Management of Depression in ALS With the Use of Methylphenidate and Sertraline

Nikunj Talati, DO, Theresa Toledo, MD, Esther Akinyemi, MD

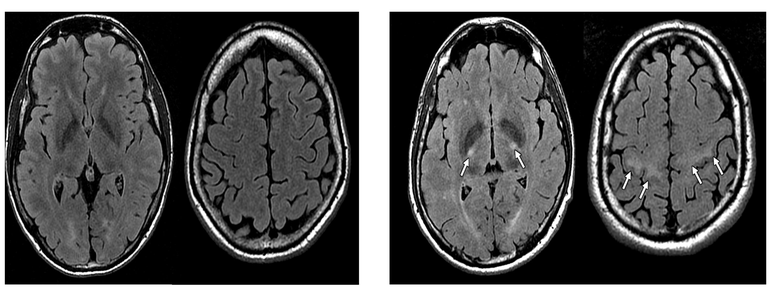
Department of Psychiatry, Henry Ford Hospital, Detroit, MI

Abstract

Amyotrophic lateral sclerosis (ALS) is now a well-known disease that was first described by Charcot in the 19th century. It is a relentlessly progressive neurodegenerative disorder, with voluntary muscle action progressively affected, people may experience muscle weakness, disability, and eventually death. The loss of motor neurons results in the primary clinical symptoms and produces impairment affecting limb, bulbar, axial, and respiratory function. The focus of research and treatment has been on the loss of motor neurons, but equally debilitating and associated problems with ALS include mood alterations such as depression and anxiety. Initial depression has been associated with shorter survival time. Quality of life appears to be more dependent on psychological factors such as depression and hopelessness being common in ALS patients. Quality of life can be improved with treatment of depression in ALS patients, however, there are no controlled trials supporting certain pharmacological treatments. Combination treatments with SSRI and methylphenidate has demonstrated enhanced clinical response in mood, well-being, higher rate of remission, and enhancement in cognitive functioning in the geriatric population. Herein we describe the management strategy for one patient with ALS and comorbid depression.

Introduction

ALS is a well-known disease that was first described by Charcot in the 19th century. It is also known as the Lou Gehrig's disease after the famous baseball player. It recently generated more awareness after social media and the “Ice Bucket Challenge.” It is a relentlessly progressive neurodegenerative disorder, with voluntary muscle action progressively affected, people may experience muscle weakness, disability, and eventually death. The loss of motor neurons results in the primary clinical symptoms and produces impairment affecting limb, bulbar, axial, and respiratory function. The focus of research and treatment has been on the loss of motor neurons, but equally debilitating and associated problems with ALS include mood alterations such as depression and anxiety. Initial depression has been associated with shorter survival time. Quality of life appears to be more dependent on psychological factors such as depression and hopelessness being common in ALS patients. The prevalence of depression among patients with ALS has been noted to be around 34%. The use of stimulants in ALS is generally not well- studied. Modafinil has shown to have overall positive effect on depression though primarily improvement in energy symptoms. Unfortunately, in ALS, modafinil has very low-quality evidence suggesting improvements in fatigue versus placebo. Other stimulants have not been studied in this population. Quality of life can be improved with treatment of depression in ALS patients, however, there are no controlled trials supporting certain pharmacological treatments. Combination treatments with SSRI and methylphenidate has demonstrated enhanced clinical response in mood, well-being, higher rate of remission, and enhancement in cognitive functioning in the geriatric population. Herein we describe the management strategy for one patient with ALS and comorbid depression.



FLAIR MR images from a patient with ALS (right) and a control subject (left), showing bilateral hyperintensities of the corticospinal tract in subcortical white matter and posterior limb of capsula internal in the ALS patient.

Case Presentation

Patient is an 80-year-old male with no history of depression or other mental illness, who presented to ALS neurology clinic around the age of 73, due to trouble balancing on one foot when drying off, after exercising, then later, difficulty to picking up his feet when he was jogging. He was diagnosed with ALS and then obtained second opinion at another institution where the diagnosis was confirmed. Since that time, his condition has been very slowly progressive.

