

## PATHOLOGICAL PHYSIOLOGY

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**Quality of life and muscle strength improvement  
in an amyotrophic lateral sclerosis patient after  
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The objective of the article was to describe a patient with amyotrophic lateral sclerosis (ALS) treated with nutraceuticals who had a better quality of life and improved muscle strength. A 65-year-old male patient with a past medical history of gout was diagnosed with amyotrophic lateral sclerosis in 2016. He received intravenous immunoglobulin and prednisone, but no improvement was observed. In 2018, he was diagnosed with multiple myeloma, submitted to a bone marrow transplant, and initiated riluzole. After 2 months, he came to our private clinic; he could not walk anymore and used outpatient nasal ventilator equipment. Beck anxiety inventory (BAI) was 20 [normal range (nr): < 8], Beck depression inventory (BDI) was 12 (nr: < 10), Bristol stool form scale (BSTS) was 5 (nr: 3–4), and there were 7 symptoms of dysbiosis. Analogic visual scale (Lickert scale) for well-being was 5.0. We suspended the colchicine, added vitamin D3, creatine, vitamin C, N-acetyl cysteine, 5-hydroxytryptamine, B1, and B6 vitamins. Dysbiosis was also treated. After 2 months, he returned feeling much better, BAI and BDI reduced BDI to 11, and BSFS normalized. Following this evaluation, a nutraceutical prescription was added: methylfolate, zinc, magnesium, green tea extract, Ginkgo biloba, lipoic acid, pyrroloquinoline quinone, vitamin E, coenzyme Q10, and resveratrol. Af-

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ter 7 months, he was feeling very well; BAI and BDI were normal, he gained weight. He felt a marked improvement in his muscle strength, and he gained again the capacity of eating alone, his quality of life improved, and AVS well-being was 8.0. This report illustrates a demonstrative case of a patient with ALS treated with nutraceuticals and improved his quality of life and muscle strength. It may be an alternative therapeutic option for such patients.

*Keywords:* amyotrophic lateral sclerosis, neurological disorders, lower neuron disease, immunity, vitamin D, nutraceuticals, supplements.

## Introduction

Amyotrophic lateral sclerosis (ALS) is the prototype motor neuron disease with the presence of degeneration of the anterior horn of the spinal cord, motor nuclei of the cranial nerves, and pyramidal cells in the motor cortex. The aetiology of ALS is unknown, although the trigger roles of repeated cranial traumas, certain infections and monoclonal gammopathies are suggested. The pathogenesis includes autoimmune links, which hypothesis is supported by the association of ALS with other autoimmune pathologies and with higher prevalence of certain HLA haplotypes in it. Autoantibodies from ALS patients sera may induce apoptotic death of motor neurons in cell culture and anterior horn damage by passive transfer to mice. Autoantibodies against voltage-dependent calcium channels and few other targets (neurofilaments, Fas receptor (CD95), fetal muscular proteins, and vascular antigens) are blamed for that. Also, T-cell/macrophageal infiltration of spinal anterior horns has been registered in cases of ALS. The targeted neurons undergo degeneration under influence of immune and other complex mechanisms, increase of intracellular calcium ions' concentration, glial activation and M1-polarization, reactive oxygen species hyperproduction, glutamate excitotoxicity, protein misfolding with ubiquitinated aggregates and disorder of proteasome functions [1–3]. This degeneration causes progressive palsy of skeletal muscles leading to a paresis of lower and upper limbs. During the progression of the illness, intercostal, phrenic and esophageal muscles may also be involved, due to involvement of medulla oblongata, with respiratory insufficiency and dysphagia, resulting in weight loss and malnutrition [1]. The median time of survival after the onset of ALS symptoms is 32 months [4].

There is no definitive treatment for ALS. The only therapeutical agent available is riluzole, a noncompetitive metabotropic glutamate receptor 1 (mGluR1) antagonist, which may prolong survival by only 2 to 3 months [5].

New modalities of treatment are therefore desired. In this line, low-risk treatments to improve life quality, prolong survival, and reduce comorbidities are extremely desired in this neurological disorder. Using a holistic approach with complementary and alternative medicine may be an additional option for such patients to improve their quality of life and some aspects of muscle strength.

The purpose of this article is to report the case of a patient with ALS who was treated using a combination of nutraceuticals and had a better quality of life and muscle strength.

