ALS Case Study
10/25/21

Summary: This is a case of a 54-year-old woman diagnosed with ALS in March 2018. Based on ALSFRS-R changes, she is categorized as a slow progressor (by comparison to a rapid progressor). She is able to walk slowly with the assistance of a walker and can lift both arms over her head. She requires assistance sitting down and standing up, is able to write with difficulty and has recently been experiencing worsening speech. She has had multiple falls. Weakness in the core is profound. Atrophy in both hands is pronounced. Minimal scapula winging. Patient reports that her progression speed has been increasing significantly over the past 10 months.

Introduction: Patient arrived October 11th for 3-weeks. She was unclear about the causes and timeline of her motor neuron disease. Given that causal relationships are crucial in determining an appropriate treatment protocol, there were multiple conversations with the patient, multiple clinical assessments, reviews of lab results, dental reports and medical notes after which a timeline was constructed:

- Herpes Simplex Virus 1 has been active since childhood with cold sores throughout adult life.
  Medication history: Valtrex anti-viral medication started more than 20 years ago, used and average of 8 times per year for 1-2 days each time to control outbreaks. Last used in January 2021.
- 2015 a root canal in the front left side of the mouth was causing pain on the left side of the face. Dental procedure was performed, patient reports significant facial tenderness in the cheek and sinus cavity below the left eye that lasted for at least one year after the procedure.
  Working Theory: (1) the infection surrounding the root canal could have been introduced into the sinus cavity from the dental procedure or due to size and proximity of the infection (2) exposure to the CNS could be through an infected sinus cavity or cranial nerve. (Reference Article: The Role of viruses in Oral Disease: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3084576/. (3) determine if an enterovirus could be a culprit given symptom overlap with ALS. (See article below regarding enterovirus and ALS symptoms.)
- 2016 bicycle accident occurred within 6 months of the 2015 root canal procedure. “In spite of riding bikes routinely, I felt like something was not right with my balance when I was riding on vacation.” Of note, patient was an avid runner and athlete at that time and noted that lunges were becoming difficult.
  The oral infection is the likely causal link; the bicycle accident should be considered the initial symptom. There was no evidence of neuromuscular or neurodegenerative symptomology prior.
- 2017 “weakness in my right foot, especially when working out and running that moved up my right side to my hand and then right arm”
- 2018 Summer - provoked heavy metal testing urine, blood and hair. Elevations in: Al, Pb, Cd and Hg
- 2018 Fall - water filtration system installed in home, no evidence of toxins in the water.
- 2018 November - 5 teeth corrected (2 teeth with veneers that were at least 10 years old, 3 root canals (performed approximately 25 years ago) with confirmed infections that were corrected/removed. One of which “was really bad, encapsulated in a cyst that was removed.”

Reference Article Excerpt April 2019:
https://als.ca/blogs/does-a-viral-infection-play-a-role-in-als-onset-and-progression/
Dr. Luo and her team have been studying enteroviruses for 15 years. Recently, they discovered that infecting motor neurons with enteroviruses produces changes with striking similarities to those seen in ALS. The similarities included TDP-43 protein abnormalities and a reduced ability for motor neurons to clear out cellular waste in a process called autophagy. "Based on our findings, we believe that enterovirus could be a causal factor or a risk factor for triggering ALS," said Mohamud.

Reference Article March 2018:
Enteroviral Infection: The Forgotten Link to Amyotrophic Lateral Sclerosis? Front. Mol. Neurosci., 12 March 2018. https://www.frontiersin.org/articles/10.3389/fnmol.2018.00063/full

Figure 1. Molecular and pathological similarities between amyotrophic lateral sclerosis (ALS) and enteroviral infection. Enterovirus (EV) infection impairs nucleocytoplasmic trafficking **(A)** *via* EV proteinase-mediated proteolysis of nucleoporin proteins, resulting in mislocalization of TDP-43 and heterogeneous nuclear ribonucleoproteins (hnRNPs) from the nucleus to the cytoplasm, where they are further cleaved to induce TDP-43 pathology **(B)** and cause RNA-processing defects **(C)**. EV infection also results in the cleavage of several critical autophagic proteins, including SQSTM1/p62, Nbr1 and SNAP29, contributing to the disruption of the autophagic pathway **(D)** and consequent accumulation of misfolded proteins/damaged organelles **(E)**. Finally, subclinical EV infection induces chronic inflammatory reaction **(F)** and promotes non-lytic viral spread and prion-like mechanism through extracellular microvesicles **(G)**.

