Bangladesh Journal of Neuroscience 2016; Vol. 32 (2): 106-110

CASE REPORT

A Rare Case Report on Distal Spinal Muscular Atrophy (SMA)

HABIBUR RAHAMAN[1], MD. RAFIQUL ISLAM[2], M A HANNAN[2], MAFTAHUL JANNAT[1]

Abstract:

Spinal muscular atrophies (SMA) are heterogeneous group of motor system disorders of alpha motor neuron clinically characterized by progressive lower motor neuron features. The distal form of SMA is an extremely rare disorder, which usually presents in the young adults and has a relatively slow progression with almost normal life-span. Differential diagnosis of this syndrome includes hereditary motor sensory neuropathy-Charcot-Marie-Tooth disease (CMT) and distal myopathies, which should be excluded before confirming this rare entity. As distal form of SMA is a very extremely rare condition so we would like to present a young male with this disorder and a short discussion of the theoretical aspects.

Key words: *Spinal muscular atrophies (SMA), Distal, Peroneo-muscular Atrophy, and Hereditary.*

Introduction:

Spinal muscular atrophy (SMA) is a relatively less frequent group of degenerative anterior horn cell disorder clinically characterized by proximal muscle weakness, muscle wasting, muscle twitching and areflexia in varying combinations. Almost all cases are genetically determined, with most being autosomal recessive due to homozygous deletions or mutation of the survival motor neuron (SMN) gene on chromosome[5]. Traditionally, SMA is classified as one of the four types based on the age at onset: SMA type 1 (infantile SMA or Werdnig-Hoffmann syndrome), SMA type 2 (intermediate SMA), SMA type

3 (juvenile SMA or Kugelberg-Welander disease), and SMA type 4 (adult-onset SMA, pseudomyopathic SMA. SMA type 1 begins within the first few months of life; children with this disease are never able to sit without support. Symptoms include severe hypotonia, limb weakness is severe, generalized, and worse proximally, a weak cry, and respiratory distress. Death from respiratory failure, pneumonia, and malnutrition usually occurs before age 2 years. The signs and symptoms of SMA type 2 usually begin between the ages of 6 and 18 months. Delayed motor milestones are often the first clue to neurological impairment, with more prominent leg weakness then arm weakness. The onset of the juvenile form of SMA is usually between 5 and 15 years presenting with slowly progressive limb-girdle weakness difficulty in walking. Adult onset SMA type 4 presents with slowly progressive limb-girdle weakness leading to difficulty in walking, climbing stairs, and rising from a chair or the floor. Fasciculations are an important finding. A new class of adult-onset SMA has recently emerged and is sometimes referred to as *SMA-5* distinguished by a distal rather than proximal pattern of slowly progressive muscular atrophy.[1]

The distal form of SMA is an extremely rare form of this entity, which presents in the young adults with predominantly distal muscle involvement in the lower limbs, which progressively involve the distal upper limbs and very slowly progressive and having almost a normal life-span.[2,3] It is inherited as both autosomal dominant and autosomal recessive form of inheritance.[3,4] Other neuromuscular disorders presenting with peroneal muscular atrophy like hereditary motor sensory neuropathy (CMT 2) and

1. MD (Neurology), Phase B.
2. Prof. of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka

distal myopathies need to be excluded before this rare entity is confirmed which can be done by physical examination, investigating muscle enzyme(S. CPK, Aldolase), NCS & EMG, CSF study, Muscle biopsy & genetic study.Physiotherapy, rehabilitation and education to the patient and parents, genetic counseling are helpful in managing these patients and preventing this disorder.

Case Report:

A 22 years male, a right-handed, first year Honors student, visited us in the outpatient department, department of neurology, Bangabandhu Sheikh Mujib Medical University, presented with insidious onset progressive weakness of all limbs with distal wasting for two years. He states that he was alright two years ago when he developed progressive distal weakness with wasting of his legs and difficulty in walking and running. Over the last six months, the weakness in his lower limbs progressed to involve the proximal lower limbs and he noted similar weakness and wasting of hand muscles. He has also history of occasional muscle cramp in leg muscles. He denied any muscle twitching in his arms and legs. He has no stiffness of limbs, muscle pain, tingling or numbness sensations, difficulty in swallowing, neck or back pain. There was no bowel or bladder dysfunction. There was no history of parental consanguinity. He has normal developmental milestones. There was no similar case in the family. On general examination, he had pes cavus deformity, normal vital parameters, no high arched palate. Neurological assessment revealed normal higher mental function, speech and cranial nerves. There was wasting of the intrinsic muscles of hands and feet with bilateral foot drop, also wasting of distal forearm and legs with relatively preserved proximal muscle groups, no fasciculation observed. There was distal hypotonia, muscle power proximally grade-4/5 and distally grade-2/5, areflexia, bilateral non responsive plantar reflexes and a high stepping gait. There was no sign of cerebellar, sensory or autonomic dysfunction. There was no abnormal spinal curvature or thickened nerves. Investigations revealed a normal hematological and biochemical profile. Muscle enzymes levels, serum creatinine phosphokinase (159 IU/L). Nerve conduction studies on the sensory and motor nerves of upper and lower limbs were within normal limits. Electromyography studies revealed features of chronic denervation with reinervation in form of increased insertional and spontaneous activity and long duration, high amplitude, polyphasic MUAP) Fig. 1,2,3,4.CMT was excluded by having no sensory complaint or findings, no nerve thickening & normal NCS findings. Distal myopathy was

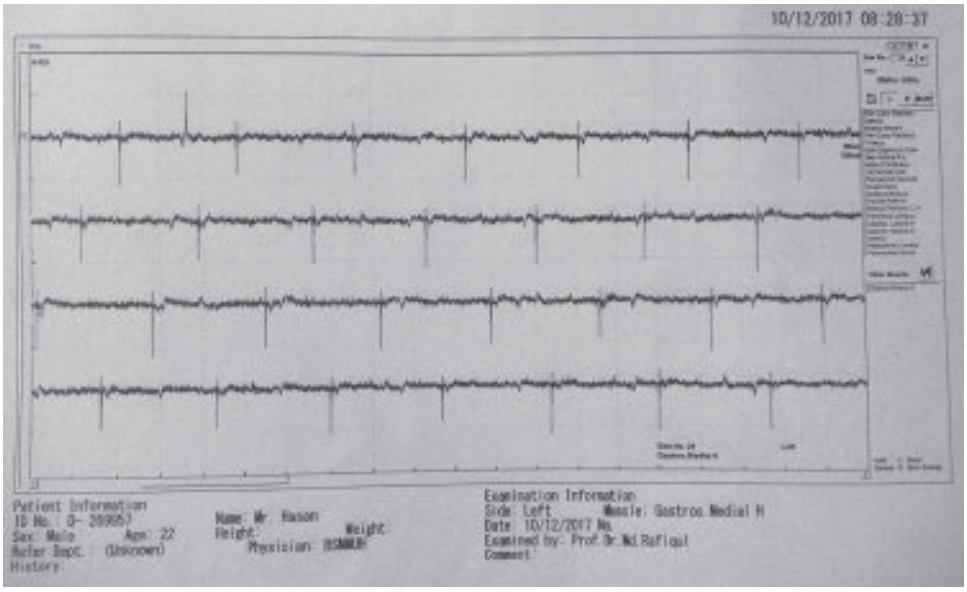

Fig.-1:

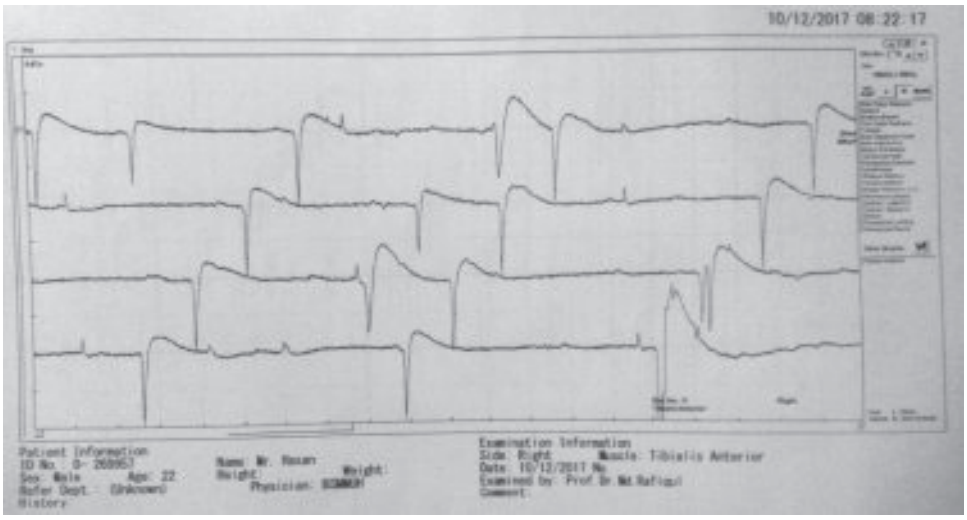

Fig.-2:

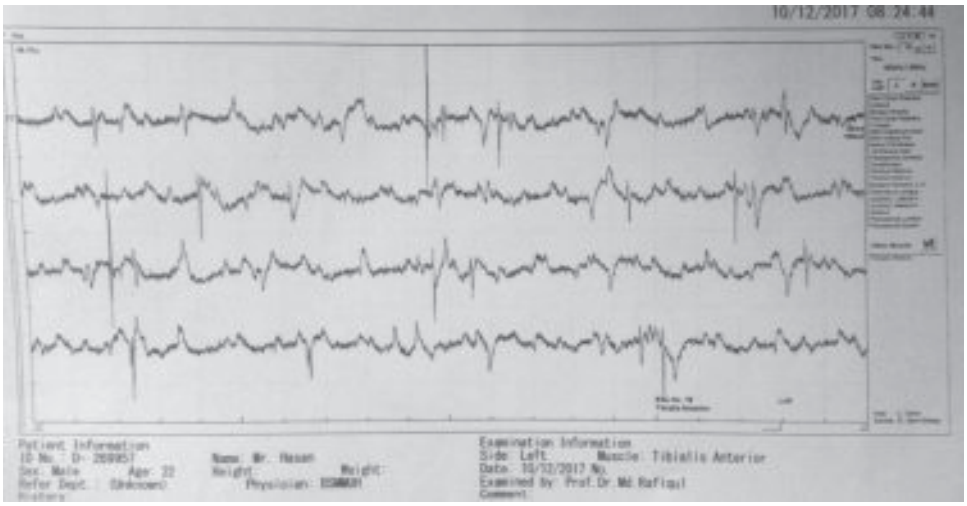

Fig.-3:

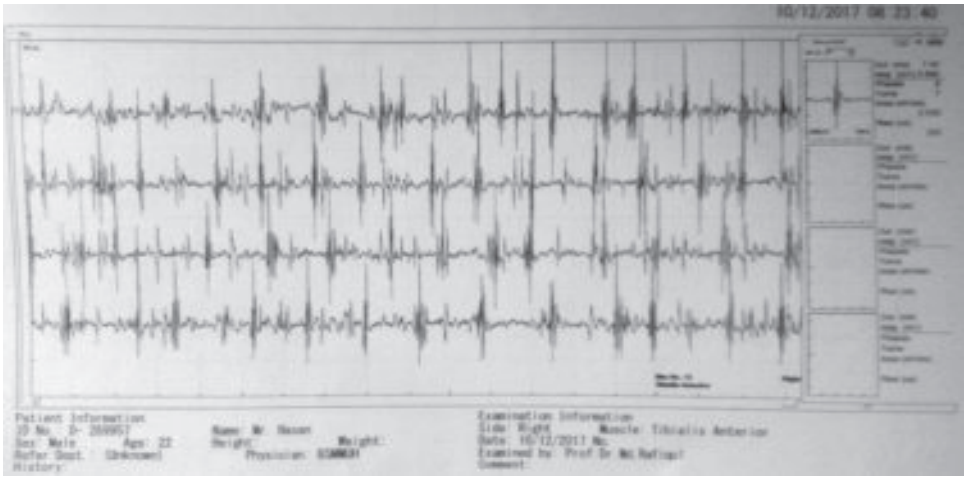

Fig.-4:

excluded by normal muscle enzyme & neuropathic EMG findings. But muscle biopsy, genetic study not done. Parents and siblings were not available for neurological assessment.

Fig 1, 2, 3 showing features of chronic denervation: (1) Fibrillation potential (2) Positive sharp wave (3) Fibrillation, positive sharp wave & fasciculation

Figure: 4 showing features of chronic active reinervation; polyphasic, high amplitude, long duration

MUAP with reduced recruitment.Discussion:
Motor system disease is a group of disorders characterized by progressive degeneration of motor neurons in the spinal cord, brainstem and motor cortex. Patient usually presents with various combinations of upper and lower motor neuron features. Progressive spinal muscular atrophy is a group of degenerative neuromuscular disorder characterized by lower motor neuron involvement features with varying combinations of weakness, muscle wasting, areflexia and muscle twitching which gradually involves the proximal muscles of the lower limbs, upper limbs, later distal part of limbs and variable neck, trunk and respiratory muscle involvement. A form of progressive spinal muscular atrophy with predominantly distal involvement (Distal SMA) is a rare subgroup of this disorder 2, 3 Distal SMA is an inherited form of SMA with autosomal recessive or dominant form of inheritance (Table 1).

