

# MuSK Antibody-Positive Myasthenia Gravis With An Overlapping Systemic Lupus Erythematosus

## *Miastenia Gravis Positiva para Anticuerpos MuSK con Lupus Eritematoso Sistémico Superpuesto*

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### Abstract

Since 1961, the overlap between myasthenia gravis (MG) and systemic lupus erythematosus (SLE) has been increasingly recognized, with MG patients facing up to 13 times the risk of developing SLE, especially after thymectomy, predominantly in young women. Thymic B cells may play a role in MG and SLE, as shown in animal models. MG often coexists with family histories of autoimmune diseases, sharing genetic risk factors with SLE, as supported by genome-wide studies. Patients with both conditions also experience higher rates of other autoimmune diseases, suggesting a potential for broader autoimmunity. Early-onset MuSK-MG strengthens this observed connection.

**Keywords:** MuSK myasthenia gravis, systemic lupus erythematosus, autoimmunity

### Resumen

Desde 1961, se ha reconocido cada vez más la superposición entre la miastenia gravis (MG) y el lupus eritematoso sistémico (LES), con pacientes con MG que enfrentan hasta 13 veces más riesgo de desarrollar LES, especialmente después de la timectomía, predominantemente en mujeres jóvenes. Las células B tímicas pueden desempeñar un papel en la MG y el LES, como se ha demostrado en modelos animales. La MG a menudo coexiste con antecedentes familiares de enfermedades autoinmunes, compartiendo factores de riesgo genéticos con el LES, como lo respaldan los estudios de genoma completo. Los pacientes con ambas afecciones también experimentan tasas más altas de otras enfermedades autoinmunes, lo que sugiere un potencial para una autoinmunidad más amplia. La MG con anticuerpos anti-MuSK de inicio temprano refuerza esta conexión observada.

**Palabras clave:** Miastenia gravis MuSK, lupus eritematoso sistémico, autoinmunidad

Rev. Ecuat. Neurol. Vol. 35, N° 2, 2026

### Introduction

Myasthenia gravis (MG) is an autoimmune disease that affects the postsynaptic membrane at the neuromuscular junction caused by antibodies against the acetylcholine receptor (AChR), muscle-specific kinase (MuSK) or other AChR-related proteins in the postsynaptic muscle membrane, localized or general muscle weakness is the predominant symptom and is induced by the antibodies.<sup>1</sup> On the other hand, systemic lupus erythematosus (SLE) is an autoimmune connective-tissue disorder due to the production of antibodies, the deposit of immune complexes and the activation of the complement cascade, leading to multiple organ damage.<sup>2</sup>

Autoimmune diseases occur together more commonly than expected by chance alone, the frequency with which MG and SLE coexist is variable and reported rates of incidence run from 3.78% of patients with SLE, up to 7.7% with a higher prevalence among women.<sup>3</sup> This phenomenon in which two or more autoimmune diseases present in a single individual is defined as polyimmunity,<sup>4</sup> herein we present the case of a patient with the coexistence of MuSK-MG and SLE.

### Clinical case

A 23-year-old woman presented to the Emergency department with symptoms that evolved over 5 months,

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with dysphagia, horizontal and vertical diplopia especially with distance vision, dysphonia that gets worse when talking too much, and weakness in all 4 limbs that appears worse at the end of the day and limits daily activities. From that time being she also refers weight loss, pruritic maculopapular rash on palms and trunk, painful ulcerative lesions in oral region, abundant hair loss, mechanical joint pain predominantly in hands, knees and ankles that is exacerbated by movement, xerophthalmia and xerostomia. She had intracranial idiopathic hypertension currently on acetazolamide.