He described onset of depression beginning after he was diagnosed with ALS. Over the following years, his physical health slowly declined and he became significantly less independent. His mood symptoms include anhedonia, decreased energy, and difficulty concentrating. He started initial treatment seeing a counselor and started on citalopram. The medication was effective for 6 weeks marked by brighter affect and reduction in anhedonia. However, the medication waned in its effectiveness over time, so bupropion was added. Citalopram and bupropion were discontinued shortly after, due to concern for worsening cognitive function and worsening withdrawal, depression, and anhedonia.

Psychiatry was curbside consulted for further assistance with medication management. Next medication options were given to either change from citalopram to sertraline for lack of effectiveness, add adjunct treatment of mirtazapine or adjunct treatment of methylphenidate. Methylphenidate was ultimately the first choice recommendation as it is often used to target symptoms of apathy, particularly in conjunction with an antidepressant. Mechanism of methylphenidate treating apathy is effect on catecholamine’s and dopamine. Methylphenidate was started by his neurologist. However, it was not further increased due to concerns for side effects in geriatric patients, and he was referred for full psychiatric evaluation and medication management.

On initial psychiatric evaluation for his mood symptoms, he was still taking methylphenidate which was providing only minimal to mild relief. He still had symptoms of depressed mood, fatigue, loss of energy, diminished concentration, anxiety, and worrying. Recommendations were made to start sertraline. Patient started to see mild improvements on sertraline including improvements in mood, irritability, anxiety, and social engagement. However, during the following video visit, patient reported being more withdrawn, feeling depressed, hopeless, and helpless. Due to worsening symptoms, sertraline was further optimized. Prior to next monthly visit, his wife reached out to describe patient being more confused, having trouble making decisions, and worsening difficulty with using a computer. Due to worsening symptoms and possible side effects, sertraline was decreased between appointments.

During the next visit, patient continued to complain of feelings of isolation, increased irritability, and being withdrawn with worsening depression. Sertraline was further decreased with plan to completely titrate off due to cognitive decline. After sertraline was discontinued, patient had major “meltdown” where he refused to go to an activity they usually go to for unknown reasons and also suicidal thoughts only during “meltdown.” Do to these thoughts, sertraline was restarted at 12.5 mg daily. This dose improved patient’s mood while cognition returned to baseline. Methylphenidate was re-initiated as previous dosing was not optimized or given full trial in conjunction with antidepressant.

One month later, at sertraline 12.5 mg and methylphenidate 5mg twice a day, patient and his wife reported increased motivation, feeling more expressive, less social withdrawal, decreased depression, and objectively more conversational on the phone. Methylphenidate was optimized to 10mg twice a day and sertraline continued at 12.5 mg once a day. He continues to demonstrate improvement in depression, with improved symptoms as listed above, and will continue to follow up on outpatient basis.