## Case report

A 65-year-old male patient with a past medical history of gout for 20 years; started to feel in December 2016 progressive mild muscle weakness in his hands, and then he noted the difficulty of cut foods and bring them to his mouth, later he felt the difficulty

of use stairs, and the symptoms progressed. His cerebrospinal fluid was normal. Electroneuromyography showed alteration of the anterior horn of the spinal cord on cervical and lumbar regions of the spine. He was diagnosed with amyotrophic lateral sclerosis by the neurologist. He had positive serological data for Lyme disease and received antibiotics (ceftriaxone 2 g/day) for 30 days but without any improvement. In January 2018, he received human polyclonal intravenous immunoglobulin G, but no change was noted. He also was treated with prednisone 80 mg/day for 8 months with progressive tapering, but no improvement was observed. In July 2018, he was diagnosed with multiple myeloma, and in August 2018, he was submitted to a bone marrow transplant and developed pulmonary thromboembolism in the post-operative transplant. Riluzole 50 mg twice a day was initiated to him. After 2 months, he came to our private clinic. He could not walk anymore. His physical examination demonstrated a pale patient using a nasal bi-level positive airway pressure (BIPAP) in an outpatient ventilator equipment. His weight was 64 kg and height 1.68 m, and body mass index (BMI) 22.7 kg/m<sup>2</sup>. He had atrophy of hand interosseous muscles and several muscle atrophies of his forearm and thigh muscle groups. Furthermore, the spasticity of lower limbs was noted on passive flexion and extension. His muscle strength was grade 3/5 in upper limbs and 2/5 in lower limbs; the legs were paretic. All reflexes were exacerbated, and fasciculations were observed in arms and legs. Blood pressure was 110 × 80 mm Hg, heart rate of 64 bpm, Cardiovascular, lung, and abdomen examination was unmarked. Beck anxiety inventory (BAI) was 20 [normal range (nr): < 8], Beck depression inventory (BDI) was 12 (nr: < 10), Pittsburgh sleep scale was 3 (nr: < 7), Bristol stool form scale (BSTS) was 5 (nr: 3–4), and there were 7 symptoms associated with dysbiosis. Analogic visual scale (Lickert scale) for well-being was 5.0 (reference: 0, worst, and 10, best). He was under methylcobalamin 50 mg subcutaneously twice a week, colchicine 1mg/day, riluzole 100 mg/day, and tauroursodeoxycholic acid 250 mg/day. Laboratory tests revealed hemoglobin 12.3 g/dL (nr: 13–18 g/dL), white blood cell 3,260 cells/mm<sup>3</sup> (nr: 4,000–10,000 cells/mm<sup>3</sup>), eosinophils were 690 cells/mm<sup>3</sup> (nr: < 500 cells/mm<sup>3</sup>), platelets 208,000 cells/mm<sup>3</sup>, creatine kinase of 1.050 U/L (nr: 32–294 U/L), vitamin D3 28.3 ng/mL [normal range (nr): > 30 ng/mL], albumin 39.7 g/L (nr: 35–47 g/L), AST 34 (nr: < 35 U/L), ALT 23 U/L (nr: < 30 U/L) and homocysteine 10.3 mmol/L (optimal range: < 8 mmol/L). Antinuclear antibodies, anti-dsDNA, anti-Sm, anti-Ro/SS-A, anti-La/SS-B, anti-U1RNP, anti-mitochondria, anti-thyroglobulin, anti-thyroperoxidase, and anti-CCP were all absent. Immunoglobulin levels were within the normal range. Magnetic resonance imaging of the brain and spinal cord gave normal images. Polysomnography revealed an index of apnea-orthopnea mildly increased and the presence of 34 episodes of desaturation. Serological data for infectious diseases, such as HIV 1 and 2, syphilis, rubella, mononucleosis, hepatitis B and C virus, cytomegalovirus, herpes type 1 and 2, toxoplasmosis — were all negative. We suspended the colchicine since this drug may induce or worsen myopathy; we added vitamin D3 10.000I U/day, creatine 5 g/day, vitamin C 500 mg/day, N-acetyl cysteine 400 mg/day, 5-hydroxytryptamine 300 mg/day, thiamine 100 mg/day, and pyridoxine 100 mg/day. For dysbiosis, we prescribed albendazole 400 mg once and an additional dose after 15 days; glutamine 5 g twice a day, quercetin 250 mg/day, and vitamin A 25.000 Iu/day for 2 months. A gluten-free diet was suggested, removing all foods with wheat, rye and barley. After 2 months, he returned feeling much better, and vitamin D increased to 48.3 ng/mL, CK reduced to 484 U/L, eosinophils normalized to 243 cells/mm<sup>3</sup>, an increase in weight was seen, BAI reduced to

16, and BDI to 11, and BSFS normalized in 3. Following this evaluation, this nutraceutical prescription was added: vitamin D3 was increased to 20.000 IU/day, methylfolate 1 mg, zinc 30 mg, iodine 500 mcg, magnesium 200 mg, green tea extract 300 mg, Ginkgo biloba 100 mg, lipoic acid 600 mg, pyrroloquinoline quinone 20 mg, and vitamin E 400 IU once a day. Coenzyme Q10 200 mg plus resveratrol 50 mg was administered transdermally once a day. D-ribose 5 g once a day. And he continues using riluzole associated with the nutraceuticals. After 7 months, he felt very well; BAI was 8, BDI was 9, he gained weight and stayed with 72.5 kg, with a BMI of 25.5 kg/m<sup>2</sup>, and his muscle strength was grade 4/5 in upper limbs and 3/5 in lower limbs; although the legs continued were paretics No evidence of myeloma multiple was seen as evidenced by the normal calcium, creatinine, total protein and serum albumin concentration. He felt a marked improvement in his muscle strength, and he gained again the capacity of eating alone, his quality of life improved, and AVS was 8.0.

