studies performed immediately after admission enable early diagnosis and optimised management.

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Systemic lupus erythematosus in patients with myasthenia gravis undergoing thymectomy: report of 3 clinical cases☆

Lupus eritematoso sistémico postimectomía en pacientes con miastenia *gravis*: a propósito de tres casos clínicos

Dear Editor:

Myasthenia gravis (MG) is an autoimmune disease characterised by muscle fatigue, most frequently caused by anti-acetylcholine receptor (anti-AChR) antibodies that target the neuromuscular junction.[1] The thymus, a primary lymphoid organ playing a fundamental role in the maturation of T cells, is the main organ involved in the formation of anti-AChR antibodies.[2] Based on recent research findings, thymectomy is an active part of the treatment of MG, and is recommended for all generalised forms in patients aged up to 65 years.[3] However, the possible effects of this procedure on immunity are unknown. Cases have been published in recent years of patients presenting such other autoimmune diseases as systemic lupus erythematosus (SLE) following thymectomy[4,5]; it has been suggested that the procedure may trigger alterations in the immune system, although the precise mechanism is unclear. We present 3 new cases of patients who developed SLE (2012 international classification criteria) following thymectomy.

Patient 1 was a 26-year-old woman diagnosed in 2009 with ocular-bulbar MG (stage IIb, according to the Osserman classification), with compatible electromyography findings and anti-AChR antibodies. A chest MRI scan showed a lesion compatible with thymic remnant tissue. Thymectomy was performed in 2010; cytology findings were compatible with thymic hyperplasia. The patient attended follow-up consultations every 6 months, showing good progression. In early 2016, she reported the appearance of photosensitivity in

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the face and polyarthritis. An analytical study including a complete blood count and coagulation and biochemistry studies yielded normal results; a specific autoimmunity study returned positive results for antinuclear antibodies (1/640), anti-DNA antibodies (1/640), anticardiolipin antibodies, β_2 microglobulin, and lupus anticoagulant, and decreased complement levels. These findings were confirmed with a second study, leading to a diagnosis of antiphospholipid syndrome, and antiplatelet treatment was started. However, the patient also presented diagnostic criteria for SLE (meeting at least one clinical and 4 immunological criteria).

Patient 2 was a 42-year-old woman diagnosed in 2003 with generalised MG (stage IIb, according to the Osserman classification), with compatible electromyography findings, positive results for anti-AChR antibodies, and normal chest MRI findings. Thymectomy was performed in 2004; cytology findings were compatible with thymic hyperplasia. Progression was poor, with the patient presenting a myasthenic crisis requiring admission to the intensive care unit and treatment with mycophenolate. As the patient planned to become pregnant, this treatment was suspended 3 years later, with no clinical worsening. In 2011, she reported photosensitivity in the face and polyarthralgia. A general blood analysis revealed severe leukopaenia, and autoimmunity study results were positive for anti-AChR antibodies. After these findings, she was diagnosed with SLE as she met 2 clinical and 4 immunological criteria.

Patient 3 was a 45-year-old woman diagnosed with bulbar MG in 2012 (stage IIa, according to the Osserman classification) after a first caesarian section; she presented no electromyography alterations, but was positive for anti-AChR antibodies and chest MRI detected minimal thymic remnant tissue. Thymectomy was performed in 2014; cytology findings were compatible with thymic hyperplasia. Symptoms were stable at 3 years of follow-up, but she presented photosensitivity and polyarthritis in 2017. A complete blood count, biochemistry study, and coagulation study detected no pathological findings, but urine sediment testing detected proteinuria. An autoimmunity study detected antinuclear antibodies (1/640), anti-DNA antibodies, and anti-Ro antibodies at very high titres. The patient met 2 clinical and 3 immunological criteria for SLE, and was diagnosed with the condition.

Approximately 5% of patients with MG present a second autoimmune disease, which represents a 13%—22% increase in risk with respect to the general population; the most frequent associations are hypothyroidism, rheumatoid arthritis, and diabetes mellitus.[6] According to some series, 1%—8% of patients with MG present SLE.[7] While it is not sufficient in itself, thymectomy has been proposed as a trigger factor for SLE, with onset occurring after a period ranging from 3 months to 19 years.[4] The pathogenic mechanisms involved are unclear; the hypothesis is based on experimental studies of animal models, which have shown that performing the procedure in mice with immune alterations accelerated disease progression; when it was performed in neonatal animals and associated with administration of B-cell activators, animals developed a lupus-like disease.[8] Thymectomy has been shown to cause an imbalance in the regulatory activity of T cells due to a loss of central tolerance, which results in excessive antibody production. This process would be modulated by environmental factors.[9] It has been suggested that CXCL13, a common activator of B cells and T cells whose levels are elevated in patients with lupus nephritis and severe MG, may be involved in the copresence of both diseases.[10]

Given the possibility that thymectomy may occasionally cause dysregulation of lymphocytes, clinical and analytical monitoring of patients undergoing the procedure is needed to detect immunological disorders.

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