HYPOPARATHYROIDISM: A RARE MIMIC OF AMYOTROPHIC LATERAL SCLEROSIS

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ABSTRACT: *Introduction*: Amyotrophic lateral sclerosis (ALS) carries a grim prognosis. Various ALS mimics have been reported and should be excluded before confirming this diagnosis. *Methods*: We report the case of a 61-year-old man who presented with progressively worsening limb weakness and dysphagia. His examination showed mixed upper and lower motor neuron signs without sensory impairment. ALS was suspected, however, atypical diffuse pain prompted diagnostic work-up to exclude other causes. *Results*: Electrodiagnostic testing was suggestive of a sensorimotor polyneuropathy with superimposed diffuse active denervation suspicious for anterior horn cell degeneration. Brain MRI showed bilateral basal ganglia and thalamic calcifications. Laboratory studies confirmed the diagnosis of hypoparathyroidism. Treatment with calcium and vitamin D resulted in significant improvement at 6 months follow-up. *Conclusions*: Hypoparathyroidism, a treatable endocrinopathy, can rarely present clinically as ALS. In atypical cases, this should be ruled out before making a final diagnosis.

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Amyotrophic lateral sclerosis (ALS), the most common type of acquired motor neuron disease (MND), carries a poor prognosis.[1] No definitive laboratory tests are available for diagnosis. Instead, it is based on a physician's clinical evaluation, electrodiagnostic testing, and exclusion of other treatable causes.[2] The only approved medical treatment for ALS provides only a slight benefit in slowing the disease course.[3,4] All efforts should be made to rule out possible MND mimics at the time of diagnosis, especially when the presentation is atypical. We report a rare case of hyoparathyroidism that presented clinically as ALS.

CASE REPORT

A 61-year-old man with a known history of diabetes and hypertension presented with progressive difficulty with walking, swallowing, and slurring of speech. He had asymmetric, left hemibody predominant weakness that was gradually progressive over 8 months and was associated with body stiffness. Four months into his illness, he started using a cane for ambulation and developed gradually worsening dysarthria and dysphagia for both solids and liquids. Two weeks before presentation, he became completely bed bound. Associated with this, the patient complained of generalized body aches but did not report any sensory symptoms, fasciculations, cramps, or falls. His family reported that he had shown decreased interest in routine activities over the preceding 3 years. He developed acute shortness of breath and fever 2 days before presentation, which led to admission to our hospital.

On examination, the patient was tachypneic. He had dysarthric speech and a weak gag reflex. Muscle bulk was preserved except for atrophy of the left first dorsal interosseous muscle. Muscle fasciculations were not visualized. Tone was increased in the left upper extremity and bilateral lower extremities. Power was Medical Research Council grade 4+/5 in the right upper limb and 4-/5 in the left upper limb proximally and distally. Detailed strength testing of the lower extremities was limited due to severe pain, but the patient could move them against gravity. Muscle stretch reflexes were brisk in all extremities. There was no ankle clonus. Plantar responses were flexor bilaterally. Neither sensory impairment or cerebellar signs were identified.

Nerve conduction studies (NCSs) revealed absent sural sensory nerve action potentials and decreased distal fibular compound muscle action potential amplitudes bilaterally. Electromyography showed severe evidence for active denervation in almost all proximal and distal muscles examined in the upper and lower extremities, and in the cervical and lumbosacral paraspinal muscles. Active denervation was not seen in the thoracic paraspinal or genioglossus muscles. A few large amplitude polyphasic motor unit action potentials (MUAPs) with reduced recruitment were seen symmetrically in distal lower extremity muscles, while normal morphology MUAPs with normal recruitment were seen in bulbar, cervical, and proximal lumbosacral myotomes. Fasciculation potentials were not observed.