## Discussion

This article reports a patient who suffered from ALS and experienced improved muscle strength and quality of life when treated with a combination of some nutraceuticals and a gluten-free diet.

From the point of view of pathology, the co-morbidity of this ALS case with multiple myeloma is remarkable. The association of these entities was noticed before, with either ALS (or related motor neuron disorders) diagnosis established prior to myeloma, or vice versa monoclonal gammopathies, including myeloma or other lymphomas, debuted before ALS elicited [6–10]. Concerning Lyme disease, it was probably a false positive serology, since the adequate treatment with ceftriaxone 2 g/day for 30 days did not change the clinical picture of the patient.

A blend of strategies was used in our patient. Indeed, we supplemented him with vitamin D since the serum levels of vitamin D were low, and, also, there is evidence in the literature about its deficiency in ALS as well as its protective role in autoimmune diseases [11; 12]. More so, significantly, low vitamin D is associated with more ALS severity [11]. The use of vitamin D supplementation in ALS was already studied. Its efficacy was supported by a study with 34 ALS subjects supplemented with 2,000 IU/day and improved functionality in these patients [13].

Concerning creatine supplementation, a study that reported using this derivative of amino acids in 28 patients with a dosage of 20 g/day for 7 days and then 3 g/day for 3–6 months showed an increase of maximal isometric power these patients [14].

Regarding vitamin C and E, an extensive prospective study of ALS prevention evaluated 957,740 healthy individuals, who regularly used vitamins E and C and was followed from 1989 to 1998, and the authors observed 525 deaths from ALS. Interestingly, regular use of vitamin E supplements was associated with a lower risk of dying of ALS. However, no significant associations were found for the use of vitamin C or multivitamins [15].

Hyperhomocysteinemia is frequently found in patients with ALS. A study that evaluated 62 patients with ALS and 88 age- and sex-matched controls verified a higher median plasma homocysteine levels (11.2 vs. 9.7 micromol/L,  $p=0.0004$ ) lower folate levels in patients compared to controls. Moreover, multivariate logistic regression revealed a robust direct association between plasma homocysteine levels and ALS presence and a shorter

interval onset ALS diagnosis [16]. A high dose of methylcobalamin, a methylating agent, was tested in ALS, showing a prolonged survival and retarding symptomatic progression without significant side effects if started early in these patients [17].

5-hydroxytryptamine was offered to the patient to improve anxiety and depression symptoms, and this good result was observed in our case. In fact, in a Cochrane review, 5-HTP had a good effect on depressive patients than controls [18].

A scheme for dysbiosis was used in the patient, with albendazole, to kill pathogenic intestinal parasites. In ALS patients, few case reports exist of ALS associated with the presence of parasites such as schistosomiasis, babesiasis, and borrelia. Moreover, the ALS clinical manifestations improved after treatment with ceftriaxone and anti-babesia therapy [19; 20].

Quercetin as well as plantar polyphenols, bioflavonoids and resveratrol are able to render therapeutic effect in ubiquitination/proteasome function disorders of ALS and similar diseases, as it was shown recently by comprehensive meta-analysis [3]. Also quercetin and vitamin A has an essential role in the intestinal epithelization process, contributing to dysbiosis improvement [21; 22].

Pyridoxine and thiamine supplementations were implemented in our patients to improve anxiety and depression symptoms. A study could show that there was a 28% thiamine deficiency in ALS patients [23]. Another study showed the effectiveness of a high dose of pyridoxine for anti-stress activity [24]. Moreover, the association of magnesium 200 mg and pyridoxine 50 mg may reduce anxiety symptoms [25]. Our patient received both elements and had a marked reduction of anxiety.

Zinc levels are inversely associated with the presence of ALS and also with ALS patients' function impairment [26]. Lipoic acid supplementation was reported in a similar case report with a good outcome [27]. However, this substance was administered together with other treatments, as in our patient. An experimental study has shown a good effect of Ginkgo biloba in mice with ALS [28].

Concerning coenzyme Q10, it is commonly used in various degenerative neurological diseases, including ALS. An exciting review of coenzyme Q10 in these neurological conditions is available (see reference 21) [29].

Future randomized and controlled studies with the combined use of several nutraceuticals as complementary therapeutics for ALS are desired to confirm our patient's excellent response.

Recently it has been demonstrated that riluzole commonly used in ALS has also some anti-neoplastic activities as regards to myeloma also [30], which makes this kind of therapy especially appropriate for comorbid cases like one described here.

In conclusion, our present ALS patient used some nutraceuticals, changed his food for a gluten-free diet, and obtained an excellent clinical response to improve muscle strength, reduce anxiety and depression symptoms, and improve his life quality.

## **Ethical statement**

The author declares that he followed the World Medical Association Declaration of Helsinki in this study. An informed consent was obtained from the patient for publication of his case. No image of him is used.

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