International Journal of Contemporary Pediatrics
Bainade KS et al. Int J Contemp Pediatr. 2022 May;9(5):501-503
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20221080

Case Report

Spinal motor atrophy in a floppy infant: a case report

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Received: 15 February 2022
Revised: 04 March 2022
Accepted: 19 March 2022

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ABSTRACT

Spinal muscular atrophy (SMA) is a progressive neuromuscular condition typically due to homozygous absence of the survival motor neuron gene (SMN1). It is characterized by progressive muscle weakness that limits motor development. Muscle weakness is associated with muscle atrophy and hypotonia, absence or marked decrease of deep tendon reflexes. Proximal muscles are more affected than distal muscles. Contractures and spinal deformity are a common impairment. Child with SMA gradually lose function over time. Electromyelography (EMG) and nerve conduction velocity shows anterior horn cells abnormality. No specific medical management is available for children with SMA. Interventions are usually supportive and may include physical therapy, occupational therapy, speech therapy, nutrition, orthotic management and possible surgery. This case report was of a 4 and half month-old female child with paucity of movement of lower limb since birth along with developmental delay.

Keywords: SMN, SMA, Nusinersen

INTRODUCTION

SMA is an autosomal recessive neuromuscular disorder characterised by degeneration of anterior horn cells of spinal cord, leading to symmetrical muscle weakness and atrophy affecting nearly 1 in 10,000 births. Two nearly identical genes survival motor neuron gene (SMN 1 and SMN 2) plays a crucial role in the survival of motor neuron. In most patients with SMA the disease is caused by homozygous deletion or mutation of the telomeric SMN 1 on chromosome 5q13. SMN 1 produces the SMN protein. This intracellular protein is found in many tissues and in particular is expressed in high levels in spinal motor neuron and plays a crucial role in survival of the motor neuron. SMN 2 is a complicated inverted repeat area displaying high instability leading to frequent deletion and gene conversion. SMN 1 and SMN 2 can only be distinguished by two single nucleotide difference ne in exon 7 and one in exon 8. The single nucleotide difference in exon 7 of SMN 2 affects mRNA splicing resulting in an altered SMN protein with a limited half-life and function.

Once a diagnosis of SMA is clinically suspected the current method of confirmation is by molecular genetic sequencing in order to identify a homozygous absence of SMN 1. While the next generation sequencing (NSG) that is now commercially available has improved our ability to detect mutation consistent with SMA compared to polymerase chain reaction (PCR). With novel therapeutics on the horizon accurate diagnosis is of the utmost importance.

CASE REPORT

4 and half month-old female child admitted complaining of paucity and weakness of lower limb since birth. The child was born at 38 weeks of gestation, meconium-stained amniotic fluid (MSAF) with birth weight of 2.5 kg born through normal delivery, the baby cried on tactile stimulation. At 2 months of age the parents noticed that the chid had difficulty in moving the lower limb along with paucity. Developmentally the child was delayed with no neck holding and complete head lag, social smile attained

at 3 months of age, identified mother at 3 and half month, follows object 180º laterally, turn towards sound and responded along with vocalization at 3 months, the developmental quotient was 50%. The child was active and alert lying comfortably on mothers' lap. On examination the child was afebrile with heart rate of 130 /minute and respiratory rate of 30 /minute. On examination of the central nervous system it was found, all the cranial nerves were normal but with generalized hypotonia and the tone of the both the lower limb were markedly reduced whereas the power of both the lower limb was 1/5.

Figure 1: 4 and half month old child with SMA.

Following the clinical examination and the history of the child magnetic resonance imaging (MRI) brain (P+C) was done to rule out cerebral palsy and any other cause and it was normal, MRI screening of the spinal cord was done and it was normal too. To find out the etiology nerve conduction velocity (NCV) and EMG was done, were the NCV showed motor nerve conduction abnormality (right median-low amplitude, right ulnar-absent, right peroneal-absent, left peroneal-low amplitude, right and left tibial-low amplitude) whereas the sensory nerve conduction was normal. The EMG showed chronic denervation in left l4 and l5 segment which was suggestive of type 1 spinal muscular atrophy.

DISCUSSION

SMA is an autosomal recessive neurodegenerative disease caused by mutation/deletion in the SMN gene on chromosome 5q affecting 1 in 11,000 live births and an estimated carrier frequency of 1 in 54.[1] The severity of the disease, onset and the clinical feature depended upon the type of the disease.[2] There was no cure to the disease but various genetic and molecular studies had led to pre-clinical models and various therapeutic approaches.[3-5] Paired with the excitement of an active therapeutic pipeline in SMA had been a focus upon understanding the natural history of this disorder as well as early diagnosis and clinical intervention. This had led to the development of clinical standards of care.[6,7] The most severe form of SMN was type 1 where there was rapid loss of respiratory motor function in 1st year of life.[8] There were studies which showed survival of this infants were up to 70% by non-invasive ventilatory support with parenteral feeding.[9-11] The gene therapy, AVXS-101 (Onasemnogene, Abeparvovec, Zolgensma^{R}) were an adeno associated viral vector that carriers SMN 1 DNA encoding functional human SMN with continuous promoter inside the cell, it caused the expression of SMN 1 mRNA thereby increasing the amount of functional SMN protein.

Treatment

The main objective of the treatment was to slow down the progression of the disease and prevent secondary impairment. Interventions were usually supportive and included physiotherapy, occupational therapy, speech therapy, nutrition and orthotic management. The focus of physical therapy was to optimize functional mobility, maintaining muscle strength, preventing contractures and deformities.

CONCLUSION

Spinal muscular atrophy is the most common disease of the spinal motor neuron. It is a neuronal disorder of infancy and childhood involving the motor component. The disease can manifest any time prior to birth to adulthood, with varying severity and disease impact. It is the most common genetic cause of death in infants. Supportive care and management can reduce the disease burden and improve the quality of life significantly.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Bainade KS, Kotrashetti V, Sonawane VB, Agarwal R. Spinal motor atrophy in a floppy infant: a case report. Int J Contemp Pediatr 2022;9:501-3.