Timeline

- **Prior to Evaluation**
  - Symptoms: Anhedonia, Decreased Energy and Concentration
  - Medication Trials: Citalopram 20mg Daily + Bupropion 300mg Daily ; Methylphenidate 5mg Daily
- **May 24, 2021**
  - Symptoms: Depressed Mood, Fatigue, Decreased Concentration, and Anxiety
  - Medications: Methylphenidate 5mg Daily and Sertraline 25mg titrated to Sertraline 50mg Daily if tolerated.
- **June 25, 2021**
  - Symptoms: Depressed Mood, Social Withdrawal and Isolation, Anxiety,
  - Medication: Sertraline 100mg Daily; Hold Methylphenidate 5mg Daily
- **July 23, 2021**
  - Symptoms: Improved Mood, Decreased Irritability and Anxiety, Fatigue
  - Medication: Sertraline 150mg Daily
- **August 27, 2021**
  - Symptoms: Isolative, Depressed Mood, Feelings of Hopelessness and Helplessness
  - Medication: Sertraline 200mg Daily
- **September 13, 2021**
  - Symptoms: Confusion, Indecisive, and Increased Difficulty using a Computer
  - Medication: Sertraline 150mg Daily, Consider Ritalin Addition
- **September 29, 2021**
  - Symptoms: Confusion, Difficulty with Computer and Paying Bills, Slower Thought Process, Irritable, Difficulty Sleeping, Depression Worsening
  - Medication: Sertraline 100mg Daily with Plans to Taper and Discontinue
- **October 22, 2021**
  - Symptoms: Increased Motivation, Meltdown - Leading to Suicidal Thoughts, Depression W/o Sertraline
  - Medication: Sertraline 12.5mg Daily and Methylphenidate 5mg Twice a Day
- **November 11, 2021**
  - Symptoms: Increased Motivation, Expressive, Decreased Social Isolation, Sleep and Mood Improved, Objectively – More Conversational
  - Medication: Sertraline 12.5mg Daily and Methylphenidate 10mg Twice a day

Discussion

Depression has a prevalence of 34% in patients diagnosed with ALS. Currently there is not data identifying utilization of medications for ALS patients for depression aside from traditional antidepressants. To the best of our knowledge, there are no case reports that have reported methylphenidate or stimulants in general as treatment adjunct to antidepressants for depressive symptoms in ALS. This patient responded to sertraline and methylphenidate combination at relatively low doses. This is noteworthy as the patient was not able to tolerate higher doses of the antidepressant sertraline and citalopram was not found to be effective. The use of stimulants was tried in a single patient, so more studies will be needed to confirm the utility of this class of medications and combination in the ALS population with depressive mood symptoms. Further literature on treatment of depression in ALS is needed including different pharmacological measures and treatment modalities. We suggest that in addition to an antidepressant, stimulants can be considered to help specific symptoms including motivation, energy, and concentration.

References

1. Teive HA, Lima PM, Germiniani FM, Munhoz RP. What's in a name? Problems, facts and controversies regarding neurological eponyms. Arq Neuropsiquiatr. 2016;74(5):423-425.
2. Ackrivo J, Hansen-Flaschen J, Wileyto EP, Schwab RJ, Elman L, Kawut SM. Development of a prognostic model of respiratory insufficiency or death in amyotrophic lateral sclerosis. Eur Respir J. 2019;53(4):1802237.
3. Gromicho M, Figueiral M, Uysal H, et al. Spreading in ALS: The relative impact of upper and lower motor neuron involvement. Ann Clin Transl Neurol. 2020;7(7):1181-1192.
4. Thakore NJ, Pioro EP. Depression in ALS in a large self-reporting cohort. Neurology. 2016;86(11):1031-8
5. Heidari ME, Nadali J, Parouhan A, et al. Prevalence of depression among amyotrophic lateral sclerosis (ALS) patients: a systematic review and meta-analysis. J Affect Disord. 2021;287:182-190.
6. Ketter TA, Wang PW, Miller S. Bipolar therapeutics update 2014: A tale of 3 treatments. J Clin Psychiatry. 2015;76(1):69-70.
7. Gibbons C, Pagnini F, Friede T, Young CA. Treatment of fatigue in amyotrophic lateral sclerosis/motor neuron disease. Cochrane Database Syst Rev. 2018;1(1):CD011005.
8. Lavretsky H, Reinlieb M, St Cyr N, Siddarth P, Ercoli LM, Senturk D. Citalopram, methylphenidate, or their combination in geriatric depression: a randomized, double-blind, placebo-controlled trial. Am J Psychiatry. 2015;172(6):561-9.
9. Mazón M, Vázquez Costa JF, Ten-Esteve A, Martí-Bonmatí L. Imaging biomarkers for the diagnosis and prognosis of neurodegenerative diseases. The example of amyotrophic lateral sclerosis. Front Neurosci. 2018;12:784.