The atypical feature of diffuse body pain, especially early in the disease course, prompted an extensive work-up to rule out an ALS mimic. Brain

Abbreviations: ALS, amyotrophic lateral sclerosis; BG, basal ganglia; MND, motor neuron disease; MUAPs, motor unit action potentials; NCS, nerve conduction study; PHP, primary hyperparathyroidism

Key words: amyotrophic lateral sclerosis; electromyography/nerve conduction studies; hypocalcemia; hypoparathyroidism; motor neuron disease

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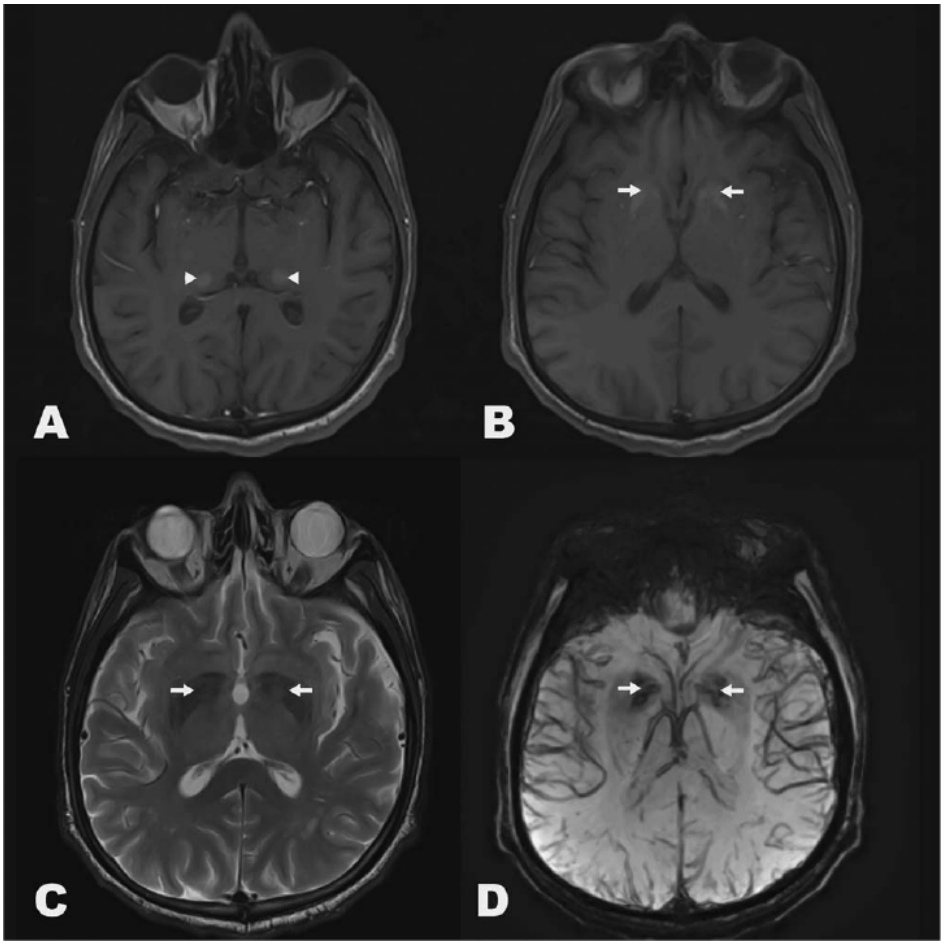

FIGURE 1. Brain MRI (axial views) showing abnormal increased bilateral basal ganglia (arrows) and thalamic signals (arrowheads): T-1 hyperintense signals**(A,B)**; T-2 hypointense signals **(C)** and signal dropout **(D)** on susceptibility weighted image.

MRI (Fig. 1) demonstrated bilateral basal ganglia (BG) and thalamic calcifications. Laboratory studies revealed a calcium level of 3.1 mg/dl (normal, 8.6–10.2 mg/dl), phosphate of 7.2 mg/dl (normal, 2.5–4.5 mg/dl), magnesium of 1.1 mg/dl (normal, 1.6–2.6 mg/dl), creatine kinase of 994 IU/L (normal, 46–171 IU/L), and vitamin D of 7.38 ng/ml (deficiency <20 ng/ml). Parathyroid hormone levels were undetectable at <3 pg/ml (normal 16–87 pg/ml). Taken together, these findings were most consistent with primary hypoparathyroidism. The patient was started on activated vitamin D along with calcium supplementation. Remarkable clinical and biochemical improvement was noted at 6 months, along with improvement in the ALS Functional Rating Scale-Revised score from 21 to 44 and near-normalization of serum calcium levels (8.5 mg/dl). The only residual deficit was some difficulty in ambulation secondary to development of a contracture in the right lower limb. The patient did not consent to repeat electrodiagnostic testing.

