq28 region[2] and occurs in childhood or adolescence; however, a neonatal form occurs from autosomal recessive inheritance. ALD affecting 1/20,000 males whose having impaired ß-oxidation of very long chain fatty acids (VLCFA) in peroxisomes, particularly hexacosanoic acid (C26:0), pentacosanoic acid (C25:0) and tetracosanoic acid (C24:0), which accumulate in tissues and body fluids[2,3]. This accumulation probably incorporated into myelin which leads to instability and dysmyelination with possible direct cytotoxic effect on oligodendrocytes. At least seven clinical subtypes have been described: childhood cerebral ALD (more severe form), adolescent cerebral ALD, adult cerebral ALD, adrenomyeloneuropathy (AMN), Addison's disease only, presymptomatic (asymptomatic) and heterozygous women[4]. Most patients are diagnosed in childhood or adolescence when they have such neurologic manifestations as cognitive dysfunction, behavioral problems, visual loss, seizures or features of adrenal insufficiency[5]. Progression is usually rapid, with the patient reaching a vegetative state within 10 years after the neurologic symptom onset. In patients with Addison's disease, diagnosis of ALD is suggested by the abrupt development of neuropsychiatric symptoms, associated with MRI confirmation of extensive, usually symmetric, white matter disease. Here we report a case of ALD.

Case report:

A 18 years old young boy from Feni was admitted at department of Neurology, Dhaka Medical College Hospital with the complaints of progressive blackening of the whole body for the last 15 years, gradual impairment of vision for last 7 years, hearing impairment and abnormal behaviors noticed for last 3 months. He started his schooling at the age of five, but failed to continue due to lack of attention, and subsequent visual impairment. Gradually he also started having hearing impairment. He had a single episode of seizure 3 months back. During his hospital stay he also had features of

a. Dr. Md. Badrul Alam Mondol, Associate Professor
b. Dr. Md. Mahmudur Rahman Siddiqui, Postgraduate Resident,
c. Dr. Luna Wahab, Postgraduate Resident
d. Dr. Md. Azharul Hoque, Associate Professor
e. Dr. Sharif Uddin Khan, Assistant Professor
f. Dr. Kazi Mohibur Rahman, Assistant Professor
g. Professor Dr. Quazi Deen Mohammad, Professor & Head of the Department

Department of Neurology, Dhaka Medical College Hospital, Dhaka.

Address of Correspondence: Dr. Md. Badrul Alam Mondol, Associate Professor, Department of Neurology, Dhaka Medical College Hospital, Dhaka.

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psychosis and complained of vertigo. His past medical history was unremarkable. Prior to his admission to the hospital he was not on any medications except for some herbal products. His family history was also unremarkable. Examination finding revealed, generalized hyper-pigmentation (Fig-1,2) of skin including pigmentation of the oral mucosa, gum, tongue and palmer creases. He has diffuse hair loss, his blood pressure was within normal limits without any postural drop. His genital examination revealed testicular atrophy. Neurological examination revealed, bilateral primary optic atrophy (confirmed by ophthalmologist), sensory-neural hearing loss in both ears (confirmed by Audiometry). All routine investigations revealed normal findings, but CSF examination revealed high protein: 208 mg/dl (normal level 15-45 mg/dl) without any change of cell count, glucose and microbiological findings. Serum electrolytes were within normal limits. On imaging abdominal USG was normal but MRI of the brain showed bilateral symmetrical hypointence signal change in T1 weighted images and bilateral symmetrical hyperintance signal changes in T2 and Flair weighted images in the sub cortical white matter of both parieto-occipital regions, which were compatible with Leukodystrophy (Fig-3,4,5). His basal cortical level was

