Annals of African Medicine
Vol. 7, No.2; 2008:88 – 90

CASE REPORTS

MYASTHENIA GRAVIS ASSOCIATED WITH AUTOIMMUNE THYROID DISEASE: A REPORT OF TWO PATIENTS

F. Bello-Sani, F. E. Anumah and A. G. Bakari

Endocrine unit, Department of Medicine, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria
Reprint requests to: Dr. Fatima Bello-Sani, Department of Medicine, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria. E-mail: otuchu2000@yahoo.com

Abstract
Myasthenia gravis (MG) is an acquired autoimmune disorder causing skeletal muscle fatigue and weakness. This is a report of one woman and her daughter presenting with myasthenia and gravis and Grave's disease. It highlights possible hereditary component of this condition which has not been commonly reported in our setting.

***Key words**: Myasthenia gravis, thyroid disease*

Résumé
Les gravis de Myasthenia (magnésium) est un désordre autoimmun acquis causant la fatigue et la faiblesse de muscle squelettique. C'est un rapport d'une femme et de sa fille présent avec le myasthenia et les gravis et la maladie de la tombe. Il accentue le composant héréditaire possible de cette condition qui n'a pas été généralement rapportée dans notre arrangement.

***Mots clés**: Gravis de Myasthenia, la maladie thyroïde*

Introduction

Myasthenia gravis (MG) is an autoimmune disease characterized by impaired neuromuscular transmission due to circulating antiacetylcholine receptor auto antibodies (AchRAB).[1] The frequent association of MG with thymic disease, such as follicular hyperplasia and thymoma, suggests that the thymus plays a role in its pathogenesis.[1-3] The clinical expression of MG varies, ranging from a mild localized disease such as ocular myasthenia gravis (OMG) to a severe generalized disease.[4]

Patients with MG may have evidence of coexisting autoimmune thyroid disease (AITD)[5-8] as well as other autoimmune disorder like type 1 diabetes, primary hypogonadism, pernicious anemia, and adrenal insufficiency. Collectively referred to as the polyglandular syndrome (PGA).

Epidemiological studies showed that AITD occur in approximately 5%-10% of MG patients.[9,10] Graves' disease (GD) is the commonest AITD associated with MG.[9,10] Graves' disease and MG are more common in females. A higher frequency of thyroid antibodies has been observed in OMG compared to generalized myasthenia gravis (GMG).[11] GD has been found to coexist with OMG in 41.0% & GMG in 28.5% of a total of 129 cases of myasthenia gravis studied.[11]

The pattern of inheritance is unknown but high frequency of human leukocyte antigen (HLA) B8 and DR 3 has been reported in both disorders.[12-14] This report highlights possible hereditary component of this condition in our setting.

Case 1

A 46-year- old woman presented in 2000 with excessive sweatiness, polyphagia, and occasional

palpitation. At the age of 18 years she had diplopia, ptosis and blurred vision. A diagnosis of MG was made and subsequently she had thymectomy.

Physical examination revealed hyperpigmentation, a warm, moist palm with tremulous hands, and a firm diffusely enlarged goiter. There was lid lag, lid retraction and exopthalmos. A diagnosis of Graves' disease was made and confirmed by high levels of thyrotrophin, thyroxin and very low thyroid stimulating hormone levels (Table 1). Serum thyroid microsomal antibodies.

She was initially treated with azathioprine 25mg 3 times daily and prednisone 2.5mg 3 times daily. Six months after her 2nd childbirth, treatment was changed to pyridostigmine 30-60mg 3 times daily and prednisone 10mg 3 times. Treatment for Grave's disease was with metimazole 15mg 3 times daily. She has two daughters; one was diagnosed to have myasthenia gravis and Graves' disease at the age of 15yearrs and is being treated.

Case 2

A 24-year-old first daughter of case 1 was diagnosed to have myasthenia gravis at the age of 15 years when she presented with weakness, ptosis and diplopia. She was commenced on treatment with marked improvement, but developed intolerance to heat, excessive eating, warm moist palms, inattention in class and proptosis after 5 years. She attained Menarche at eleven years of age with regular menstrual flow.

Physical examination showed lid lag, lid retraction, and exophthalmos in addition to a diffuse goiter. A diagnosis of Graves' disease was made and confirmed by high levels of thyrotrophin, thyroxin and low thyroid stimulating hormone (Table 1). Serum thyroid microsomal antibodies was high. She was placed on methimazole 10mg 3 times daily and pyridostigmine 30mg 3 times daily. She has remained well at follow up. Her only sister is apparently well and thyroid antibody negative.

Table 1. Result of thyroid function and thyroid antibodies in the two patients

Tests	Normal values	Case 1	Case 2
T3	0.2-2.3ug/ul	4.2ug/ul	3.4ug/ul
T4	38-98ng/ul	160ng/ul	155ng/ul
TSH	1.0-5.2miu/l	0.74miu/l	0.86miu/l
STA		Negative at 1:600 dilutions	Negative at 1:600 dilutions
STMA		Positive at1:6400 dilutions	Positive at 1:6400 dilutions

T3: thyrotropin; T4:Thyroxin; TSH: thyroid stimulating hormone; STA: serum thyroglobulin antibodies; STMA: serum thyroid microsomal antibodies

Discussion

Myasthenia gravis is an autoimmune neuromuscular disorder often associated with thymic disease.[1-3] The coexistence of other autoimmune diseases in MG is well recognized,[6,7] including the association with AITD.[6-8] However, the influence of AITD on the clinical expression of MG has not been defined. Whether AITD is more frequently association with OMG (as in this cases) or GMG has not been evaluated and whether the clinical expression of MG with coexistent AITD is related to thyroid disease per se or to its autoimmune component remains to be clarified.

