Abstract
Spinal muscular atrophy (SMA) is a genetic disease that attacks the motor neurons of the spinal cord. This results in the progressive wasting of the voluntary muscles of the limbs and trunk. We present a 26 year old girl diagnosed with SMA since last ten years. The diagnosis was confirmed on the basis of muscle biopsy and electromyography (EMG) showing anterior horn cell involvement. In view of the same; the patient was given intrathecal autologous bone marrow derived stem cell therapy as part of the neuron regenerative rehabilitation therapy (NRRT) protocol. The patient showed functional improvements in her disability post therapy. A detailed case report is presented here with.

Key words: Spinal Muscular Atrophy, autosomal, motor neurons, bone marrow, neuroregeneration.

Introduction
Spinal Muscular Atrophy is a recessive autosomal disorder caused by mutations of the survival motor neuron (SMN) gene located on chromosome 5q13, resulting in a marked reduction in SMN protein and characterized by degeneration of motor neurons associated with muscle paralysis. Although SMN is a ubiquitously expressed protein, mutations, in SMN specifically cause the targeted deterioration of motor neurons of the spinal cord. The clinical features of SMA result from skeletal muscle denervation, loss of anterior horn cells in the spinal cord and cranial nerve nuclei. The incidence of spinal muscular atrophy is about 1 in 10,000 live births with a carrier frequency of 1 in 50. The disorder can be subdivided into three groups according to age of onset, the severity of symptoms (assessed by the achievement of motor milestones) and age at death. SMA type I and II are severe forms of SMA with an early onset while SMA type III (Kugelberg-Welander disease) is the mildest form of the disorder with a late onset. In order to be diagnosed with Spinal Muscular Atrophy, symptoms need to be present. In most cases a diagnosis can be made by the SMN gene test, which determines whether there is at least one copy of the SMN gene by looking for its unique sequences (that distinguish it from the almost identical SMN2) in exons 7 and 8. In some cases, when the SMN gene test is not possible or does not show any abnormality, other tests such as an EMG or muscle biopsy may be indicated.

In spite of worldwide efforts, there is as yet no cure for SMA. Principal approaches to
find out an effective treatment or indeed a cure have been aimed at either manipulating the genetic material implicated in the pathophysiology of SMA, or at restoring the lost or damaged motor neurons via cellular replacement. Autologous hematopoetic stem cell transplantation (HSCT) has been used as a treatment for such diseases along with Physiotherapy and Occupational therapy. Before the discovery of Adult Stem Cells, Spinal Muscular Atrophy (SMA) had no cure or treatment. Normally the only thing an SMA patient can do is try to keep the status quo and try to prevent it from getting worse. However, thanks to great advances made in Adult Stem Cell research, Spinal Muscular Atrophy is now able to be improved. The case we are presenting is a good example of this. She presented with tongue fasciculations, respiratory muscle fatigue and lordotic gait with predominant abdominal weakness. The muscle biopsy and EMG suggested the diagnosis of Spinal Muscular Atrophy with anterior horn cell involvement.

Case report
We present a 26 year old girl suffering with Spinal Muscular Atrophy with a history of frequent falls while walking and progressive left extremity weakness and difficulty while getting up from squatting position. She had tongue fasciculations and respiratory muscle fatigue. She had a lordotic gait and predominant abdominal muscle weakness. She also had a difficulty in overhead activities and occasional misarticulation of few words was also observed. Her genetic tests did not show any abnormality. Hence, her Muscle Biopsy and EMG were carried out. The Quadriceps Muscle Biopsy indicated Denervation Atrophy from spinal origin and EMG showed very chronic motor axon degeneration affecting all the four limbs predominantly proximal muscles. Lower limb proximal muscles and trunk muscles were most affected. The site of involvement was the Anterior Horn Cell level which indicated Spinal Muscular Atrophy.

Materials and Methods:
NRRT Protocol: Patients selection and protocol design has been based on the inclusion criterion as per paragraph 32 of the World Medical Associations Helsinki declaration. The protocol had been reviewed and approved by the Institutional committee for Stem cell Research and therapy (IC-SRT). The patient was informed about the procedure and a duly filled informed consent form was obtained from her. Blood Tests, MRI were performed one week before the transplantation. The investigations were repeated prior to the second transplant as well. G-CSF injections were administrated 48 hours and 24 hours before Bone Marrow derived Stem Cell Transplantation. Autologous bone marrow derived MNCs were transplanted according to the NRRT protocol. Bone marrow (100ml) was aspirated from the iliac bone. Mononucleocytes (MNC) were obtained after density gradient separation. Viable count of the isolated MNCs was taken. The MNCs were checked for CD34+ by FACS analysis. Approximately 64 x 10^6 MNC were immediately injected post separation, intrathecally in L4-L5 intervertebral space using a lumbar puncture needle and catheter. Along with Neuroregeneration, Neuro Rehabilitation, Physical Therapy and Occupational Therapy were also given to the patient. This therapy emphasizes the role of stem cells.
in taking advantage of the brain’s capacity for repair & recovery. Rehabilitation interventions seek to promote recovery & independence through neurofacilitation.

Observation:
Clinical improvements
After the stem cell therapy, the patient had no side effects and was evaluated at a regular time period. On follow up, improvement was observed in the strength of the upper extremity. Her hand grip had improved significantly bilaterally. Her stamina had improved along with the sitting balance. Improvement was observed in her walking and frequency of falling had decreased. She could now climb stairs better with minimal support. Her speech had also improved significantly. Her over all muscle strength had improved. She has become more confident in doing her daily activities. According to her the quality of life has improved significantly.

Discussion:
Spinal Muscular Atrophy (SMA) is a neuromuscular disease characterized by degeneration of motor neurons\textsuperscript{14}, resulting in progressive muscular atrophy (wasting away) and weakness. The clinical spectrum of SMA ranges from early infant death to normal adult life with only mild weakness. In all of its forms, the primary feature of SMA is muscle weakness, accompanied by atrophy of muscle. This is the result of denervation, or loss of the signal to contract, that is transmitted from the spinal cord. This is normally transmitted from motor neurons in the spinal cord to muscle via the motor neurons axon, but either the motor neuron with its axon, or the axon itself, is lost in all forms of SMA.

Since, many potential therapies have not been successful in treating the disorder, Adult Stem Cell (Autologous bone marrow derived MNC’s) transplantation was carried out. The adult bone marrow stem cells per se have no side effects and are very safe. This treatment showed significant improvements in the case. She could walk better and her muscle strength had improved significantly. She was advised to do physical therapy to enhance the benefits of the stem cells even more. While the stem cells may not have cured her completely, they have definitely helped and hopefully she is now on the road to a full recovery.

The present data provide clear evidence that Autologous Hematopoietic Stem Cell Transplantation along with Neuro-rehabilitation can result in significant improvements in the case of Spinal Muscular Atrophy with no side effects.

References:


