Retrospective study of a cohort of 508 patients affected by myasthenia gravis: from diagnosis to management

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BACKGROUND

Myasthenia gravis (MG) is an autoimmune neuromuscular condition in which antibodies directed against neuromuscular junction targets cause symptoms of fatigable weakness[1]. Disease-modifying therapies for MG include chronic immunosuppression; exacerbations of MG often require plasma exchange or intravenous immunoglobulin (IVIg) [1]. The natural history of MG is unpredictable. In the first few years the disease course is worst, with subsequent gradual disease stabilization [2].

PATIENTS AND METHODS

We retrospectively evaluated 508 patients, aged from 12 to 95 years old, referred to our clinic from 1994 to 2014 and affected by MG.
- 418 patients: AChR abs positive (221 females and 197 males)
- onset: <40 years old in 118 patients
- 25 patients: antiMuSK abs positive (16 females and 9 males)
- 65 patients: seronegative (38 females and 27 males)

Atypical presentations of MG: 3 % of cases

Diagnosis: clinical evaluation, antibodies' dosage, neurophysiological analysis (SFEMG/RNS), thorax CT scan.

RESULTS

- Details about the different MG forms are reported in Tables 1 and 2.
- Triggers for relapses are reported in Table 3.
- 1 % of patients developed a recrudescence of thymoma, even 8 years later the extended thoracic surgery.
- Immunosuppressants drugs:
  - AZA : 65% of patients
  - CYCLOSPORIN : 4% of patients
  - RITUXIMAB: 1 % of patients

  Atypical phenotypes: 3%, as isolated distal upper limb muscles weakness at onset (Fig. 1 a); isolated weakness of the triceps brachii (Fig. 1 b); isolated peroneal muscle weakness (Fig. 1 c); MG involving upper limbs, associated to cervico-inflammatory myositis (Fig. 1 d).
- 44 patients had one or more pregnancies (see Table 4).
- 15% of remission, without treatment - symptomatic and/or immunosuppressive (all AChR positive or seronegative).

Table 1: AChR Abs positive and AChR and MuSK Abs negative MG patients

MG	Patients	Thymic surgery: hyperplasia/tymoma	Ab AChR + (pts)	Seronegative	Treatment
Type 1	110	8/2	61	49	PDN + AChEI
Type 2	305	98/62	295	10	PDN + AChEI + AZA/ cyclosporin
Type 2B	39	6/8	33	6	PDN + AChEI + AZA/ cyclosporin +IgG i.v./Pheresis
Type 3A	16	5/3	16	0	PDN + AZA/cyclosporin +IgG i.v./Pheresis
Type 3B	8	3/3	8	0	PDN + AZA/cyclosporin +IgG i.v./Pheresis
Type 4	3	0/0	3	0	PDN + AZA/cyclosporin +IgG i.v./Pheresis
Type 5	2	0/1	2	0	PDN + AZA/cyclosporin +IgG i.v./Pheresis + intubation

Table 2: MuSK Abs positive MG patients

MGAb MuSK +	Patients	Thymic pathology	Treatment
Type 1	3	-	PDN + AZA
Type 2A	8	-	PDN + AZA/cyclosporin/ IgG i.v./ Pheresis/rituximab
Type 2B	10	-	PDN + AZA/cyclosporin/ IgG i.v./ Pheresis/rituximab
Type 3A	3	-	PDN + AZA/cyclosporin/ IgG i.v./ Pheresis/rituximab
Type 5	1	-	PDN + AZA/cyclosporin/ IgG i.v./ Pheresis/rituximab

Table 3: Triggers for relapses

Triggers for relapses	%
Antibiotics – Quinolones (ciprofloxacin, levofloxacin..)	4%
Puerperium	2%
Immunosuppressants' reduction	13 %
Emotional stress (bereavement, divorces)	1%

Table 4: Pregnancies and MG

Pregnancies	Ab AChR + MG	Ab MuSK+ MG
N. of patients	42	2
Transient MG neonatal form	3	-
% of worsening in puerperium	3	1
% of pts on AZA	26	-
Worsening with AZA	-	-

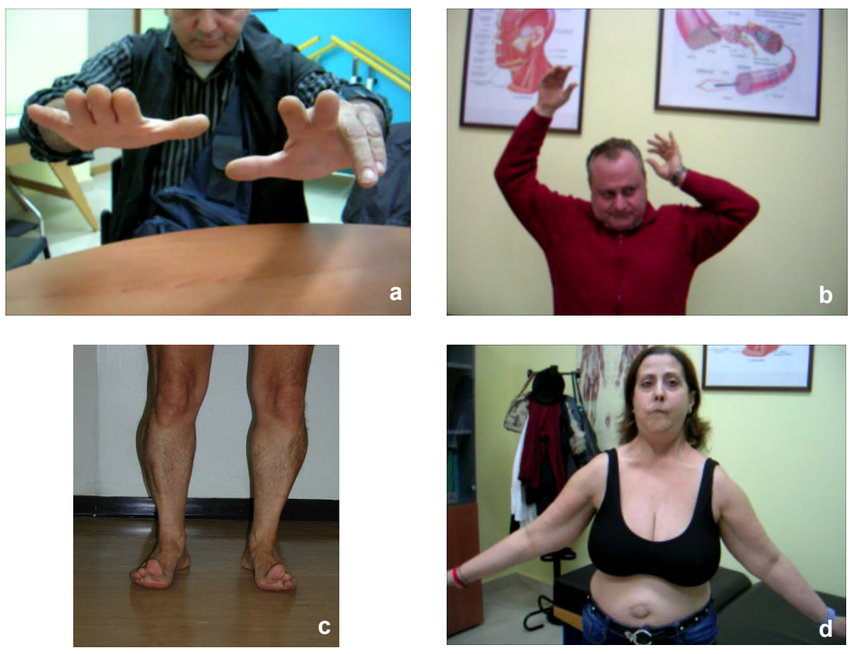

Fig. 1 - atypical MG phenotypes: a) isolated distal upper limbs muscle weakness at the onset; b) isolated weakness of the triceps brachii; c) isolated peroneal muscle weakness; d) MG involving the arms associated to a cervico-inflammatory myositis

CONCLUSIONS

- Despite of MG diagnosis is usually confortable, in some cases it could be difficult, especially when oculo-bulbar muscles are spared, and the main symptoms consist of muscles weakness and excessive fatigability in atypical sites. Electrophysiological studies must include SFEMG and RNS, that should be performed on the involved muscles.
- In our cohort, the risk of exacerbations was unpredictable and it occurred after prolonged clinical quiescence, often related to the reduction of immunosuppression. Triggers for MG were treatment with antibiotics (>> Quinolones - ciprofloxacin, levofloxacin...), puerperium, immunosuppressants' reduction, emotional stress (bereavement, divorces)
- Treatment for MG included symptomatic and/or immunosuppressive medications, such as AChEI, steroids, AZA, cyclosporin, IgG iv, pheresis and rituximab. We also confirm the stabilizing role of the thymectomy in patients with a generalized MG form, if performed within the first years from onset.
- There were no reported side effects induced by AZA during pregnancy and no fetal malformations. AZA remains the immunosuppressant of first choice; the percentage of non-responders cases to AZA is, in our cohort, 5% (all MuSK+ MG). Rituximab is a useful therapy for refractory MG forms.

REFERENCES

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