In the present report clinical presentation of MG associated with AITD was characterized by neuromuscular involvement restricted to eye muscles. Garlepp et al[5] reported increased association between OMG and thyroid immunity and greater frequency of thyroid antibodies in OMG than GMG. Marino et al demonstrated that Graves' disease patients with clinical evidence of ophthalmopathy had a higher frequency of ocular MG (51.8%) than GD patients without clinical ophthalmopathy (16.6%).[11] That report[11] also demonstrated milder clinical expression of MG in patients with associated AITD than in those without thyroid auto immunity.

The reason for the association of AITD with ocular MG is unknown, but several hypotheses have been considered. First, OMG and GMG might actually represent separate diseases.[15,16] Second, an immunological cross-reactivity against epitopes or autoantigen shared by the thyroid and the eye muscles might be the basis for this association.[17,18] Several experimental data suggest that the thyroid antigens are presents in ocular tissues. Circulating autoantibodies directed to eye muscles components have been identified in GD with MG.[19,20] Explanation for the higher frequency of OMG in AITD could be that these disorders have a common genetic background.[11] Also a high frequency of human-leukocyte antigen B8 and DR3 has been reported in both disorders.[11]

The present report is a reminder that the clinical features of autoimmune diseases can overlap. The presence of one autoimmune disease should prompt a search for other autoimmune diseases. It is desirable that family members are screened to exclude autoimmune disease.

References

1. Drachman DB. Myasthenia gravis: medical progress. N Engl J Med. 1994;330:1797-1810.
2. Kao I, Drachman DB. Thymic muscles cells bear acetylcholine receptors: possible relation to myasthenia gravis. Science. 1977;195:74-75.
3. Schluep M, Wilcox N, Vincent A, Dhoot GK, Newsom-Davis J. Acetylcholine receptors in human thymic myoid cells in situ: an immunohistological study. Ann Neurol. 1987;22:212-222.
4. Osserman KE. Myasthenia gravis. Grune and Stratton, New York. 1953; 80.
5. Garlepp MJ, Dawkins RI, Christiansen FT. Autoimmunity in ocular and generalized myasthenia gravis. J Neuroimmunol. 1981;1:325-332.
6. Rennie GE. Exophthalmic goiter combined with myasthenia gravis. Rev Neurol Psychiatry. 1908;6:229-233.
7. Drachman DB. Myasthenia gravis and the thyroid gland. N Engl J Med. 1962;15:330-333.
8. Tola MR, Caniatti LM, Casetta I, et al. Immunogenetic heterogeneity and associated autoimmune disorders in myasthenia gravis: a population-based survey in the province of Ferrara, Northern Italy. Acta Neurol Scand. 1994;90:318-323.
9. Kiessling WR, Finke R, Kotulla P, Schleusener H. Circulating TSH-binding inhibiting immunoglobulins in myasthenia gravis. Acta Endocrinol (Copenh). 1982;101:41-46.
10. Pacey SR, Belchetz PE. Grave's disease associated with ocular myasthenia gravis and thymic cyst. J R Soc Med. 1993;86:297-298.
11. Marino M, Ricciardi R, Pinchera A, et al. Mild clinical expression of Myasthenia gravis associated with autoimmune thyroid diseases. J Clin Endocrinol Metab. 1997;82:438-443.
12. Weetman AP, McGregor AM. Autoimmune thyroid disease: further developments in our understanding. Endocr Rev. 1994;15:788-830.
13. Pirskanen R, Tilikainen A, Hokkanen E. Histocompatibility (HLA) antigens associated with myasthenia grais. A preliminary report. Ann Clin Res. 1972;4:304-306.
14. Feltkamp TEW. Van Der Berg- Loonen PM, Nijenuis LE. Myasthenia gravis, autoantibodies and HLA antigens. BMJ. 1974;1:131-133.
15. Bartoccioni E, Scuderi F, Evoli A, Provenzano C, Flamini G. Ocular myasthenia gravis: two different disease. Lancet. 1986;1:1038-1039.
16. Zimmermann CW, Eblen F. Repertoires of autoantibodies against homologous eye muscle in ocular and generalized myasthenia gravis differ. Clin Investig. 1993;71:445-451.
17. Schumacher M, Camp S, Maulet Y, et al. Primary structure of Torpedocalifornica acetylcholinesterase deduced from its cDNA sequence. Nature. 1986;319:407-409.
18. Ludgate M, Swillens S, Mercken L, Vassart G. Homology between thyroglobulin and acetylcholesterase: an explanation for pathogenesis of Graves' ophthalmopathy? Lancet. 1986;2:219-220.
19. Ludgate M, Dong Q, Soreq H, Mariotti S, Vassart G. The pathophysiological significance of a thyroglobulin-acetylcholinesterase shared epitope in patients with Graves' ophthalmopathy. Acta Endocrinol (Copenh). 1989;121:38-45.
20. Ludgate M, Owada C, Pope R, Taylor P, Vassart G. Cross-reactivity antibodies to human thyroglobulin, and torpedo acetylcholinesterase in patients with Graves' ophthalmopathy. In: Pinchera A, Ingbar SH, McKenzi JM, Fenzi GF (Eds). Thyroid autoimmunity. Plenum Press, New York. 1987; 271-273.