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CLINICAL CHARACTERISTICS AND TREATMENT MANAGEMENT IN SERONEGATIVE MYASTHENIA GRAVIS: A SYSTEMATIC REVIEW OF THE LITERATURE

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BACKGROUND

Seronegative myasthenia gravis (SNMG) usually refers to MG cases lacking detectable AChR and MuSK antibodies using standard assays.

The clinical presentation is typically heterogeneous, and there aren't currently standardized diagnostic or treatment guidelines.

AIM: to define clinical characteristics, diagnostic strategies, treatment management and disease outcomes of SNMG patients

METHODS

Selection Criteria: Original English-language articles published between 2001 and June 2024 with 2 core criteria and at least 1 ancillary criterion:

Core criteria

1. Clinical findings consistent with Myasthenia Gravis.
2. undetectable anti-AChR and anti-MuSK antibodies (dSNMG) OR undetectable anti-AChR, anti-MuSK and anti-LRP4 antibodies (tSNMG) tested by the best available assay in each study analyzed.

Ancillary criteria

1. Findings consistent with MG on ENMG.
2. response to pharmacological testing (edrophonium or neostigmine test).
3. clinical response to therapeutic anticholinesterase inhibitor drugs.
4. clinical response to immunotherapy.

31 studies included

RESULTS

Clinical Characteristics

A total of 712 patients with seronegative myasthenia gravis (SNMG) were included.

Female to male ratio: 2:1

Mean age at onset: 42 years (range 2-83 years)

Diagnostic Criteria

The testing method for anti-AChR and anti-MuSK antibodies was specified in 448/712 (63%) patients: all tested negative by RIA, and only 213/712 (30%) were additionally tested and confirmed negative by live CBA.

Anti-LRP4 antibodies were tested and found negative in 288/712 (40%) patients.

Figure 1: MGFA classification at disease onset of SNMG patients

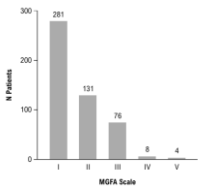
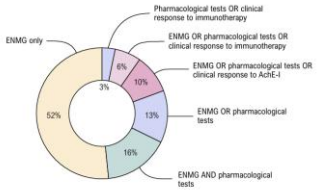


Figure 2: Ancillary Criteria used for the diagnosis of SNMG



Abbreviations: AChE- I = Acetylcholinesterase inhibitor; ENMG = Electroneuromyography;

Immunotherapy and outcome of SNMG patients.

Of 333 patients, 271 (81%) underwent immunotherapy, varying in the number of agents administered (A). Clinical outcome data were available for 394 SNMG patients. According to MGFA-PIS, 249/394 (63%) patients achieved a favourable outcome defined as "Improved or Better" (B). Among the 220 patients with follow-up and treatment data, 52/220 (24%) were treatment-refractory[1,2] . Clinical outcome data were avaiable in 42 of these refractory SNMG patients, according to three different types of immunotherapies (n =16 RTX; n = 16 EFG; n = 10 CNI) (C).

Abbreviations: CNI=calcineurin; EFG=Efgartigimod; MGFA – PIS = Myasthenia Gravis Foundation of America – Post Intervention Status; NSIST = non-steroidal immunosuppressive therapy; RTX= rituximab; SNMG = Seronegative Myasthenia Gravis.

CONCLUSIONS

SNMG is confirmed to have an early onset of disease compared to seropositive MG. However, the majority of patients required immunotherapy, with the outcome rates that were less favourable and a higher proportion for treatment-refractory MG patients when compared to the rates generally reported in AchR+ MG.

Furthermore, this systematic review highlights the substantial heterogeneity in the diagnostic management of SNMG in current clinical practice. The lack of standardized diagnostic criteria not only limits comparability between cohorts but raises a significant concern regarding potential misdiagnosis and the possibility of overtreatment.

Our findings underscore the urgent need for standardized diagnostic criteria incorporating high-sensitive serological and neurophysiological tools, as well as for prospective studies to clarify the immunopathogenesis and optimal management of these patients.

REFERENCES

1. Narayanaswami P, Sanders DB, Wolfe G, Benatar M, Cea G, Evoli A, et al. International Consensus Guidance for Management of Myasthenia Gravis. Neurology: 2021;96:114–122.
2. Mantegazza R, Antozzi C. When myasthenia gravis is deemed refractory: clinical signposts and treatment strategies. Ther Adv Neurol Disord: 2018;11:1756285617749134..

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