CASE REPORT

Kugelberg-Welander disease

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Abstract

Spinal muscular atrophy (SMA) is a group of genetically determined disorders affecting spinal and cranial motor neurons, characterized by proximal and distal wasting, fasciculation and weakness of muscles. This patient presented with the features of slow progression of weakness and wasting of limbs, involuntary muscle twitching & without sensory impairment. No definitive treatment is yet to be discovered. SMA in adulthood is very rare. Most cases are detected in childhood and adolescence period. Sooner the diagnosis can be done, better the prognostic value.

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Introduction

Spinal muscular atrophy a genetic defect in the SMNI gene that codes SMNI, a protein widely expressed in all eukaryotic, cells. SMNI is essential for survival of motor essential neurons, as diminished abundance of the protein results in death of neuronal cells in the anterior horn of the spinal cord and subsequent system-wide muscle wasting.

The symptoms vary greatly depending on the SMA type involved, the stage of the disease and individual factors and commonly include areflexia, particularly in extremities, overall muscle weakness, poor muscle tone, limpness or a tendency to flop (the "floppy baby" syndrome), difficulty in achieving developmental milestone, difficulty in sitting/standing/walking in infants, adopting of a frog-leg position when sitting hips abducted and knees flexed), loss of strength of the pulmonary muscles: weak cough, weak cry (infants), accumulation of secretions in the lungs or throat, respiratory distress, Bell-shaped torse (caused by using only abdominal muscles for respiration), Clenched fists with sweaty hands, head often tilted to one side, even when lying down, fasciculations (twitching) of the tongue, difficulty in sucking or swallowing, poor feeding, arthrogryposis (multiple congenital contractures), weight lower than normal.

SMA is rare disease, overall incidence is I per 10,000 individuals. Though it is genetically determined some (24%) sporadic forms are also reported from spinal muscular atrophy (Genetic Home).

Case study

Mr. Al Mamun of 24 years age, a sailor, unmarried, non hypertensive, non diabetic, non alcoholic, smoker, hailing from Zianagar, Pirojpur admitted in Khulna Medical College Hospital with the complaints of gradual weakness of limbs, initially lower limbs followed by upper limbs. The weakness is less severe, slowly progressive but for the last I year he cannot stand from sitting and lying position without the assistance of his hands.

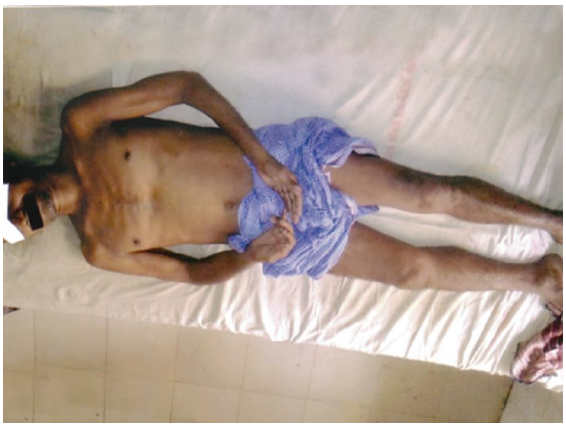

Fig-1 : Muscular atrophy of both upper & lower limbs.

He also noticed of involuntary muscle twitching of all limbs especially thigh and shoulder muscles at rest for last 3 yrs. He also complains of gradual wasting of limbs especially thighs and arms muscle for the last 2 years (Fig-1). His bowel,

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bladder habit & sleep patterns are normal. He has no history of dysarthria, dysphagia, nasal regurgitation, heat intolerance, unconsciousness, diplopia, polyphagia, polyurea, nocturia etc. There is no previous history of trauma in headneck, childhood polio, no neurological deficit in past and no history of contact with tubercular patient. On general examination he is anxious looking, mildly anaemic with below average physical built, Pulse-78bpm, BP-110/80 mm of Hg & RR-16/m & temp 980F.

