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Letter to the Editor

Coexistence of Amyotrophic Lateral Sclerosis and Myasthenia Gravis

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We read with interest Wang *et al*.'s article about a case series of five Chinese patients (patient-1: 62yo male, patient-2; 56yo male, patient-3: 71yo female, patient-4: 58yo male, patient-5: 47yo male) diagnosed with the double trouble sporadic amyotrophic lateral sclerosis (sALS) and myasthenia gravis (MG) [1]. In two patients (patient-1, patient-5) the ALS occurred before the onset of MG. In two patients (patient-2, patient-3) the MG initially manifested itself with bulbar symptoms [1]. Only three patients (patient-2, patient-3, patient-4) were positive for acetyl-choline receptor antibodies (AchR-abs) [1]. All five patients responded positively to cholineesterase inhibitors, but only four patients received immunosuppressive treatment [1]. The study is excellent, but some points need discussion.

The first point is that AchR-abs were negative in patient-3 and patient-5 [1]. In seronegative MG, differential diagnoses mimicking ALS and MG should be thoroughly excluded. One of these differential diagnoses is a paraneoplastic syndrome. In particular, in patient-5 who had a transient response to intravenous immunoglobulins (IVIG), it is imperative to rule out an occult neoplasm. Has the patient undergone screening for malignant neoplasms? Additional differential diagnoses that must be ruled out in patient-3 and patient-5 include myasthenic syndrome, mitochondrial disorder, beta-oxidation defect, congenital myasthenic syndrome, and myotonic dystrophy. Did patient-3 and patient-5 undergo single-fiber EMG to document increased jitter or number of blocks? Were patient-3 and patient-5 subjected to high-frequency repetitive nerve stimulation to document an increment?

A second point is that the El Escorial criteria were used to diagnose ALS in patient-1 [1]. Since the introduction of the El Escorial criteria, several revisions have been published, such as the revised El Escorial criteria and the Awaji Shima criteria. Currently, the Gold Coast criteria are generally recommended for diagnosing ALS [2]. We should know whether patient-1 also met these criteria or not. We should also know what criteria were used to diagnose ALS in the other four patients.

A third point is that in patient-2 who received tacrolimus for MG, side effects of this medication were not sufficiently ruled out. Tacrolimus has been reported to be complicated by muscle cramps, muscle weakness, and myopathy [3]. We should know what dosage of tacrolimus the patient received for MG and whether he had renal or liver insufficiency.

A fourth point is that family history was not reported for any of the patients [1]. Particularly in patient-3 and patient-5 with seronegative MG it is important to report whether any of the first-degree relatives suffered from a neuromuscular disorder.

A fifth point is that patient-3 did not receive immunosuppressive treatment. Since she was diagnosed with seronegative MG and responded positively to acetylcholine-esterase inhibitors, it might have been prudent to try immunosuppression. What was the reason for not using such therapy?

A sixth point is that no long-term results have been reported. Knowing the long-term outcome is crucial as progression was noted in all five patients.

A seventh point is that none of the five patients had a chest CT performed to determine whether there was an indication for thymectomy due to thymic hyperplasia or thymoma, which represents a real option of MG therapy, especially in patients under 60 years of age.

An eight point is that the speculation presented in the introduction that ALS is an immunological disease, is not sufficiently supported in the literature. To date, there is limited evidence that immunological processes play a primary role in the pathophysiology of ALS [4]. A strong argument against this speculation is that immunosuppressive treatment is ineffective in ALS.

Some other points should be clarified. Patient-3 had peripheral facial nerve palsy, which is neither a proven manifestation of ALS nor MG. What is the cause of peripheral facial palsy in patient-3? Were AchR-abds repeatedly determined in patient-1, patient-2 and patient-4? Were the antibodies still elevated at follow-up? Both examinations, the measurement of antibody level

and the repetitive nerve stimulation, do not have 100% sensitivity [5]. Was this taken into account in the analysis? Did patient-4 die from ALS, MG, or both?

In summary, the excellent study has limitations that should be addressed before final conclusions are drawn. Clarifying the weaknesses would strengthen the conclusions and improve the study.

Keywords: Amyotrophic Lateral Sclerosis, Myasthenia Gravis

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