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CASE REPORT

Co-existence of Myasthenia Gravis and Addison's Disease Without Thymoma: A Case Report

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Abstract

INTRODUCTION: Myasthenia Gravis (MG) and Addison's Disease (AD) co-existing is very rare. The estimated prevalence of this co-occurrence is less than 1 in 100 000, underscoring its clinical significance. We present a female case with coexisting AD and MG. A 45-year-old female arrived at our clinic complaining of breathing difficulties for a month, a drooping left eyelid, and swallowing difficulties for 10 days. She has been treated with 5 mg/day prednisone for AD for three years. Long-term corticosteroid therapy may modulate immune responses and influence the timing of MG onset. Neurological evaluation revealed partial ptosis in the left eye and mild tetraparesis (4/5 strength).

CASE REPORT: Cortisol level was 0.8 µg/dL, and adrenocorticotropic hormone (ACTH) level was 987 ng/L, an adrenal crisis was excluded. The anti-acetylcholine receptor antibody (anti-AChR antibody) level was 8.37 nmol/L (> 0.4 nmol/L). Repetitive nerve stimulation, neostigmine, and Simpson tests were compatible with MG. Therefore, she was diagnosed with MG.

CONCLUSIONS: Acetylcholine antibodies in MG may indicate that other autoimmune diseases may be added to the clinic in these patients. Keeping in mind the presence of the underlying MG may be life-saving for those who do not react well to therapy or in the case of newly added findings in AD patients.

INTRODUCTION

Myasthenia gravis (MG) is associated with other autoimmune diseases. Large cohort studies suggest up to 15% of MG patients have at least one additional autoimmune endocrinopathy, most commonly thyroiditis (Zhu *et al.* 2003; Fichtner *et al.* 2020). We are presenting a very uncommon case of a female patient with MG and Addison’s Disease (AD) coexisting. This report aims to highlight potential shared immunopathogenic mechanisms and to review management considerations in dual autoimmune endocrine-neuromuscular syndromes.

CASE PRESENTATION

A 45-year-old female was brought into our clinic complaining of a drooping left eyelid, ten days of dysphagia and one month of dyspnea. Three years ago, She presented to the internal medicine department due to skin hyperpigmentation in the axillae and mucous membranes. Notably, she had no personal or family history of neuromuscular disorders or other autoimmune diseases. Laboratory analysis: adrenocorticotrophic hormone (ACTH): 803 ng/L (7.2-63.3), in the ACTH stimulation test, 0th minute = 3.02 ng/L, 30th minute = 4.57 ng/L, 60th minute = 3.25 ng/L; cortisol: 2 µg/dL (4.82-19.5), aldosterone: 3.7 ng/dL, Follicle-Stimulating Hormone:108 IU/L, Luteinizing hormone:55.6 IU/L. Adrenal imaging by CT showed bilateral adrenal atrophy without enlargement or nodularity, confirming autoimmune adrenalitis." She was diagnosed with AD; Fludrocortisone and prednisolone 5 mg/day were advised. Hydrocortisone dosing was adjusted to mimic diurnal cortisol rhythm, and patient education on adrenal crisis prevention was provided. Neurological examination revealed 4/5 tetraparesis and mild left eyelid ptosis. No bulbar muscle atrophy or fasciculations were observed, and cranial nerve examination was otherwise normal. The fatigue test was positive. Repetitive nerve stimulation at 3 Hz demonstrated a decremental response greater than 10%, supporting the diagnosis of MG. ACTH: was 987 ng/L and cortisol was 0.8 µg/dL. AD crisis was excluded. Anti-acetylcholine receptor antibody (anti-AChR antibody) was high at 8.37 nmol/L (> 0.4 nmol/L). She was diagnosed with MG, and pyridostigmine was started, and clinical symptoms resolved entirely. No thymic hyperplasia or thymoma was found. Chest MRI performed to rule out thymoma was unremarkable.

