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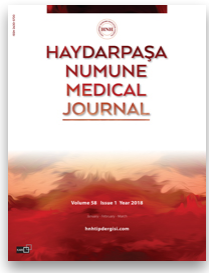

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ORIGINAL ARTICLE

Association of Myasthenia Gravis and Autoimmune Thyroid Disease

Gülbün Asuman Yüksel, Ceyhun Sayman, Hülya Tireli

Department of Neurology, Haydarpasa Numune Training and Research Hospital, Istanbul, Turkey

Abstract

Introduction: Autoimmune thyroid disease (AITD) frequently accompanies myasthenia gravis (MG). The aim of the present study was to evaluate the clinical and serological features of MG associated with AITD.

Methods: Thirty patients diagnosed with MG between 2012 and 2016 were followed. All patients' clinical and demographic features were analyzed, and acetylcholine receptor antibody (AChRAb) and antimicrosomal antibody were evaluated. There were 30 (21 female and nine male) patients suffering from MG. Age range was 13–78 years. Age range at disease onset was 11–75 years. Duration of disease range was 1–38 years.

Results: Of the 30 patients, 17 (56.7%) were positive for AChRAb, and 7 (23%) were positive for antimicrosomal antibody. Among 17 AChRAb (+) patients, both diagnoses of generalized (14/23 (60.9%)) and ocular (3/7 (42.9%)) myasthenia were present. Of the 17 AChRAb (+) patients, 6 were also positive for antimicrosomal antibody. All seven antimicrosomal antibody (+) patients had generalized myasthenia.

Discussion and Conclusion: It is really important to think coexisting MG in patients with autoimmune disorders and neuromuscular weakness. The presence of AChRAb in patients with MG is associated with a frequent risk for other autoimmune diseases.

Keywords: Acetylcholine receptor antibody; autoimmune thyroid disease; myasthenia gravis.

Myasthenia gravis (MG), an autoimmune neuromuscular disorder, the muscular weakness and fatigability that are the hallmarks of the disorder, is caused by antibodies directed against the nicotinic acetylcholine receptor (AChR) localized at the postsynaptic membrane of the cholinergic synapses [1]. Epidemiological, clinical, and serological studies have suggested that ocular MG (OMG) and generalized MG (GMG) may be separate diseases [2].

The relationship between MG and other autoimmune conditions is less clear. The association of MG with other autoimmune diseases sometimes occurs coincidentally. Approximately 13% of patients with MG reported other coexisted autoimmune diseases. Although the occurrence of conditions, such as autoimmune thyroid diseases (AITDs), appears to occur more frequently in patients with MG than in the general population, any association with acetylcholine receptor antibody (AChRAb) positivity is uncertain [3].

MG probably results from an autoimmune blockade or destruction of the receptor at the neuromuscular junction. The autoimmune attack appears to be performed by both an anti-AChR autoantibody and a cellular immune response to the receptor [4]. Further, many patients with MG show a clinical manifestation indicating extramuscular involvement. Most frequently affected is the thyroid gland. Thus,

Correspondence (İletişim): Ceyhun Sayman, M.D. Haydarpasa Numune Egitim ve Arastirma Hastanesi, Noroloji Anabilim Dali, İstanbul, Turkey
Phone (Telefon): +90 555 625 89 29 **E-mail (E-posta):** ceysayman@yahoo.com.tr

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MG may be associated with an AITD, including Grave's disease (GD) and chronic thyroiditis (Hashimoto, HT), based on the common immunological derangement [5,6].

The coexistence of thyroid disease and MG is not uncommon. Furthermore, a 4.2% incidence of HT and a 7.7% incidence of GD were reported [7].

The aim of the present study was to evaluate the clinical and serological features of MG associated with AITD.

Materials and Methods

Patients attending the neuromuscular disease outpatient clinic who were suffering from MG between 2012 and 2016 were included in the present study. Analysis of clinical and demographic features was made.

Tests for AChRAb and antimicrosomal antibody (anti-thyroid peroxidase (TPO)) had been requested in all patients.

Statistical Analysis

Statistical analyses were performed using the SPSS version 15 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used to present patient characteristics. Frequency and percentage were used to summarize categorical data, and quantitative data were expressed as mean and standard deviation.

Results

There were 30 (21 female and nine male) patients suffering from MG. Age range was 13–78 (average 46.2±15.7) years. Age range at disease onset was 11–75 (average 40.2±15.9) years. Duration of disease range was 1–38 (average 6±7) years. Of the 30 patients, 23 had GMG, and seven had OMG (Table 1).

Of the 30 patients, 17 (56.7%) were positive for AChRAb, and 7 (23%) were positive for anti-TPO.

