Myasthenia gravis in secondary progressive multiple sclerosis: an underestimated comorbidity?

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Introduction

The co-occurrence of Myasthenia Gravis (MG) and Multiple Sclerosis (MS) is rarely observed, and epidemiological studies for such comorbidity are scarce. One meta-analysis [1] found only one study showing higher prevalence of MG/MS (291/100000), compared to the prevalence of MG in the general population 5-15/100000.[2] More than 50% of the described cases affected by both MS and MG lack of significant biomarkers for MG.

Here we report on a case of a female patient affected by Secondary Progressive (SP)MS and in treatment with beta-interferon, who developed severe MG.

Case Report

A 48 year-old woman, affected since 15 years by secondary progressive (SP)MS, had never presented optic or brainstem symptoms over the course of the disease and showed EDSS 6 in the last five years, under beta-interferon 1b. **(Figure 1)**

In November 2016, beside upper limb strength worsening, she started to complain about dysphagia for fluids, and dysphonia. Unexpectedly, marked bilateral ptosis was observed.

In suspicion of MS relapse, high dosage steroid was administered, but a deterioration appeared, with complete dysphagia, aphonia and severe dyspnoea, requiring tracheal intubation.

At the electromyography (EMG), abnormal decrements to repetitive stimulation (around 20% reduction of CMAP amplitude at 2 Hz stimulation rate) were demonstrated, together with positive assay for anti Acetylcholine Receptor (AChR) antibodies (titre 5,2 pmol/ml). No thymic enlargement was detected at Computed Tomography (CT) scan. Neoplastic staging was also performed, due to a previous history of breast carcinoma, without detection of secondary lesions.

According to these results and to the absence of significant new lesions at brain MRI which could explain brainstem symptoms, the diagnosis of MG was made (type IVB according to the Osserman classification,[4] rapidly evolving to V).

In addition to piridostigmine and oral prednisone taper, the patient underwent to six courses of plasma exchange (PLEX) with ptosis improvement. intravenous immunoglobulins (IVIg) 0.4 g/Kg/daily for 5 days were administered immediately after, persisting bulbar signs and upper limbs hyposthenia, with marked and progressive improvement, although respiratory aid for the following two months was maintained.

Since March 2017, the clinical picture has been characterized by the previous known symptoms and signs compatible with SPMS and Azathioprine was chosen as treatment.

