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Coexistence of myasthenia gravis and amyotrophic lateral sclerosis in a Bosnian male: an unusual clinical presentation

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Purpose. Myasthenia gravis (MG) and amyotrophic lateral sclerosis (ALS) are two different diseases. The coexistence of both of them is extremely rare and represents a diagnostic challenge which requires thoughtful interpretation of clinical characteristics.
Case report. We present the case of a 46-year-old Bosnian male who developed ALS five months after MG. Diagnosis of MG was based on elevated titers of anti-AchR antibodies, positive edrophonium test, and decremental responses on a repetitive nerve stimulation test while the diagnosis of ALS was based on clinical and neurophysiological findings: upper motor neuron signs in the lumbar region, lower motor neuron signs in the bulbar and cervical regions, generalized fasciculations and muscle atrophy and progressive asymetric muscle weakness together with active and chronic denervation in the cervical and lumbosacral region determined by electromyoneurography.
Conclusions. The coexistence of MG and ALS is rare and request an adequate interpretation of clinical symptoms. The relationship between these two diseases in as interesting phenomen to present.

Key words: myasthenia gravis, amyotrophic lateral sclerosis, coexistence

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Conflict of interest
The Authors declare no conflict of interest

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Introduction

Myasthenia gravis (MG) is an autoimmune disorder of the neuromuscular junction that is usually caused by antibodies against nicotine acetylcholine receptors (AchR) and occasionally by antibodies against muscle-specific kinase (MuSK). Clinical characteristics of MG are fluctuating muscle weakness and easy fatigability of volontary muscles. MG follows a slowly progression course. By contrast, amotrophic lateral sclerosis (ALS) is as a progressive neurodegenerative disorder affecting motor neurons in the cerebral cortex, brainstem, and spinal cord. Studies of ALS have revealed defects in expression of acetylcholine receptors (AChRs) in skeletal muscle that occur even in the absence of motor neuron anomalies [1]. The co-occurence of MG and ALS has been described in a few reports, suggesting a possible association of the two diseases [2,3]. A recent study reported that 0,75% of patients with ALS were also affected by MG [4]. We report the case of a patients with seropositive MG who within 5 months developed ALS.

Case report

A 46-year-old Bosnian male developed difficulties in swallowing, and dysarthria in April 2019. Difficulties with swallowing and chewing as well as pronouncing words were getting worse with more activities and in the evening and improved with rest. These symptoms he noted five months before he was referred to Department of Neurology. He had no family history of neuromuscular disorders. On neurological examination, his pharyngeal reflex was reduced. Eyelid ptosis, ocular and facial motility deficits were not evident on neurological examination. There was no muscle weakness, atrophy, or fasciculations in any of his extremities. Deep tendon reflexes were normal, and Babinski signs were absent. Sensory abnormalities were not detected. His biochemical investigations, thyroid function test and tumor markers were normal. Acetylcholine receptor antibodies (AchR level 2.85 nmol/l; normal values < 0.5 nmol/l) were elevated. The MuSK antibodies were not tested. Computed tomography scans of the chest did not reveal remarkable abnormalities (Fig. 1). An edrophonium test showed improvement in a way that patient could speak better and swallowed better without any side effects. Repetitive nerve stimulation performed on the ulnar nerve at 3 Hz showed a 25% decrease in musculus abductor digiti minimi amplitude after 1 minute, and 60% after 3 minutes compared to baseline. The coumpound muscle actional potential (cMAP) after first stimulation was 2.5 mV, after second 1.8 mV and the value of the highest cMAP was 4mV. We discharged our patient from the hospital with diagnosis of Myasthenia gravis based on elevated titers of anti-AchR antibodies, positive edrophonium test, and decremental responses on a repetitive nerve stimulation test. We prescribed oral prednisolone, pyridostigmine and azatioprine. Our patient was feeling much better during the follow-up. Quantitative Myastenia gravis score before therapy was 8, and on therapy was 4. Five months later, he was again referred to our institution because he developed new symptoms such as initial tongue atrophy and fasciculations, moderate muscle weakness detected in the neck and all extremities as well as fasciculations in the upper limbs. On neurological examination, jaw jerk and snout reflex were hyperactive, and Babinski reflex was positive. An edrophonium test was again positive while titer of anti-AchR antibodies decreased to 0.85 nmol/l. Repetitive nerve stimulation showed a decrement response in the abductor digiti minimi muscle (25%). Needle electromyography showed fibrillation potentials, positive sharp waves, and fasciculation potentials with chronic denervation in the triceps brachii, biceps brachii, first dorsal interosseus muscles and chronic deinervation in the lumbosacral regions. Needle electromyography of the tongue could not be done since it caused discomfort to the patient and he could not stand this diagnostic procedure. Brain MRI (Fig. 2) and cervical spine MRI showed no abnormalities (Fig. 3). He was diagnosed with clinically probable ALS, according to the revised El Escorial criteria [5]. We prescribed him Riluzole and so far he shows no progression.

