ALS Case Study

A Case Report of Amyotrophic Lateral sclerosis in a patient with familial occurrence that carries the pathogenic repeat expansion of C9ORF72

Abstract:

This is a case of a 56-year-old female patient with familial ALS diagnosed in November 2018. She is positive for mutation C9ORF72. Initial symptoms were cramping in the legs and right foot drop. The patient's mother and maternal aunt developed ALS at ages 55 and 60 respectively. Both women deceased approximately 18 months post-diagnosis with ALS related complications. Genetic testing for C9ORF72 was performed and found to be positive in both mother and aunt. The patient has two siblings, a brother, and a sister, neither of whom suffer from neurodegenerative disease. The patient was started on Riluzole shortly after diagnosis in December 2018 and continued on 50mg twice per day until September 2019 when she elected to discontinue, citing lack of benefit. The patient started the BodyScience ALS protocol in March 2020. Results to date include improved function and a 6-point increase in the Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R).

Introduction:

Amyotrophic Lateral Sclerosis (ALS) is a relentlessly progressive neurodegenerative disorder that causes muscle weakness, disability, and eventually death from respiratory failure. The hallmark of ALS is the combination of upper motor neuron and lower motor neuron involvement. The lower motor neuron findings of weakness, atrophy, and fasciculations are a direct consequence of muscle denervation, hence the term "amyotrophic." The upper motor neuron findings of hyperreflexia and spasticity result from degeneration of the lateral corticospinal tracts in the spinal cord, which are gliotic and hardened to palpation at autopsy, hence the term "lateral sclerosis."ALS is one specific type of the more general group of motor neuron diseases. These disorders variably affect motor neurons located in the anterior (ventral) horn regions of the spinal cord, the cranial nerve motor nuclei in the pons and medulla, and the frontal cortex. Familial ALS accounts for approximately 5 to 10 percent of all ALS cases. More than 20 causative genes have been identified. Among these, the two most common are C9ORF72 and SOD1, which together make up nearly 50 percent of familial ALS. Familial ALS is phenotypically and genetically heterogeneous. Although most familial ALS cases follow an autosomal dominant inheritance pattern, recessive and X-linked forms have been described. Adult-onset autosomal dominant inheritance is more common than juvenile onset caused by recessive transmission.

Clinical findings:

Family History: The patient's mother and maternal aunt developed ALS at 55 and 60 respectively. Both deceased approximately 18 months post-diagnosis with ALS related complications. The patient has two siblings, a brother, and a sister, neither suffers from this neurodegenerative disease. Medical history: The patient was a schoolteacher and administrator for 7 years and stopped working in June 2019 due to diagnosis; environmental exposures with pesticides the suspected cause. Breast reduction in 1981, surgical correction for anal prolapse, and total hysterectomy in 2014. Symptoms preceding diagnosis included edema in legs, lower back pain, muscle cramps, fatigue, hot flashes, and cold spells. The muscle cramps started in February 2017, they occurred in the gastrocnemius muscles bilaterally. In September 2017 she developed pain in the right ankle and began to limp after developing foot drop in May 2018. The patient visited a Neurologist in July 2018 who performed an EMG with abnormal findings that led to a second EMG in November 2018 when ALS was diagnosed. The patient was taking Riluzole for 10 months after diagnosis, without any noticeable improvements, and decided to stop taking it. Upon physical examination performed on March 9, 2020, there was noticeable muscle weakness and atrophy. Orthotics were worn on both calves/feet to address foot drop, right hip flexor was too weak to lift right leg, poor core balance and strength, and positive retropulsion. Foot drop was observed bilaterally once orthotics were removed. The upper body was relatively well preserved with measurable weakness in the right forearm and noticeable weakness and atrophy in both hands. Initial ALS Rating scale was performed. At that time the patient complained of early eating difficulty including occasional choking, slow or sloppy handwriting, slow and clumsy cutting food, and handling utensils. She required intermittent assistance for dressing and hygiene, was unable to move or turn in bed, walked with assistance, and was unable to climb stairs. ALS Rating Scale Score (ALSFRS-R) was 32.

Treatment modalities:

A cycled, step-wise peptide therapy regimen was used to initially stimulate muscle growth and rotated to include neuroprotection, immune regulation, improve mitochondrial dysfunction, and restore cellular function. Localized, intramuscular amino acid injections were used to improve retropulsion, walking, core balance, dexterity, and fine motor skills. Intravenous administration for immune support and nutritional health. Antioxidant bolus dosing.

Discussion:

The ALS database of all variables such as biomarkers collected from individual studies is named The Pooled Open Access Clinical Trials Database (PRO-ACT) As per the data collected in the PRO-ACT database, patients are denoted as fast and slow progressing patients, with the estimated average 6-month drop in the ALSFRS-R score being 20 points (3.3 points per month) for fast-progressing patients, and 3 points (0.5 points per month) for slow-progressing patients. Keeping in mind that our patient is slowly progressing, the data states that she should have lost 3 points in the last six months. Not only did the patient not lose any points in the last 6 months during treatment, but she actually gained 6 points. Of note, our patient was not on any other therapy during the time of assessment (March 2020 – present). Most recent assessment report: noticeable improvements in swallowing, cutting food, better efficiency with dressing, hygiene, turning in bed, walking, and standing up. Total score in the Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R) improved by 6 points to 38. Initial ALSFRS-R performed 6-months ago was 32. Strength Tests of individual muscle groups showed a 1-point increase in the most atrophic muscles. The most noticeable improvement by the patient during a recent physical therapy session where it was noted that the patient recovered mobility of the flexor digitorum longus of the right foot after 2 years having lost the ability to move it.

	Initial ALSFRS-R	Recent ALSFRS-R
Speech	4	4
Salivation	4	4
Swallowing	3	4
Handwriting	3	3
Cutting food and handling utensils	3	4
Dressing and hygiene	2	3
Turning in bed and adjusting bed clothes	0	2
Walking	1	2
Climbing stairs	0	0
Dyspnea	4	4
Orthopnea	4	4
Respiratory insufficiency	4	4
TOTAL	32	38