Case report

Spinal Motor Atrophy in a floppy infant: a case report

ABSTRACT: Spinal Muscular Atrophy is a progressive neuromuscular condition typically due to homozygous absence of the Survival Motor Neuron Gene(SMN1) .It is characterised by progressive muscle weakness that limits motor devlopment. 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 is common impairement. Child with SMA gradually lose function over time. Electromyelography 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 is of an 4 and half month old female child with paucity of movement of lower limb since birth along with devlopmental delay

KEY WORDS- SMN, SMA,NUSINERSEN

Spinal Muscular Atrophy (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 nealy 1 in 10,000 births. Two nearly identical genes SMN 1 and SMN 2 plays a crutial role in the survival of motor nueron. In most patients with SMA the disease is caused by homozygous deletion or mutation of the telomeric Survival Motor Neuron gene(SMN1) on chromosome 5q13. SMN1 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 crutial role in survival of the motor neuron. SMN2 is a complicated inverted repeat area displayig high instability leading to frequent deletion and gene conversion .SMN1 & SMN2 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 SMN2 affects mRNA splicing resulting in an altered SMN protein with a limited half life and function

Once a diagnosis of SMA is clinically suspected th current method of confirmation is by molecular genetic sequencing in order to identify a homozygous absence of SMN1. While the Next Generation Sequencing (NSG) that is now commercially available has improved our ability to detect mutation consistent with SMA compared to PCR. With novel therapeutics on the horizon accurate diagnosis is of the utmost importance .

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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, MSAF with birth weight of 2.5 kg born through normal delivery, the baby cried on tactile stimulation. At 2months of age the parents noticed that the chid had difficulty in moving the lower limb along with paucity. Devlopmentally the child was delayed with no neck holding and complete head lag,social smile attained at 3 months of age , identifies mother at 3 and half month , follows object 180* laterally , turn towards sound and responds along with vocalization at 3months , the developmental quotient is 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 where as the power of both the lower limb was 1/5. Following the clinical examination and the history of the child 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 Electromyelography (EMG) was done , were the NCV showed motor nerve conduction abnormlity (Right median-low amplitude, right ulnar- absent, right peroneal-absent,left peroneal-low amplitude,right and left tibial-low amplitude) where as the sensory nerve conduction was normal .The EMG showed chronic denervation in left l4 & 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.[1-3]Without any form of respiratory support the historical median life expectancy for a child with SMA type is approximately 2 years .[1-4]Due to the development of new therapies the natural history of SMA continues to change rapidly. Research continued into other SMA therapies and a gene replacement therapy was FDA approved in 2018 for the treatment for SMA . This gene therapy ,AVXS-101(Onasemnogene ,Abeparvovec,Zolgensma[R)] is an adeno associated viral vevtor that carriers SMN1 DNA encoding functional human SMN with continuous promoter inside the cell , it causes the expression of SMN1 mRNA thereby increasing the amount of functional SMN protein.

Treatment-The main objective of the treatment is to slow down the progression of the disease and prevent secondary impairement .Interventions are usually supportive and include physiotherapy,occupational theraphy,speech therapy,nutrition and orthotic management.The focus of physical therapy is to optimize functional mobility,maintaining muscle strength , preventing contractures and deformities

References

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