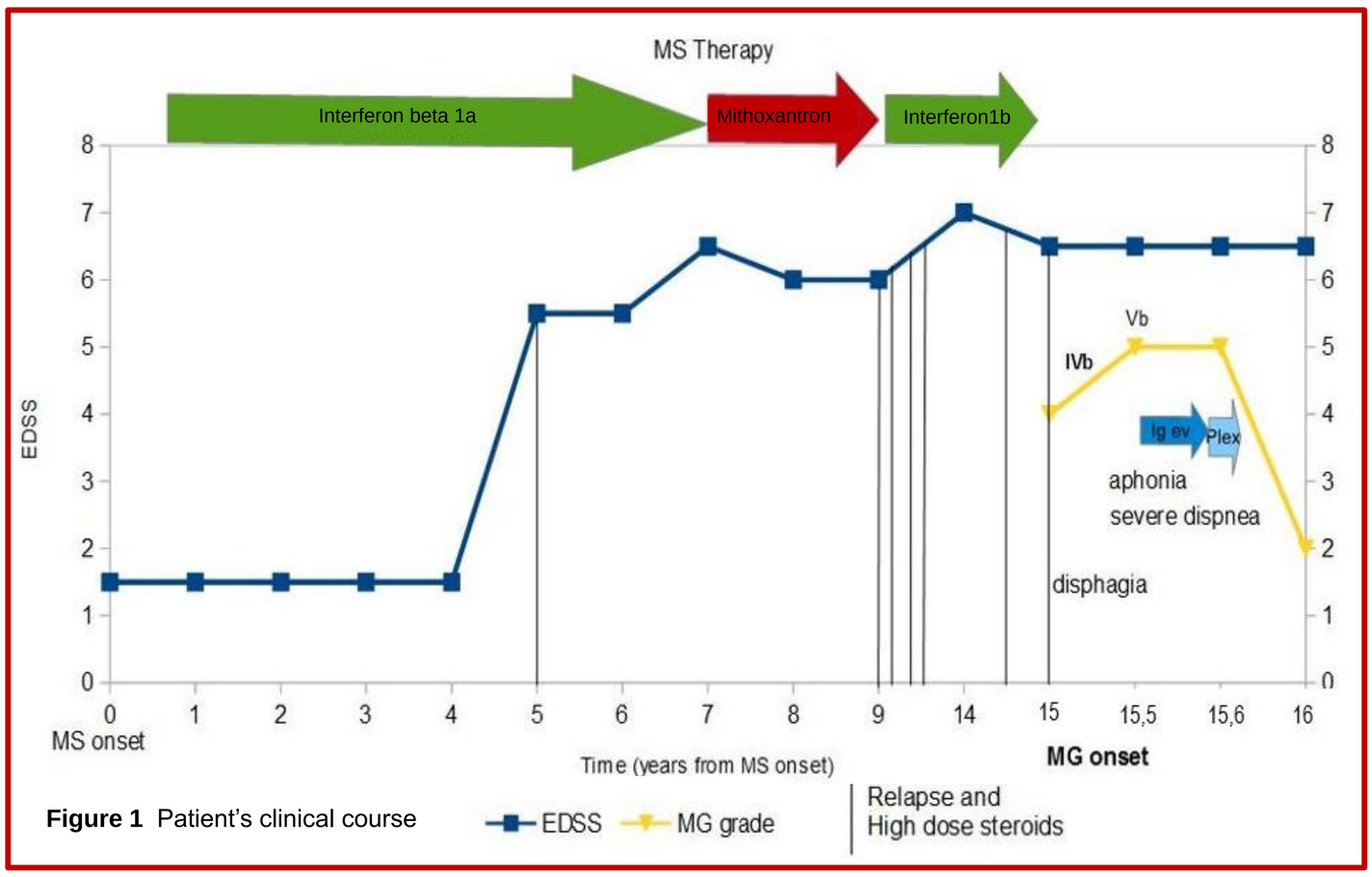

Figure 1 Patient's clinical course

AChR Ab	Pos - titre 5,2 pmol/ml
EMG repetitive stimulation	around 20% reduction of CMAP amplitude at 2 Hz stimulation rate
Thymic enlargement	No
Onset MG symptoms	bulbar
MG grade	IVb-V

Table 1 biomarkers and MG clinical features in our case

Discussion

Myasthenia gravis and MS are both autoimmune disorders, but with different target tissues, MS involving the myelin sheath while MG the neuro-muscular junction.

There are some shared features between MS and MG, such age and sex distribution, and associations with HLA types (DR3, B8, A1, and A2).[9] Both cell-mediated and humoral autoimmunity play a role in the pathogenesis of these two diseases.

Epidemiological data about MS developing MG during the primary disease or the contrary are still not exhaustive in terms of real incidence, time of onset, severity of the diseases and biological and instrumental markers. The clinical course of both MS and MG seems to be mild in most patients described, with some exception.[6]

Notably, in the case we described, MG started 15 years after MS onset, when the course of the disease was progressive. The clinical MG diagnosed in our patient was type IVb, rapidly evolving to V [4], with significant decrements to repetitive stimulation EMG and positive assay for AChR antibodies.

The patient had been treated with Beta interferon for a long time which can slip the immunity towards T-helper II predominant pathways and thus raise the susceptibility to autoantibody-mediated disorders.[8,9]

Conclusion

- ❖ We reported a case of a female patient affected by Secondary Progressive (SP)MS and in treatment with beta-interferon, who developed severe MG
- ❖ In contrast to other cases described,[3,6,7] our diagnosis of MG is more specific on the instrumental and lab point of view.
- ❖ Both MS and MG were severe and MG responded completely to treatments.

Conclusion

- ❖ Our case minds that association MG-MS should be investigated in cases of unusual brainstem signs, particularly without MRI strategic lesions and with worsening in steroid treatment.
- ❖ Such comorbidity is probably underestimated due to lack of studies and could be diagnosed in all MS subtypes, at any time during MS course and under exposition of immunomodulatory drugs such as beta -interferon.

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