Fig-2: *Generalized hyper pigmentation.*

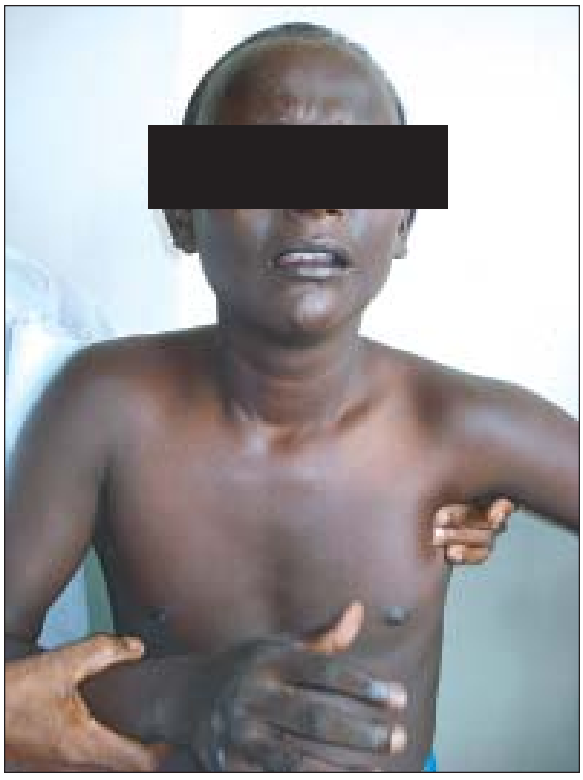

Fig-1: *Generalized hyper pigmentation.*

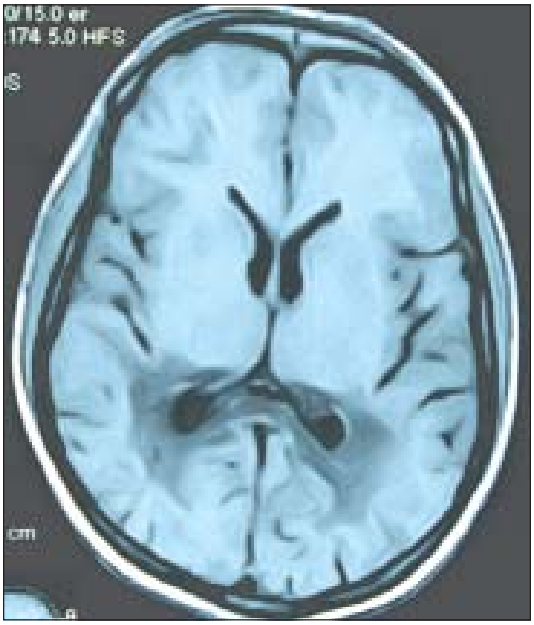

Fig-3: *Axial T1 weighted MRI of brain showing bilateral, symmetrical hypointence signal change in the sub cortical white matter of both occipito-parietal regions.*

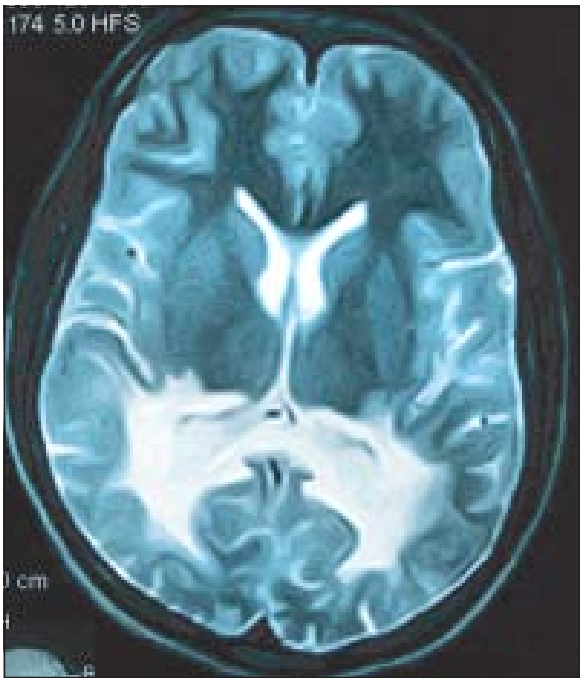

Fig-4: *Axial T2 weighted MRI of brain showing symmetrical, bilateral hyperintence signal changes in sub cortical white matter of both occipito-parietal regions.*

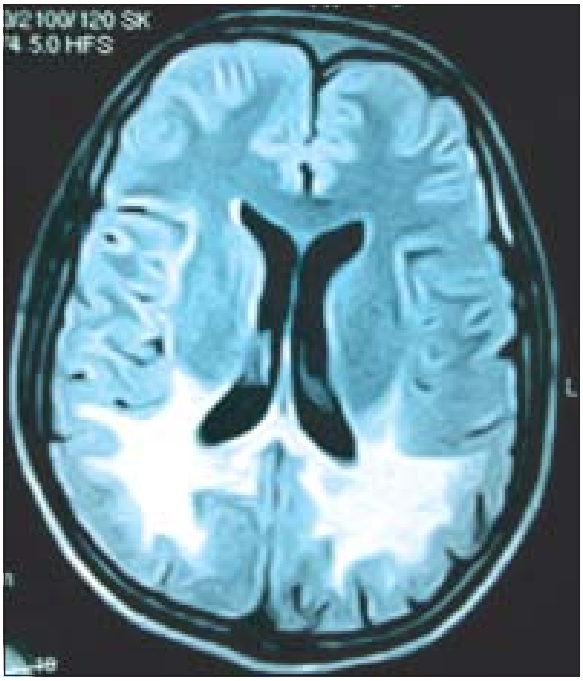

Fig-5: *Axial Flair MRI image of brain showing hyperintense signal change in the same regions.*

1.95 micg/dl at 9.00 AM (normal level 5-25 micg/dl at morning), serum ACTH level was >1250 pg/ml (normal level 5-46 pg/ml). The diagnosis of adrenoleukodystrophy was strongly suggested from the medical history, biochemical and radiological (MRI of head) findings. Then treatment was started with antipsychotic and prednisolone with good control of symptoms. Now he is in regular follow up.