Autosomal recessive form distal SMA is the more common form and occurs with a greater frequency in products of consanguineous marriages but parental consanguinity and similar illness in other siblings was not found in our patients .4, 5. It manifests as a very gradually progressive distal muscular weakness with slow clinical progression and having an almost normal life-span. Lower limbs are preferentially involved and below-knee atrophy with foot drop is commonly seen, as in our patient. Hands and proximal limbs are involved much later and to a lesser degree which was also found in our patient. However there is a type of distal SMA where upper limb predominance is seen (Type V).6 Carriers of the disease may be clinically normal though subtle EMG abnormalities may be the evident. The importantdifferential diagnosis of this peroneal muscular atrophy syndrome is peripheral neuropathies like HMSN (Charcot-Marie-Tooth II), where there is axonal type of involvement with almost normal conduction velocities. Chronic inflammatory demyelinating polyneuropathy (CIDP) and distal myopathies should be considered in the differential diagnosis.5 Differentiation from CMT is possible as there is always some degree of clinical or electrophysiological sensory nerve involvement in CMT. Distal myopathies can be differentiated by presence of high CPK and LDH levels and EMG findigns of myopathy. Muscle biopsy is conclusive evidence of the nature of muscular involvement. In neurogenic disorders, there is evidence of "group atrophy" with intervening muscle fibres normal or at times hypertrophic. In extreme forms of neurogenic atrophy, the muscle fibres may be

Table-I

World Federation of Neurology Classification of Hereditary Motor Neuropathies (Distal Spinal Muscular atrophy) 5

Type	Inheritance	Age of onset	Gene	Age of unableto walk	Life expectancy
Type I (Juvenileonset)	AD	2-20 yr	Unknown	Rare	Normal
Type I I(Adultonset)	AD	20-40 yr	*HSP22*,*HSP27*	Rare	Normal
Type III (Mildjuvenile)	AR	2-10 yr	Unknown	Rare	Normal
Type IV (Severejuvenile)	AR	4m-20yr	Unknown	30yr	?
Type V (Upperlimb predominant)	AD/ sporadic	5-20yr	*GARS*,*BSCL2*	Never	Normal
Type VI (Severeinfantile)	AR	infancy	*IGHMBP2*	Unable to walk	<1 yr
Type VII (Withvocal cord palsy)	AD	10-20yr	Unknown	Rare	Normal

replaced by fibrocollagenous tissue. The distal form of SMA has a relatively better prognosis compared to other forms of this disorder. Though the initial progression is rapid, the disease stabilizes in the later stages with patients remaining ambulant and having a normal life span. Since genetic inheritance is well known, genetic counseling of the carriers helps in preventing the disease. There is no definitive therapeutic modality available. Management of this disorder involves active multi-disciplinary approach with neurologist, occupational and physical therapist and rehabilitation experts. Respiratory support and care of the bed-ridden is seldom required in the natural course of distal SMA. Patient education about the natural course of the disease and its prognosis is important to involve the patient in the management process. Recent advances in gene therapy can pave way for a possible genetic treatment for this untreatable entity.

In conclusion, distal SMA is an extremely rare form of motor system disease. Other common causes of similar presentation of peroneo-muscular syndrome can be excluded by clinical, electrophysiological, and biochemical methods. Prognosis of this entity is relatively better than other forms of SMA. Patient education with multi-disciplinary approach to rehabilitate these patients is pertinent in managing these patients.

References:

1. Russman B S, Spinal Muscular Atrophy: Clinical Classification and Disease Heterogeneity. Journal of child Neurology, 2007, 946-951.
2. Harding AE, Thomas PK. Hereditary distal spinal muscular atrophy. A report of 14 cases and a review of literature. J Neurol Sci 1980; 45:337-48.
3. Pearn J, Hudgson P. Distal spinal muscular atrophy. A clinical and genetic study of 8 kindreds. J Neurol

Sci 1979;43:183-91.

4. Viollet L, et al. Mappjng of autosoma recessive chronic distal spinal muscular atrophy to chromosome 11q13. Ann Neurol 2002;51:585-92.
5. Boylan KB, Cornblath DR. Werdnig-Hoffmann disease and chronic distal spinal muscular atrophy with apparent autosomal dominant inheritance. Ann Neurol 1992; 32:404-7.
6. Dyck T, Thomas PK. Peripheral Neuropathies. III Ed WB Saunders. 1990:1058-59.