Adrenomyeloneuropathy with bulbar palsy: A rare association

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Abstract

Adrenomyeloneuropathy (AMN) is a variant of adrenoleukodystrophy (ALD), an X-linked recessive peroxisomal disorder associated with accumulation of very long chain fatty acids (VLCFA). Mutations of this gene lead to abnormal peroxisomal β-oxidation, which results in the harmful accumulation of VLCFAs in affected cells. Neurological symptoms occur due to progressive demyelination and destruction of cerebral white matter and primary adrenal insufficiency. Bulbar palsy in a case of AMN is very unusual. We report a case of a 22-year-old male with AMN who developed adrenal insufficiency at the age of 4 years successfully treated by gluco- and mineralocorticoids followed by features of myeloneuropathy with bulbar palsy. AMN with prominent bulbar symptoms emphasizes the diverse clinical manifestation of this disease.

Key Words

Adrenal insufficiency, adrenomyeloneuropathy, bulbar palsy

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Introduction

Adrenoleukodystrophy (ALD) is the most common peroxisomal disorders with X-linked recessive trait with an incidence of 1 in 20,000 male births.[1,2] Adrenomyeloneuropathy (AMN) a variant of ALD, is a non-inflammatory axonopathy of the spinal cord that involves descending corticospinal tracts in the thoracic and lumbosacral regions and the ascending posterior columns in the cervical region.[1] The characteristic clinical picture is a slowly progressive spastic paraparesis and mild polyneuropathy in adult men (in their late 20s), with or without sensory symptoms and sphincter disturbances. Rare cases of cerebellar involvement have also been described in 1% of cases.[3] Bulbar palsy is very rare in AMN.

Case Report

This 22-year-old male born out of non-consanguineous marriage with normal birth and developmental history developed generalized hyperpigmentation of body since 4 years of age, which started as knuckle pigmentation and the whole body eventually became hyperpigmented over 4-5 months [Figures 1 and 2]. There was history of recurrent episodes of giddiness with transient loss of consciousness lasting for few seconds without tonic-clonic movements of limbs, tongue bite, and urinary incontinence. Adrenocorticotropic hormone (ACTH)-stimulated serum cortisol was 1 pg/dl. Diagnosis of Addison's disease was made, and treatment was started with gluco- and mineralocorticoids with reversal of hyperpigmentation and subsidence of syncopal attacks.

One year later, he developed insidious onset, gradually progressive weakness of all four limbs, which started in lower limbs distally and 3-4 months later involved upper limbs. Weakness was predominantly distal and associated with wasting. Patient was ambulatory only with support. Then, he developed dysphagia more for liquids with occasional nasal regurgitation and slurred speech with nasal intonation. There was cognitive decline in the form of learning difficulty and poor academic performance. There was no history of sensory symptoms, sphincter incontinence, headache, vomiting, or twitching of muscles.

Neurological examination revealed mini-mental status examination (MMSE) score of 26/30, spastic dysarthria with nasal intonation, left lateral pterygoid weakness, normal jaw jerk, bilateral 7th, 9th, and 10th cranial nerve palsy with decreased gag reflex, spastic paraparesis, and fissured tongue [Figure 3].

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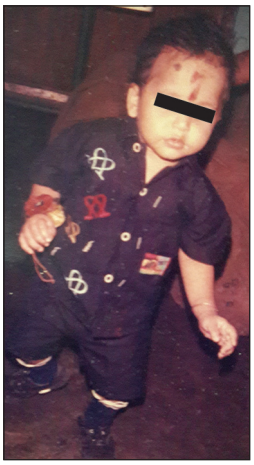

Figure 1: Photograph of the patient at the age of 3 years

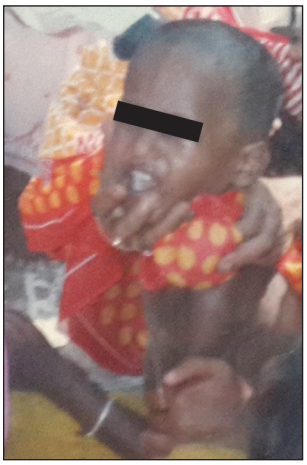

Figure 2: Photograph of the patient at the age of 4 years (generalized hyperpigmentation)

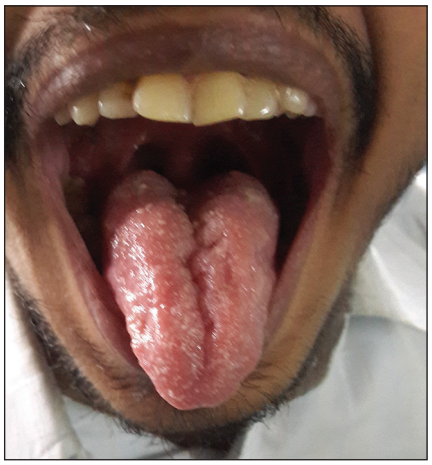

Figure 3: Small, spastic, and fissured tongue

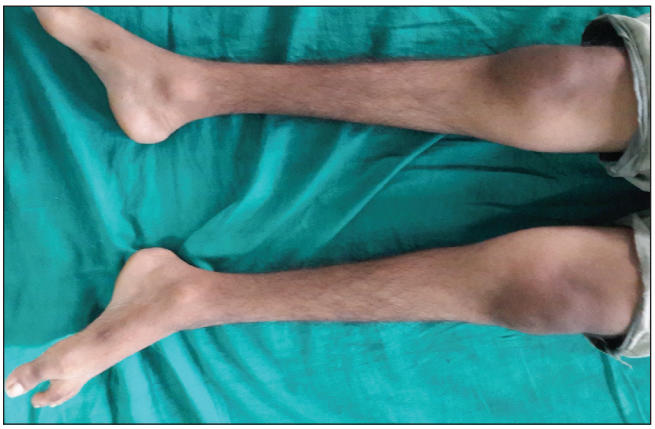

Figure 4: Wasting of extremities

There was distal predominant wasting of all extremities [Figure 4], marked hypertonia in lower limbs, generalized hyperreflexia, and bilateral extensor plantars. Sensory and cerebellar examination was normal.

In laboratory evaluation complete hemogram, blood sugar, liver and renal function tests, and electrolytes were within normal range. Brain and cervical magnetic resonance imaging (MRI) scan was normal. Nerve conduction studies showed symmetric motor and sensory predominantly axonal type of polyneuropathy. Electromyography (EMG) showed denervation pattern. Visual-evoked potential and brainstem auditory-evoked response studies were normal. Serum analysis showed elevated very long chain fatty acids (VLCFA) confirming the diagnosis of AMN.

Discussion

AMN, the adult phenotype of ALD, is an X-linked recessive disorder of fatty acid metabolism secondary to a mutation on ABCD1 gene located on Xq-28.[1,2] A defect in β-oxidation of saturated VLCFA in peroxisomes leads to the accumulation of tetracosanoic (C24:0) and hexacosanoic (C26:0) acid in tissues and body fluids in affected patients leading to damage of central and peripheral myelin and adrenal glands.[2] Pathologically, myelin degeneration is observed, often symmetrically, in various parts of the cerebrum, brainstem, optic nerves, and sometimes the spinal cord with extensive astrocytic gliosis. The myeloneuropathy of AMN is a central-peripheral distal (dying-back) axonopathy.[4]

AMN usually presents in the third and fourth decade and is characterized primarily by involvement of long ascending and descending tracts of the spinal cord and peripheral neuropathy, which leads to spastic quadri- or paraparesis and urinary dysfunction.[1,5] AMN is generally considered to be a milder variant of ALD with slower progression. Patients of AMN generally do not have clinically significant cerebral involvement, and only up to 20% of males with AMN can have evidence of cerebral demyelination on MRI.[1]

The specific laboratory marker of the disease is an excess of VLCFAs. In particular, three quantities are of value: the absolute level of hexacosanoic acid (C26), the ratio of C26 to tetracosanoic acid (C26:C24), and the ratio of C26 to docosanoic acid (C26:C22) in plasma, erythrocytes, leukocytes, or cultured fibroblasts.[6] Studies have shown that up to 35% of patients with presumed idiopathic adrenal

insufficiency have elevated VLCFA levels and experience AMN in later life.[7]

Our case had rare features, in that it presented in the first decade instead of third or fourth decade, it had significant bulbar features, which are very rare in AMN, and cortical involvement in the form of cognitive decline, which is also uncommon in AMN patients. AMN has varied clinical presentation and bulbar palsy occurs very infrequently. The wide spectrum of presentation of AMN complex emphasizes the need to consider these conditions when dealing with a progressive multisystem neurologic illness of unknown origin. To our knowledge, this represents the first reported case of AMN with predominant bulbar palsy.

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