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Post-thymectomy myasthenia gravis 2 years after thymoma removal: a case report and literature review

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INTRODUCTION AND AIMS

Myasthenia Gravis (MG) is associated with thymoma in around 10-15% of the cases, its onset usually preceding thymoma diagnosis. A few patients **develop MG after thymectomy, a condition known as 'post-thymectomy myasthenia gravis (PTMG)'.** In this study we report **a case of post-thymectomy myasthenia gravis (PTMG) and the results of a literature review on the topic**.

RESULTS

Case report

- In 2022, a 74-year-old woman underwent radical thymectomy with wedge resection of the left upper lobe for a B1/B2 thymoma (Masaoka-Koga stage IIIA), followed by radiotherapy (60 Gy cranially and 52.8 Gy caudally, in a total of 30 sessions).
- **Despite being AChR Ab+ (4.33 nmol/L), she remained asymptomatic until >2 years later (810 days)**, when she developed MG with marked bulbar involvement (MGFA IIb). Chest CT ruled out thymoma recurrence.
- Initial therapy with pyridostigmine and azathioprine provided partial benefit, but azathioprine was discontinued due to side effects; other immunosuppressive drugs including steroids were contraindicated due to infectiology risk**,** so **efgartigimod was started** and induced **marked and sustained clinical improvement** for the following 5 months. (Fig.1A)
- While AChR Ab titres remained substantially stable (**5.34 nmol/L**) during the disease course, the degree of complement activation induced by patient serum against both AChR isoforms was higher at MG onset (T1) than at thymoma diagnosis (T0) (Fig.1B),

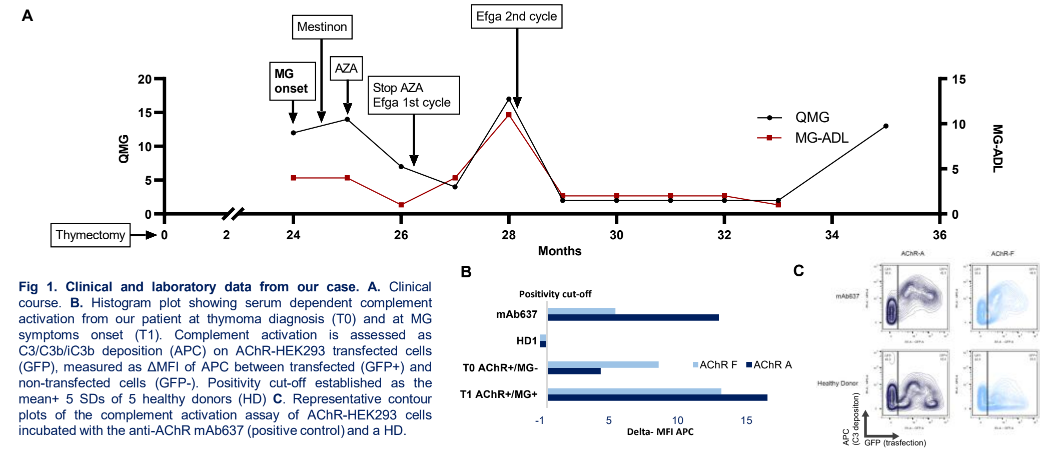

Fig 1. Clinical and laboratory data from our case. A. Clinical course. **B.** Histogram plot showing serum dependent complement activation from our patient at thymoma diagnosis (T0) and at MG symptoms onset (T1). Complement activation is assessed as C3/C3b/iC3b deposition (APC) on AChR-HEK293 transfected cells (GFP), measured as ΔMFI of APC between transfected (GFP+) and non-transfected cells (GFP-). Positivity cut-off established as the mean+ 5 SDs of 5 healthy donors (HD) **C**. Representative contour plots of the complement activation assay of AChR-HEK293 cells incubated with the anti-AChR mAb637 (positive control) and a HD.

Literature review

A literature review using PubMed and EMBASE identified 16 studies, comprising **1503 thymoma patients without preoperative MG**.

- **PTMG** developed in 57/1503 (**3.8%**) thymoma patients, between **3 days and 15 years** after surgery (median: 1.5 yrs). (Fig. 2A). M:F=1:1; mean age at onset: 51.3 yrs (range 23-82).
- AChR Ab testing before thymectomy was reported in 626/1503 (41.7%) patients**: 141/626 (22.5%) were AChR Ab+** (median value 5.44 nmol/L, range <0.3–54.2). (Fig.2B)
- **PTMG** developed in **32/141 (22.7%)** AChR Ab+ patients and **12/485 (1.9%)** AChR Ab- patients **(p<0.001, χ²test; OR=11.57, 95%CI 5.77-23.20).** (Fig.2C)
- **At the onset of PTMG, all patients were AChR Ab+** (median value 10 nmol/L, range 0.3–280), including those negative pre-thymectomy, with a significant increase in AChR Ab titres (p<0.0001, Fig.2D). Thymoma recurrence was detected at PTMG onset in 4/57 (7%) cases.

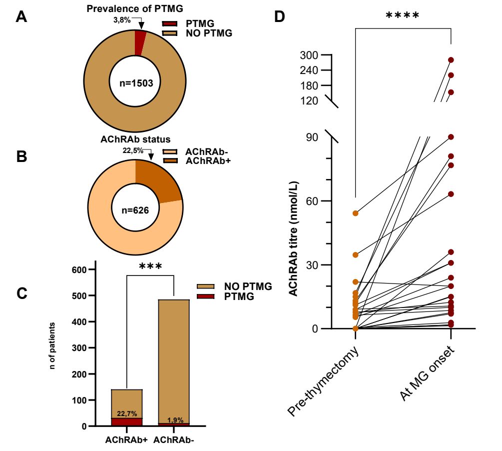

Fig.2 Results from the literature review. A. Frequency of PTMG among thymoma patients. **B**. Pre-thymectomy AChR Ab status of patients presenting without MG **C**. PTMG development based on AChR Ab status **D.** Comparison of AChR Ab titres (RIA) before thymectomy and at MG onset. ***=p<0.001, ****=p<0.0001

DISCUSSION AND CONCLUSIONS

- Based on the literature review, **AChR Ab+ pre-thymectomy was associated with higher risk of developing PTMG**, with antibody titers increasing at MG onset compared to pre-thymectomy. **Antibody testing should be performed in all patients** before thymectomy, including those without MG symptoms.
- In this case, **PTMG onset was associated with increased AChR Ab–mediated complement activation**. Complement activation assessment could represent a novel prognostic biomarker of PTMG, warranting systematic investigation in future studies.
- Further studies will clarify the changes in the antibody and B cell repertoire underlying PTMG development.

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