DISCUSSION

To our knowledge, fewer than 20 cases of MG co-occurring with AD have been described, with the majority involving thymoma. The existence of an adrenal–thymus axis has been proposed. Thymic hyperplasia was observed, improving response to ACTH and cortisone administration in animals with adrenalectomy. These animal studies suggest bidirectional crosstalk between the adrenal cortex and thymic immune microenvironment. Authors have shown that giving ACTH to MG patients reduces thymus volume (Dumas *et al.* 1985). Therefore, they proposed the existence of an adrenal-thymus axis. Clinically, this axis may explain why exogenous glucocorticoid therapy can induce thymic involution and transiently ameliorate MG symptoms. The coexistence of MG and AD might be explained by the adrenal-thymus axis. Dumas reported a male and a female patient with AD were subsequently found to have MG (Dumas *et al.* 1985). Conversely, Skedros (Skedros *et al.* 2011) and Seker (Seker *et al.* 2009) discussed the presence of MG, which manifests later in AD patients. A female MG patient was later reported to have developed AD (Okada *et al.* 1994). Most reported patients with AD and MG had coexisting thymomas, whereas our patient had no thymic hyperplasia or thymoma on chest MRI. Seker suggested that MG manifested following thymectomy and that thymoma may contribute to coexisting AD and MG (Seker *et al.* 2009). Additionally, other authors claimed that thymectomy in MG patients alters their immunological status and can lead to the development of other autoimmune disorders (Okada *et al.* 1994). High AChR titers were detected in all reported cases of MG-AD coexistence, similar to our case. The high levels of AChR autoantibodies in these reported cases suggested that they may be a sign of co-existing autoimmune disorders.

Recent studies demonstrate ectopic germinal center formation within the thymus as a site of AChR autoantibody generation. Elevated B-cell activating factor (BAFF) levels and dysregulated T follicular helper cells have been implicated in cross-organ autoimmunity, potentially linking adrenal insufficiency and neuromuscular autoimmunity (Chen *et al.* 2024).

B cells have an important role in autoantibody-mediated autoimmune diseases. B cells produce anti-AChR autoantibodies and contribute significantly to autoantigen presentation, proinflammatory cytokine production, T cell interaction via costimulatory molecule expression, and ectopic germinal center development in autoimmune disorders (Fichtner *et al.* 2020). Some autoimmune disorders, including those with distinct autoantibodies, chemokines, and cytokines, may be predisposed to by ectopic germinal centers. It seems possible that ectopic germinal centers have developed in MG patients with anti-AChR antibodies. Genetic studies in polygenic autoimmune syndromes reveal HLA-DRB1*04 predisposition in both MG and AD, suggesting shared antigen-presentation pathways (Kurian *et al.*2024; Lundtoft *et al.* 2023).

CONCLUSION

We presented a rare co-existing autoimmune AD with MG in a female patient. Despite being extremely uncommon, it is unclear if this link is a coincidence or represents a distinct syndrome. Prospective registries of autoimmune polyendocrine and neuromuscular disorders are needed to determine true incidence and causality. For individuals who do not respond well to treatment or in the event of recently discovered signs in the clinic in patients with identified autoimmune MG, determination of the existence of the underlying AD condition may be life-saving. The presence of acetylcholine receptor antibodies in MG patients may indicate ectopic germinal center activity, potentially contributing to the generation of additional autoantibodies and the development of further autoimmune disorders. Routine screening for adrenal autoantibodies

(21-hydroxylase) in MG patients with atypical fatigue or hyperpigmentation should be considered.

Further research is required to elucidate the immune mechanisms driving this autoimmune association, particularly those operating within ectopic germinal centers in patients with coexisting MG and AD. Understanding these pathways could inform the development of targeted immunomodulatory strategies aimed at regulating germinal center activity and preventing multi-organ autoimmunity.

Written informed consent was obtained from the patient.

FINANCIAL DISCLOSURE AND CONFLICT OF INTEREST FOR EACH AUTHOR

None.

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