Neurologic examination revealed bilateral ophthalmoparesis with subtle eyelid ptosis, without curtain sign or ice pack test, dysphonia, and fluctuating proximal weakness in 4 limbs and positive fatigability test. A comprehensive investigation revealed mild lymphopenia and anemia, normal creatine kinase, proteinuria, antinuclear antibodies positive 1:1280, and hypocomplementemia, with normal thyroid function, HIV was negative; CSF studies were normal, and MRI brain showed no signs of abnormality. Electromyography (EMG) with single-fiber and repetitive stimulation tests were unrevealing. Serum antibodies against muscle-specific kinase confirmed the diagnosis of MuSK MG associated with SLE, and immunotherapy with systemic corticosteroid was initiated. She was discharged with immunomodulatory treatment with a corticoid, azathioprine and an antimalarial drug, together with symptomatic treatment with pyridostigmine.

### Discussion

Since MG-SLE overlap was first reported in 1961<sup>5</sup> its association has been more common than previously thought with up to 13-fold increased risk for diagnosis of SLE in patients with MG compared to patients without MG, and even higher among MG patients who had undergone a thymectomy,<sup>6</sup> with a predominance in young females as the majority of autoimmune diseases.<sup>7</sup> The pathophysiological mechanism by which thymectomy predisposes to autoimmune disease have not been established, however, it seems plausible that thymic B cells play a role in MG and SLE,<sup>8,9</sup> as some data has demonstrated in murine models of type 1 diabetes<sup>10</sup> and lupus.<sup>11</sup>

Patients with MG are more likely to have a family history of autoimmune diseases, suggesting that the disease may well share a genetic basis with other autoimmune diseases and consequent shared pathobiological disease mechanisms.<sup>12</sup> That being the case MG is observed in the first-degree relatives of SLE patients nearly three times more often than in patients without the disease.<sup>13</sup> Furthermore, several shared putative risk genes for MG and SLE have been found when comparing associated single nucleotide polymorphisms (SNPs) in genome-wide association studies (GWAS), association that has been supported by Mendelian randomization.<sup>6</sup>

An increased incidence of other autoimmune diseases has also been found among patients with MG and SLE, diseases like autoimmune thyroid disease, autoimmune hemolytic anemia, rheumatoid arthritis, and ankylosing spondylitis are more common than in the general population.<sup>14</sup> This association to both organ specific as well as a systemic autoimmune disease may constitute a form of polyglandular autoimmunity that has not been previously recognized.<sup>6</sup>

MuSK-MG typically has an early age of onset and rarely occurs after 60 years of age<sup>15</sup> which reinforces the association between SLE and the early onset MG over the late onset MG, furthermore the typical course of MuSK-MG demonstrates acute onset, with rapid progression within a few weeks,<sup>16</sup> with craniobulbar muscle involvement, however, its clinical spectrum also includes a syndrome of fatigable generalized weakness closely resembling acetylcholine receptor-MG.<sup>17</sup>

### Conclusion

The co-existence of MG and SLE represents a clinical challenge due to the possible differential diagnoses that may be involved, even though it is not common for these diseases to present together, it is important to assess for MG should be considered in SLE patients with unexplained muscular weakness and fatigability, and among patients with both SLE and MG, there should be careful vigilance for additional autoimmune diseases.

### References

1. Gilhus NE, Tzartos S, Evoli A, Palace J, Burns TM, Verschuuren J, et al. Myasthenia gravis. *Nat Rev Dis Primers*. 2019;5:30. <https://doi.org/10.1038/s41572-019-0079-y>.
2. D'Cruz DP, Khamashta MA, Hughes GR. Systemic lupus erythematosus. *Lancet*. 2007;369:587-596. [https://doi.org/10.1016/S0140-6736\(07\)60279-7](https://doi.org/10.1016/S0140-6736(07)60279-7).
3. Bekircan-Kurt CE, Tuncer Kurne A, Erdem-Ozdamar S, Kalyoncu U, Karabudak R, et al. The course of myasthenia gravis with systemic lupus erythematosus. *Eur Neurol*. 2014;72:326-329. <https://doi.org/10.1159/000365568>.
4. Rojas-Villarraga A, Amaya-Amaya J, Rodriguez-Rodriguez A, Mantilla RD, Anaya JM. Introducing polyautoimmunity: secondary autoimmune diseases no longer exist. *Autoimmune Dis*. 2012;2012:254319. <https://doi.org/10.1155/2012/254319>.
5. Isaacs P. Myasthenia with systemic lupus and palmo-plantar keratosis. *Br Med J*. 1971;4(5783):339-340. <https://doi.org/10.1136/bmj.4.5783.339>.
6. Igoe A, Merjanah S, Harley ITW, Clark DH, Sun C, Kaufman KM, et al. Association between systemic lupus erythematosus and myasthenia gravis: a population-based national study. *Clin Immunol*. 2024;260:109810. <https://doi.org/10.1016/j.clim.2024.109810>.