DISCUSSION

ALS is a heterogeneous disorder with clinically variable presentations, age of onset, distribution of weakness, and rate of progression.[1] Multiple ALS mimics have been described,[5–7] possibly accounting for both high false-positive (up to 10%) and false-negative rates (up to 44%) of diagnosis.[8]

The simultaneous presence of gradually progressive, asymmetric weakness with mixed upper and lower motor neuron signs in a middle aged man, involving multiple segments of the neuraxis, and evidence of dysfunction of motor neurons or their axons on electrodiagnostic studies, led us to initially suspect ALS. Asymmetric muscle weakness with upper motor neuron signs has also been reported with hypoparathyroidism.[9] Body aches and pain were a significant complaint and made us consider an alternate diagnosis. Bilateral BG calcifications, seen on subsequent brain MRI, led us to suspect parathyroid endocrinopathy. Laboratory studies confirmed the diagnosis of primary hypoparathyroidism.

Pathological BG calcifications can be seen in a variety of infectious, genetic, and metabolic diseases, of which the commonest are parathyroid endocrine disorders.[10] The most common sites of cerebral calcifications in hypoparathyroidism are the BG followed by the cerebral cortex and cerebellum.[11]

Reversible neuropathy of predominantly an axonal variety has been reported in hypoparathyroidism.[12] Electrodiagnostic testing in our patient suggested sensorimotor axonal neuropathy, which could have been due to either hypoparathyroidism or concomitant diabetes mellitus.[13] In the hypoparathyroid-ALS patient reported by Scarpitta et al.,[14] electrodiagnostic studies showed denervation and fasciculation potentials in both upper and lower limbs and a diffuse neurogenic pattern characterized by a reduced number of polyphasic motor unit potentials during voluntary movements. No abnormality was seen in sensory or motor NCSs. Electrodiagnostic studies of our patient revealed diffuse active denervation but no fasciculation potentials. Changes of chronic denervation and reinnervation were seen in distal foot and leg muscles symmetrically and were much more likely secondary to longstanding neuropathy rather than the acute process causing the diffuse active denervation. Many authors have studied abnormalities in calcium regulation by neurons and the resultant motor neuron toxicity, but no definite causal relationship has been established.[15,16]

Generalized body pain, a predominant complaint in our patient, is among the early features of hypocalcemia.[17] Although body aches and pain have also been found to be associated with ALS, they are usually not a prominent clinical feature early in the disease course.[18]

Neuropsychiatric manifestations associated with hypoparathyroidism include depression, impaired concentration, impaired memory, emotional lability, and hallucinations.[9] In a large cohort study by Murphy et al., cognitive and behavioral changes were also seen in ALS, ranging from mild impairment (54.2% and 14.1%, respectively) to frank changes consistent with possible frontotemporal dementia (6.5% and 16.5%, respectively).[19] The patient's family noticed that he had stopped deriving pleasure from previously enjoyable activities in the years preceding his debilitating motor symptoms. Although formal neuropsychological assessment was not done during his hospitalization, in view of the overall reversibility of the underlying disease process, these behavioral symptoms were also likely secondary to hypoparathyroidism.

Although primary hyperparathyroidism simulating ALS is a known phenomenon,[20,21] hypoparathyroidism mimicking ALS is a rare occurrence.[14] Being a potentially treatable endocrinopathy, hypoparathyroidism should be actively looked for in patients who present with what appears to be an atypical variant of ALS.