Among the 17 AChRAb (+) patients, both GMG (14/23 (60.9%)) and OMG (3/7 (42.9%)) were present. Of the 17 AChRAb (+) patients, 6 were also positive for anti-TPO. All seven anti-TPO (+) patients had GMG (Table 2).

There were six (four female and two male) patients suffering from MG with co-occurrence of AChRAb and anti-TPO. Age range was 34–65 (average 48.8±10.8) years. Age range at disease onset was 32–54 (average 44.3±10.9) years. Duration of disease range was 1–10 (average 4.5±3.5) years. All patients suffered from GMG (Table 3).

Table1. Demographic features of patients suffering from MG

Sex (F/M) (n, %)	21 (70)/9 (30)
Age (year) (mean±SD)	46.23±15.69
Disease onset (year) (mean±SD)	40.20±15.86
Duration (year) (mean±SD)	6.03±6.93
Clinic (n, %)	GMG: 23 (76.67)
	OMG: 7 (23.33)

Table 2. Occurrence and co-occurrence of autoantibodies in patients suffering from MG

	Clinic-Autoantibodies n (%)	AChR-Ab(+) n (%)	Anti-TPO(+) n (%)	AChR-Ab(+), Anti-TPO(+) n (%)
GMG	23 (76.67)	14 (60.87)	7 (30.43)	6 (26,07)
OMG	7 (23.33)	3 (42.86)	0	0
MG	30	17 (56.67)	7 (23.33)	6 (20)

Table 3. Demographic features of patients with MG with co-occurrence of AChRAb and anti-TPO

Sex (F/M) (n ,%)	4 (66.67)/2 (33.33)
Age (year) (mean±SD)	48.83±10.8
Disease onset (year) (mean±SD)	44.33±10.86
Duration (year) (mean±SD)	4.5±3.45
Clinic (n, %)	GMG: 6 (100)
	OGM: 0

Discussion

MG is now regarded as one of the major autoimmune diseases. It was demonstrated that a deficiency in neuromuscular transmission in the disease results from an autoimmune response to postsynaptic AChR, and that the deficiency is occasionally associated with various autoimmune disorders, such as systemic lupus erythematosus, pernicious anemia, HT, and GD [8,9]. Many studies have also shown that AITDs, such as GD and HT, are most frequently associated with MG [5,6,8].

Autoantibodies against thyroglobulin have been particularly helpful in the diagnosis of AITD, such as HT and GD.

Epidemiological studies showed that AITDs occur in approximately 5%–10% of patients with MG, whereas a fairly low incidence of MG has been reported in patients with AITD. A higher frequency of thyroid antibodies has been observed in OMG compared with GMG, but this increased association between OMG and thyroid autoimmunity has not been confirmed. Thus, the question of whether the clinical expression of MG associated with AITDs is different from that observed in MG without thyroid autoimmunity remains unresolved.

AITD constitutes >30% of all organ-specific diseases. HT and GD are the majority of the AITDs. Other autoimmune diseases are detected at 9.67% in GD and 14.6% in HT [10].

Epidemiological studies showed that AITDs occur in approximately 5%–10% of patients with MG, whereas a fairly low incidence of MG has been reported in patients with AITD. Autoimmune overlap between MG and other autoimmune disorders reflects common pathogenic mechanisms [9,11,12].

Moreover, a higher frequency of thyroid antibodies has been observed in OMG compared with GMG, but this increased association between OMG and thyroid autoimmunity has not been confirmed. Thus, the question of whether the clinical expression of MG associated with AITDs is different from that observed in MG without thyroid autoimmunity remains unresolved. However, several hypotheses can be considered, such as OMG and GMG are different spectra of similar conditions or same genetic background. On the other hand, an immunological cross-reactivity against epitopes or autoantigens shared by the thyroid and the eye muscles could be the basis of this association [2,12].

Feltkamp et al. [13] reported a marked increase in several organ-specific autoantibodies in patients with MG. Twenty-two percent of a large group of patients with MG were found to have skeletal muscle autoantibodies, 6% gastric parietal cell autoantibody, 8% thyroid colloid, 9% thyroid plasma, and 24% antinuclear antibodies to human thyroid.

Kanazawa et al. [14] found that approximately 20% of patients with MG have associated autoimmune disease, and that AITDs are most predominant. Similarly, our study revealed that 23% of patients with MG have also AITD.

Furthermore, 35.3% (6/17) of patients with MG with AChRAb were in association with anti-TPO. On the other hand, 85.7% (6/7) of patients with MG with anti-TPO were also in association with AChRAb.

It is really important to think coexisting MG in patients with autoimmune disorders and neuromuscular weakness. The presence of AChRAbs in patients with MG is associated with a frequent risk for other autoimmune diseases.

The limitation of the present study should be acknowledged. Increasing the number of patients is necessary to confirm the results.

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