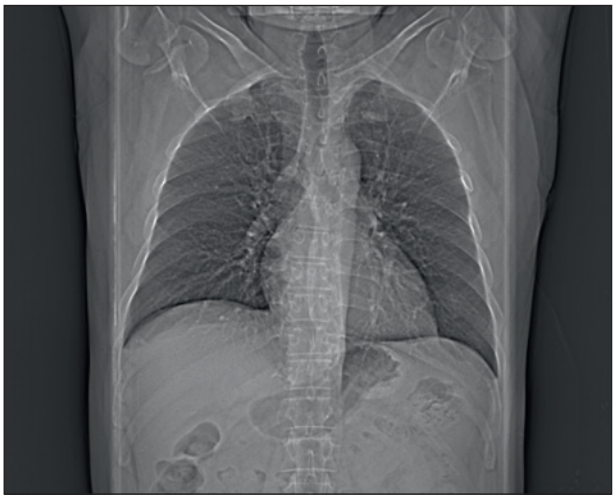

Figure 1. CT scan of the thorax.

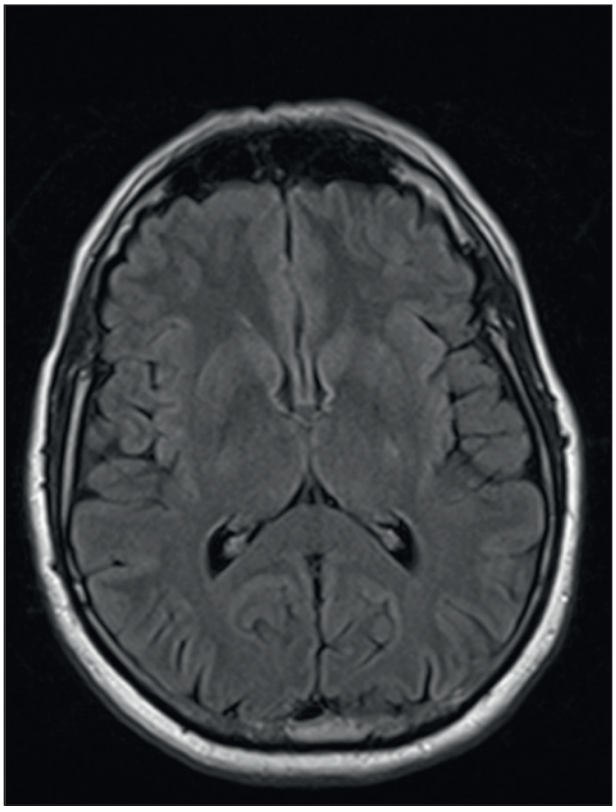

Figure 2. MRI of the brain.

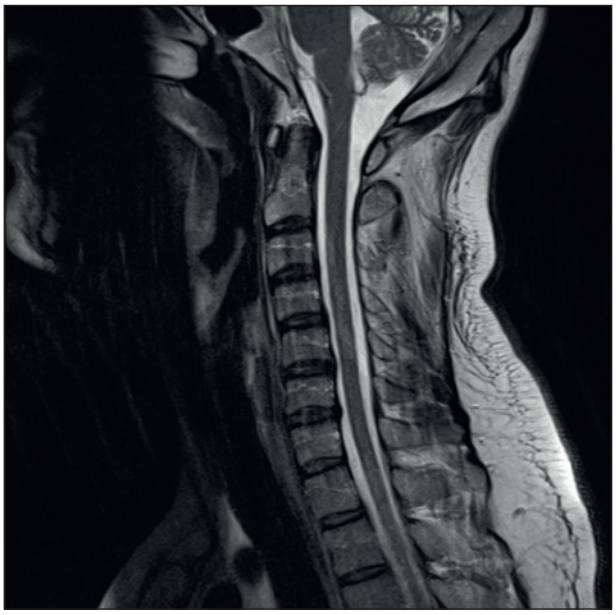

Figure 3. MRI of the cervical spine.