REFERENCES

1. Traxinger K, Kelly C, Johnson BA, Lyles RH, Glass JD. Prognosis and epidemiology of amyotrophic lateral sclerosis: Analysis of a clinic population, 1997–2011. Neurol Clin Pract 2013;3:313–320.
2. Brooks BR, Miller RG, Swash M, Munsat TL. El Escorial revisited: revised criteria for the diagnosis of amyotrophic lateral sclerosis. Amyotroph Lateral Scler Other Motor Neuron Disord 2000;1:293–299.
3. Lacomblez L, Bensimon G, Leigh PN, Guillet P, Powe L, Durrleman S. et al. A confirmatory dose-ranging study of riluzole in ALS. Neurology 1996;47(Suppl 4):242S–2450S.
4. Couratier P, Sindou P, Esclaire F, Louvel E, Hugon J. Neuroprotective effects of riluzole in ALS CSF toxicity. Neuroreport 1994;5:1012.
5. Turner MR, Talbot K. Mimics and chameleons in motor neuron disease. Pract Neurol 2013;13:153–164
6. Baek WS, Desai NP. ALS: pitfalls in the diagnosis. Pract Neurol 2007; 7:74–81.
7. Rison RA, Beydoun SR. Amyotrophic lateral sclerosis-motor neuron disease, monoclonal gammopathy, hyperparathyroidism, and B12 deficiency: case report and review of the literature. J Med Case Rep 2010;4:298.
8. Brooks BR. Earlier is better: the benefits of early diagnosis. Neurology 1998;53(Suppl 5):S53–S54.
9. Sabau M, Comanescu A, Maghiar T, Dinulescu D. Hypoparathyroidism diagnosed by neurological signs and widespread intracerebral calcifications. Rom J Neurol 2010;9:44–50.
10. Basak RC. A case report of basal ganglia calcification - a rare finding of hypoparathyroidism. Oman Med J 2009;24:220–222.
11. Bhadada SK, Bhansali A, Upreti V, Subbiah S, Khandelwal N. Spectrum of neurological manifestations of idiopathic hypoparathyroidism and pseudohypoparathyroidism. Neurol India 2011;59:586–589.
12. Goswami R, Bhatia M, Goyal R, Kochupillai N. Reversible peripheral neuropathy in idiopathic hypoparathyroidism. Acta Neurol Scand 2002;105:128–131.
13. Said G. Diabetic neuropathy–a review. Nat Clin Pract Neurol 2007;3: 331–340.
14. Scarpitta A, Pisciotta G, Fierro B. Basal ganglia calcifications and ALS syndrome. Ital J Neurol Sci 1994;15:249–251.
15. Grosskreutz J, Van Den Bosch L, Keller BU. Calcium dysregulation in amyotrophic lateral sclerosis. Cell Calcium 2010;47:165–174.
16. Jaiswal MK. Calcium, mitochondria, and the pathogenesis of ALS: the good, the bad, and the ugly. Front Cell Neurosci 2013;7:199.
17. Pravina P, Sayaji D, Avinash M. Calcium and its role in human body. Int J Res Pharm Biomed Sci 2013;4:659–668.
18. Chiò A, Canosa A, Gallo S, Moglia C, Ilardi A, Cammarosano S, et al. Pain in amyotrophic lateral sclerosis: a population-based controlled study. Eur J Neurol 2012;19:551–555.
19. Murphy J, Factor-Litvak P, Goetz R, Lomen-Hoerth C, Nagy PL, Hupf J, et al. Cognitive-behavioral screening reveals prevalent impairment in a large multicenter ALS cohort. Neurology 2016;86:813–820.
20. Carvalho AA, Vieira A, Simplicio H, Fugygara S, Carvalho SM, Rigueiro MP. Primary hyperparathyroidism simulating motor neuron disease: case report. Arq Neuropsiquiatr 2005;63:160–162.
21. Michael D. Sirdofsky LK. Neurologic complications of parathyroid gland disorders. In: Biller J, editor. The interface of neurology & internal medicine. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2008. p 479.