- clim.2023.109810.
7. Bekircan-Kurt CE, Tuncer Kurne A, Erdem-Ozdamar S, Kalyoncu U, Karabudak R, et al. The course of myasthenia gravis with systemic lupus erythematosus. *Eur Neurol.* 2014;72(5-6):326-329. <https://doi.org/10.1159/000365568>.
  8. Christensson B, Biberfeld P, Matell G. B-cell compartment in the thymus of patients with myasthenia gravis and control subjects. *Ann N Y Acad Sci.* 1988;540:293-297. <https://doi.org/10.1111/j.1749-6632.1988.tb27079.x>.
  9. Mackay IR, Masel M, Burnet FM. Thymic abnormality in systemic lupus erythematosus. *Australas Ann Med.* 1964;13:5-14. <https://doi.org/10.1111/imj.1964.13.1.5>.
  10. Greaves RB, Chen D, Green EA. Thymic B cells as a new player in the type 1 diabetes response. *Front Immunol.* 2021;12:772017. <https://doi.org/10.3389/fimmu.2021.772017>.
  11. Hidalgo Y, Nunez S, Fuenzalida MJ, Flores-Santibanez F, Saez PJ, Dorner J, et al. Thymic B cells promote germinal center-like structures and the expansion of follicular helper T cells in lupus-prone mice. *Front Immunol.* 2020;11:696. <https://doi.org/10.3389/fimmu.2020.00696>.
  12. Green JD, Barohn RJ, Bartoccioni E, Benatar M, Blackmore D, Chaudhry V, et al. Epidemiological evidence for a hereditary contribution to myasthenia gravis: a retrospective cohort study of patients from North America. *BMJ Open.* 2020;10(9):e037909. <https://doi.org/10.1136/bmjopen-2020-037909>.
  13. Kuo CF, Grainge MJ, Valdes AM, See LC, Luo SF, Yu KH, et al. Familial aggregation of systemic lupus erythematosus and coaggregation of autoimmune diseases in affected families. *JAMA Intern Med.* 2015;175(9):1518-1526. <https://doi.org/10.1001/jamainternmed.2015.3528>.
  14. Thorlacius S, Aarli JA, Riise T, Matre R, Johnsen HJ. Associated disorders in myasthenia gravis: autoimmune diseases and their relation to thymectomy. *Acta Neurol Scand.* 1989;80(4):290-295. <https://doi.org/10.1111/j.1600-0404.1989.tb03881.x>.
  15. Sanders DB, El-Salem K, Massey JM, McConville J, Vincent A. Clinical aspects of MuSK antibody positive seronegative myasthenia gravis. *Neurology.* 2003;60(12):1978-1980. <https://doi.org/10.1212/01.WNL.0000065882.63904.53>
  16. Guptill JT, Sanders DB, Evoli A. Anti-MuSK antibody myasthenia gravis: clinical findings and response to treatment in two large cohorts. *Muscle Nerve.* 2011;44(1):36-40. <https://doi.org/10.1002/mus.22006>.
  17. Evoli A, Tonali PA, Padua L, Lo Monaco M, Scuderi F, Batocchi AP, et al. Clinical correlates with anti-MuSK antibodies in generalized seronegative myasthenia gravis. *Brain.* 2003;126(Pt 10):2304-2311. <https://doi.org/10.1093/brain/awg223>.

**Conflict of interests:** *The authors have no conflict of interests to declare.*