Initial Treatment Objectives (based on Week-1 findings):

1. Patient reports that her ALS progression had been slow since onset with increased progression speed noted since the beginning of 2021. Due to her cold sore outbreaks (increased HSV1 IgM titers) she has been on antiviral medication a minimum of 8 times per year for at least 10 years. This treatment was stopped in January 2021 at the recommendation of a clinical provider. HSV1 is known to cause encephalitis.
    a. Working theory: Consider a viral-related causal relationship in this patient's motor neuron disease (likely introduced into the CNS from the oral/sinus cavity infection). Slower progression is most probably the result of on-going anti-viral medication. Increased progression speed since January 2021 coincides with the discontinuation of anti-viral medication at that time.
2. Patient reports that she has tested positive for Lyme disease but is unsure of which pathogen and/or coinfections. She has an active HSV1 lesion currently. Given that Lyme infections can have a triggering/blooming effect on herpetic viruses and vice-versa, comprehensive Tick Borne infections, coinfection and viral pathogen testing with titer levels for IgG (dormant) and IgM (active) to be established and used to follow infection load/determine efficacy of treatment. Provoked pathogen testing to be performed after 15-21 days of IV provocation depending on response testing to include fungal, viral and bacterial pathogens.
3. Initial treatment strategy: anti-pathogen treatment to include IV provocation, IV light therapy with alternating days of UVA/UVC in combination with methylene blue for excitatory benefit. LL37 to be rotated along with anti-pathogen IVs and antioxidants/neuroprotective IV to support

the immune system. Mitochondrial, peroxisomal and lysosomal targeting IVs to determine area of cellular damage.

4. Removal of Mirena IUD to reduce synthetic progestin and eliminate any unnecessary foreign objects/synthetic hormones that may contribute to inflammation. Blood labs for hormone levels, progesterone and testosterone therapy to be added for maximum muscle health.
5. Evaluations: ALSFRS-R, Myometry and Spriometry to establish baselines for muscle strength and respiratory function

Week 2 Treatments:
UVA, Red, Green, Blue and Amber wavelengths used intravenously last week in combination with both anti-inflammatory and anti-pathogen IV treatments. One of the goals in Week-2 was to attempt to identify potential areas of infections/inflammation. NAD+ IVs were run twice during Week-2, both slow and rapid drip speed, in order to target areas of cellular inefficiency, pinpoint cells that may be most senescent and those with errors in autophagy/autophagic proteins. During NAD+ treatment when drip was increased to elicit cellular response, patient experienced a very localized "tightness in the back of her neck and a headache at the base of her skull" that resolved once speed was slowed. During the second treatment two days later "there was no tightness, but a headache all over the head in the back and sides and a very stuffy nose", she "could only breath out of her mouth".
Given that localized neck stiffness is a very unusual location to be reported, that it coincides with the suspected localization of the hypothesized infection entry point, and that it has proximity to sinus cavity, oral cavity and location of HSV-1 outbreaks, this may be an important finding in the identification of the trigger pathogen and development of a prioritized anti-pathogen treatment once pathogen test results are complete.

Additional Clinical Findings in Week-2
Patient has a rigid gait and describes stiffness in both legs for at least one year. A mild, low amplitude intention tremor is present in her right hand and can be seen when picking up/holding a water bottle. Tremor is not axial/there is no tremor when the bottle is brought towards the face.

Working theory: Intention tremor in combination with rigidity is suggestive of basal ganglia/mid-brain involvement. Consider that the substantia nigra, globus pallidus and/or subthalamic nucleus may be affected by the same pathogen(s) and that basal ganglia involvement could provide a structure landmark (in concert with the NAD+ provocation findings) to help determine the type of infection and possibly a cranial nerve entry track. Given that the Basal Ganglia is the area affected in Parkinson's Disease, a similarly misfolded protein disease, consider that individuals with motor neuron disease who also have symptoms of rigidity and intention tremor may share similar pathophysiology.

a. Due to tremor and rigidity, start amantadine for both rigidity/slowness and as an antiviral
b. Review pathogens known to target the midbrain structures and consult with neurology if needed
c. Consider sLORETA EEG to confirm basal ganglia involvement, track therapeutic efficacy and measure reduction in pathogen load over the next 6 months.