On neurological examination patient is conscious, well oriented, mentally sound and all cranial nerves are intact. But there is fasciculations and wasting of proximal upper & lower limbs muscle, muscle tone normal, muscle power 4/5 on upper limbs & 3/5 on lower limbs, clonus absent, all deep reflexes are absent except both ankle jerks and all superficial reflexes are normal, sensory function intact, no abnormal cerebellar function and Gower's sign positive. Other systemic examination reveals no abnormality.

By proper history & clinical evaluation the following potential disorders are excluded namely-amyotrophic lateral sclerosis, where upper limbs present with lower motor neuron type of lesion and lower limbs present with upper motor neuron type of lesions; Primary lateral sclerosis where usually all the jerks are exaggerated and diabetic amyotrophy by absence of history of diabetic mellitus and laboratory evaluation.

Complete blood count revealed the 12.5g/dl of hemoglobin level, random blood sugar 5.6mmol/dl, serum creatinine 1.3mg/dl, X-Ray chest normal, Serum creatine kinase normal, normal CT scan of brain and Electromyogram show fibrillation and muscle denervation but Genetic testing not done due to non-availability.

Discussion

Spinal muscular atrophy has an autosomal recessive pattern. of inheritance which is linked to a genetic mutation in the SMNI gene. Human chromosome 5 contains two nearly identical genes at location 5ql3:a telomeric copy SMNI and a centromeric. copy SMN2.1 In healthy individuals, the SMNI gene codes the survival of motor neuron protein (SMN) which, as its name says, plays a crucial role in survival of motor neurons. In the long run, however, reduced availability of SMN protein results in gradual death of motor neuron cells in the anterior horn of spinal cord and the brain. Consequently, muscles undergo progressive atrophy. Muscles of lower extremities, spine and neck are involved and in more severe cases, pulmonary and muscle of mastication. Proximal muscles are always affected earlier and in a greater degree than distal.

Spinal muscular atrophy present as a significant diagnostic feature. But diagnostic & genetic testing will show bi-allelic deletion of exon[7] of the SMNI gene. This is conclusive of the disease which is not possible in our country. There is no definitive treatment of spinal muscular atrophy. Palliative care, present in Bangladesh is the main treatment. With the exception of infantile form, progression is slow and prognosis is better than motor neuron disease. Generally, patients tend to deteriorate over time, but prognosis varies with the SMA type and disease progression shows a great degree of individual variability.

Prenatal screening is controversial, because of its cost on the one hand, and the severity of the disease on the other hand. Some researchers have concluded that population screening for SMA is not cost-effective.[2] Others conclude that SMA meets the criteria for screening programs and relevant testing should be offered to all couples.[3] Very severe SMA (type-1) can be sometimes evident by reduction in fetal movement in the final months of pregnancy; else, it manifests within the first few weeks or months of life when abnormally low muscle tone is observed (the "floppy baby syndrome"). Further, for all SMA types, patient will present with hypotonia associated with absent reflexes.

Electromyogram. will show fibrillation and muscle denervation.[4] Serum creatine kinase may be normal or increased, Genetic testing will show bi-allelic deletion of exon 7 of the SMNI gene- this is conclusive of the disease. There is no known cure for spinal muscular atrophy. So palliative care is the main treatment Main areas of concern are orthopaedics - physiotherapy and occupational therapy. Respiratory care, nutritional care, mobility-assistive technologies, mental health and emerging therapies since the underlying genetic mechanism of SMA was described in 1990 several therapeutic approaches have been proposed and investigated. The main therapeutic pathways under research as in December 2011 include-Gene therapy, Stem cell therapy, SMN2 activation, SMN2 alternative splicing modulation, SAW stabilisation, neuroprotection.

SMA is very rare in adulthood. Any patient present with weakness of limbs or limping should be considered as Spinal Muscular Atrophy.

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