Discussion

We present the case of a Bosnian patient who developed ALS symptoms five months after MG. Diagnosis of MG was based on elevated titers of anti-AchR antibodies, positive edrophonium test, and decremental responses on a repetitive nerve stimulation test. We did not test for MuSK antibodies; however the coexisistence of AchR and MuSK antibodies is rare [6]. Diagnosis of ALS in our patient was based on clinical and neurophysiological findings: upper motor neuron signs in the lumbar region, lower motor neuron signs in the bulbar and cervical regions, generalized fasciculations and muscle atrophy and progressive asymetric muscle weakness together with active and chronic denervation in the cervical and lumbosacral region determined by electromyoneurography. It has been suggested that autoimmune diseases, including MG, are associated with a small but increased risk for ALS [7]. The prevalence of MG and ALS are 11.8 [8] and 7-11 [9] cases per 100.000 people, respectively. Therefore, co-occurences of MG and ALS are extremely rare. Males were affected twice compared with females, which might reflect a higher incidence of ALS in the male population [3]. The onset period between MG and ALS is variable, ranging from 3 months to 41 years [3,4]. Despite of their rarety, co-occurence of these two diseases have been presented in several case reports. The cases can be divided into two groups: first group in which MG patients developed ALS symptoms, and second where ALS patients developed myasthenic symptoms. Naik et al reported the development of ALS in a patient with established seropositive MG, 38 years after the onset [10]. Sawicka et al. showed the case of ALS that developed 3 months after thymectomy in a patient wih MG [11]. Virmot et al. investigated if muscle dynein is involved in neuromuscular junction (NMJ) formation and in ALS. They found that the overall muscle differentiation process and differentiation of the post-synapse and the maintenance of NMJs are dependent on dynein. They conclude that the NMJ loss in ALS or in dynein-related neuromuscular disorders can be due in part to a defect in MuSK turnover at the NMJ [12]. We can conclude that clinicians should not exclude the involment of ALS when patients with MG show aggravated symptoms.

References

1. Palma E, Reyes-Ruiz JM, Lopergolo D, et al. Acetylcholine receptors from human muscle as pharmacological targets for ALS therapy. Proc Natl Acad Sci U S A 2016;113:3060-3065. https://doi.org/10.1073/pnas.1600251113
2. del Mar Amador M, Vandenberghe N, Berhoune N, et al. Unusual association of amyotrophic lateral sclerosis and myasthenia gravis: a dysregulation of the adaptive immune system? Neuromuscul Disord 2016;26:342-346. https://doi.org/10.1016/j.nmd.2016.03.004
3. Tai H, Cui L, Guan Y, et al. Amyotrophic lateral sclerosis and myasthenia gravis overlap syndrome: a review of two cases and the associated literature. Front Neurol 2017;8:218. https://doi.org/10.3389/fneur.2017.00218
4. Yamashita S, Fujimoto A, Mori Y, et al. Coexistance of amyotrophic lateral sclerosis and myasthenia gravis. J Neuromuscul Dis 2014:1:111-115. PMID: 27858665
5. Ludolph A, Drory V, Hardiman O, et al. A revision of the El Escorial criteria, 2015. Amyotroph Lateral Scler Frototemporal Degener 2015;16:291-292. https://doi.org/10.3109/21678421.2015.1049183
6. Ohta K, Shigemoto K, Kubo S, et al. MuSK antibodies in AchR Ab-seropositive MG vs AchR Ab-seronegative MG. Neurology 2004;62:2132-2133. https://doi.org/10.1212/01.wnl.0000129274.12702.92
7. Turner MR, Goldacre R, Ramagopalan S, et al. Autoimmune disease preceding amyotrophic lateral sclerosis: an epidemiological study. Neurology 2013;81:1222-1225. https://doi.org/10.1212/WNL.0b013e3182a6cc13
8. Murai H, Yamashita N, Watanabe M, et al. Characteristics of myasthenia gravis according to onset-age: Japanese nationwide survey. J Neurol Sci 2011;305:97-102. https://doi.org/10.1016/j.jns.2011.03.004
9. Atsuta N, Watanabe H, Ito M, et al. Age of onset influences on wide-ranged clinical features of sporadic amyotrophic lateral sclerosis. J Neurol Sci 2009;276:163-169. https://doi.org/10.1016/j.jns.2008.09.024
10. Naik KR, Saroja AO, Mahajan M. Unusual occurance of amyotrophic lateral sclerosis in myasthenia gravis. Amyotrophic Lateral Sclerosis 2012;13:477-478. https://doi.org/10.3109/17482968.2012.711836
11. Sawicka E, Bojakowski J. Syndrome of amyotrophic lateral sclerosis after thymectomy perfomed for myasthenic syndrome. Neurol Neurochir Pol 1985;19:43-47. PMID: 4022238
12. Vilmont V, Cadot B, Vezin E, et al. Dynein disruption perturbs post-synaptic components and contributes to impaired MuSK clustering at the NMJ: implication in ALS. Sci Rep 2016;6:27804.