Additional treatment in Week 2

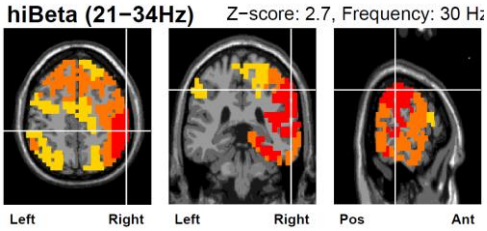
a. Nootropic stacking therapy for neuron enhancement and motor neuron protection to reduce/prevent pathogen-related damage during treatment

b. Start progesterone 50mg SR qHS (blood level is below detectable level). LH and FSH have been measured, menopause confirmed.
c. Lower back pain is disrupting sleep at night. Address with localized muscle vitamin injections. Of note, patient is now able to easily stand up straight, balance has improved and height of walker has been increased. Back pain may be resulting from dis-use/lack of conditioning due to poor posture/leaning forward as a compensation posture to prevent falling backwards. Floor exercises and stretching have been recommended.
d. Continue provocation protocol.

Week 3:
Continue treatment, testing and assessments.

Follow-up steps:

1. Review test results once complete to develop a targeted treatment strategy. Consider a molecular approach such as antisense/SOT as one part of the protocol depending on the type of pathogens. Increase perfusion in the CNS prior to any treatment to ensure optimized therapy penetration.
2. Spoke to patient's functional practitioner to discuss working theories. He agreed that an enterovirus is a reasonable hypothesis and in line with his clinical findings. He has been working with this patient using ART to address pathogen load. I asked that he focus on enterovirus and target the oral cavity, back of neck and head and he agreed. Forward lab results to him once complete.
3. Consider sLORETA EEG neuro-imaging if mapping is required to confirm mid-brain structures as viral targets and to determine when pathogen has been eliminated. Expected initial findings:



4. Schedule follow-up with the patient in three weeks to review all findings and discuss next steps.
5. Prior to next treatment run a comprehensive cytokine panel including IL1, 2, 4, 6, 8, 17, 23, TNF and Interferon gamma to track and confirm inflammatory reduction as infections are treated.
6. Once infection loads are controlled and progression speed has been reduced or corrected, heavy metal burden should be considered as well as biofilm disruption and gut health.
7. Continue to follow up with patient regarding emotional support to ensure she is able to find the resources needed.
8. Home protocol to include nootropic, muscle growth and immune regulating peptides in addition to Amino Supreme powder (1 scoop twice daily for adequate amino acid support). Bicarb Supreme to maintain proper pH balance and prevent lactic acid build-up (1 cap three times per day). Discontinue TUDCA and replace with Chaparone 1 (complete bile acid to provide heat shock protein and mitochondrial support). Digestive Enzyme 1 and Digestive Enzyme 2 for gut support and to improve and regulate bowel movements (2 caps of DE1 and 1 cap of DE2 with each meal). All caps can be crushed into powder if needed. List of supplements taken prior to treatment has been reviewed and approved for continued use.

Supplemental Background Information:

- Mental, Emotional and Spiritual Health: this is an area that has been identified as requiring additional support. Reports very high emotional stress chronically for over 5 years. Has been working with a professional. Addition of meditation and an increased focus in emotional balance has been recommended and will be followed.
- Had been exercising with Chi Gong for 90 minutes each day but stopped recently due to a fear of falling. Discussed an in-home harness system to allow stretching exercises to be re-started.
- Covid infection mid-Sept that resolved in approximately 3 weeks. Fatigue, cough and diarrhea. Sense of smell and taste have partially returned. Hastened progression/weakness over the past month may be a result of this infection, especially given the relationship between Covid and herpetic viruses. Provide covid-recovery protocol for home use.
- No significant medical history prior to diagnosis of ALS
- Lyme disease has been suggested by another provider but has not been confirmed
- Diet has largely consisted of processed meats and cheeses for over 10 years
- Water source: well water
- Known exposures: excessive fungal exposure at work
- Residence: home is 21 years old. No reported illnesses in family members living in residence

Family history:
There is no family history of MND, RA, Lupus or Parkinson's Disease.
Alzheimer's – maternal grandmother was diagnosed at in her early 70's. No shared living with this relative. Mother is showing signs of dementia starting in her 70's

Diagnostic Studies: (all with negative findings)
2017 three MRIs: 1 brain, 2 spine to rule out MS
2018 EMG

Summary

Given the heterogeneity of this disease, the creation of a categorization system whereby clinical presentation, location of initial symptoms and progression speed can be used to define a specific combination of motor neurotoxins. The development of this system could improve symptom pattern recognition leading to faster treatment selection in individuals with this highly diversified disease presentation. The individual in this case study is a slower progressor, understanding the reasons why progression has been slow may have important implications in the treatment of others with ALS.

This case study has been prepared by Amy Jaramillo. BodyScience.