Discussion:

The clinical course in adrenoleukodystrophy is characterized by behavioral disorders, ataxia, visual loss, decreased hearing, and epileptic seizures, followed by mental deterioration, psychosis and death. Adrenal insufficiency is a usual finding, but does not always precede neurologic disease [5,6]. Abnormal skin pigmentation and other features of adrenal insufficiency may become apparent before neurological symptoms. In some cases adrenal symptoms will never appear [7]. Most common cause of primary adrenal insufficiency are either autoimmune adrenal failure (about 75% to 80%) or tuberculosis (about 20%) [1], other etiologies such as ALD are thought to be distinctly uncommon [1]. We should think of ALD when adrenal insufficiency associated with neuropsychiatric manifestations, like our patient.

Typically demyelination begins bilaterally in the occipital region, extending across the splenium of the corpus callosum. Gradually the process spreads outward and forward as a confluent lesion, affecting the parietal, temporal, and finally, the frontal white matter, cerebellar white matter, cerebellar peduncles, and corticospinal and corticobulbar tracts. Calcium deposition can also be found. MR is more sensitive than computed tomography to detect these demyelinating plaques. Plain MRI show hypointense signal on T1 and hyperintense signal on T2 and flair images. Post contrast study shows contrast enhancement at the outer margins due to active demyelination and disruption of blood brain barrier [7]. VLCFA can be measured in plasma, which will be raised. Features of primary adrenal insufficiency (Serum ACTH, ACTH stimulation test, Serum. Cortisol, Serum. testosteron & gonadotropin level) should be measured [8].

The prognosis of ALD can be estimated on the basis of age and the severity of the brain MRI abnormality, but there are exceptions to these rules, and some patients

may remain stable with no further progression for up to 12 years after the initial neurological symptoms [9]. Although childhood cerebral form, causing a severe disability that leads to death early. On the other hand the adrenomyeloneuropathy is a milder adult form with involvement of mainly the spinal cord and peripheral nerves, having a slow progression with better prognosis.

Treatment is symptomatic, for example, steroid use for adrenal insufficiency and psychotropics for psychiatric symptoms. No clear effective treatments are available, although Lorenzo's oil (4:1 glyceryl trioleate and glycery trierucate) can be used before the age of 6 may reduce the probability of develop neurological deficit in late life[2,8]. Statins can reduce VLCFA level, but no influence in neuronal and endocrine functions [2,8]. Fatty diet should be restricted. Bone marrow transplantation is an option in patient with early neurological features, abnormal magnetic resonance imaging scans and neuropsychological dysfunction but is not recommended in the severely affected group (i.e. performance IQ580) and has a significant morbidity and mortality [2,8]. As ALD is an X-linked recessive disorder, genetic counseling of family members may be advisable. Early diagnosis also brings the possibility of genetic counseling; carrier detection and antenatal diagnosis and thus we can reduce the incidence of this devastating disease.

References:

1. Sydney AW. Adrenomyeloneuropathy presenting in adulthood. WJM 1998; 168(1): 45-47.
2. Sagarika M, Elizabeth N, John NH. Adrenomyelo-neuropathy in patients with 'Addison's disease': genetic case analysis. J R Soc Med 2006; 99: 245–49.
3. Antonio A, Simonetta P, Glorgio C, Leopoldo S, Aldo I et al. Rapid decline of fertility in a case of Adrenoleukodystrophy. Human reproduction 1998; 13(9): 2474-79.
4. Moser HW, Bergin A, Naidu S, Ladenson PW. Adrenoleukodystrophy. Endocrinol Metab Clin North Am 1991; 20:296-318.
5. Castellote A, Vera J, Vazquez E, Roig M, Belmonte JA et al. MR in Adrenoleukodystrophy: Atypical Presentation as Bilateral Frontal Demyelination. AJNR 1995; 16: 814–15.
6. Lee AG, Olson RJ, Bonthius DJ, Phillips PH. Increasing exotropia and decreasing vision in a school aged boy. Surv Ophthalmol 2007; 52(6):672-79.
7. Shuang W, Ji-Min W, Yuan-Shen C. Asymmetric Cerebral Lesion Pattern in X-linked Adrenoleuko-dystrophy. J Chin Med Assoc 2006; 69(8):383-86.
8. Monika S, Regina TG, Stan VU, Hasnain MK. Adrenomyeloneuropaty as a cause of primary adrenal insufficiency and spastic paraparesis. CMAJ 2004; 171 (9): 1073-77.
9. Doris EB, Rosalyn D, Steve J, Frank ME, Peter R et al. An Unusual Case of X-Linked Adrenoleukodystrophy with Auditory Processing Difficulties as The First And Sole Clinical Manifestation. J Am Acad Audiol 2004, 15:152–60.