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Familial Autoimmune Myasthenia Gravis

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ABSTRACT

Familial Autoimmune Myasthenia Gravis (FAMG) is rarely reported. We present a mother and son with late-onset mild to moderate ocular disease, low acetylcholine receptor antibody titre and the absence of a thymoma. Both responded well to low doses of anticholinesterase. HLA typing revealed that they did not share the usual HLA antigens or haplotypes with that previously reported in Caucasian and Chinese sporadic Myasthenia Gravis. Chinese FAMG may be associated with HLA antigens different from that of sporadic MG.

Keywords: Familial Autoimmune Myasthenia Gravis, Chinese, HLA

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INTRODUCTION

Familial Autoimmune Myasthenia Gravis (FAMG) has rarely been reported in literature. A familial incidence occurs in 4% of MG patients, but this prevalence includes cases of Congenital Myasthenia Gravis[1]. FAMG shares the characteristic presence of acetylcholine receptor antibodies (AChR ab) with the sporadic disease and is therefore distinct from Congenital Myasthenia Gravis in which there is a hereditary defect in neuromuscular transmission and an absence of AChR ab.

Distinct HLA antigens are associated with different phenotypes of sporadic MG. We describe here a Chinese family with MG present in a mother and son. An HLA analysis was performed on them to determine if their clinical phenotype reflected the antigens and haplotypes previously reported in sporadic MG.

CASE REPORT

The mother was a 63-year-old housewife with a 3-year history of intermittent partial ptosis and diplopia. There was no dysphonia, dyphagia or limb weakness. She had a long standing history of Rheumatoid Arthritis which had been in remission for the past few years. Her neurological examination revealed fatiguable bilateral ptosis. The extra-ocular movements were moderately limited but no truncal or limb weakness was demonstrable. Her reflexes were normal. The rheumatoid factor was less than 20 U/ml, the ESR was 25 mm/hr and an SLE diagnostic screen was negative. There was no evidence of Diabetes Mellitus or thyroid dysfunction. Her AChR ab titre was 3.29 nmol/l (normal <0.4 nmol/l). The antiskeletal muscle antibody was negative and there was no thymic mass on her CT thorax. A stimulated single fiber EMG showed a mean jitter of 30.8 μs (normal <20 μs) which was compatible with a mild to moderate dysfunction of neuromuscular transmission. She was started on pyridostigmine 10 mg tds that led to moderate improvement of the ptosis and extra-ocular movements. The dose was gradually increased to 30 mg tds and she remained asymptomatic except for the mild irreversible ophthalmoplegia. She had A24/A26, B60/-, CW7/- and DR4/DR12 antigens on HLA typing.

Her son was a 38-year-old with a 2-week history of diplopia and bilateral partial ptosis with diurnal variation. Like his mother, he did not show any evidence of extra-ocular involvement. There were no clinical or biochemical features of concomitant autoimmune diseases. He had a mean jitter of 25.5 μs on his stimulated single fiber EMG which was consistent with a mild to moderate defect in neuromuscular transmission. A CT thorax showed some increased vascularity in the anterior mediastinum probably representing a hyperplastic thymus gland, but no well defined mass was seen. He had a normal thyroid function test and a negative rheumatoid factor. His AChR ab titre was 0.82 nmol/l. He dramatically improved with pyridostigmine 30 mg tds, and remained well despite defaulting treatment for 3 months. His HLA typing revealed the following: A3/A26, B38/B60, CW7/- and DR4/DR7.

DISCUSSION

The HLA antigens associated with sporadic autoimmune MG in female Caucasians with early onset disease, high titres of AChR ab, and thymic hyperplasia are the A1, B8, DR3 and DQ2. In late onset MG, there is a slightly increased frequency of B7 and DR2[2]. Chan

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SH et al[3] have reported an association between B46, DRB1*14 and DRB1*1202 haplotypes and distinct phenotypes in Singaporean Chinese MG. B46 was the commonest haplotype associated with the disease and was manifested by a younger onset, low AChR ab titres, ocular lesions and normal thymus histology. This was also noted by Hawkins et al[4] in Hong Kong Chinese MG. B5 and B15 were more prevalent in adult-onset disease.

Both the mother and son presented as late onset ocular MG with low AChR ab titres, the absence of a thymoma and rapid response to low doses of anticholinesterase. The mother displayed irreversible ophthalmoplegia as a result of a prolonged delay in seeking treatment. She also had an associated autoimmune disease but did not have the usual HLA antigens reported in Singaporean Chinese with Rheumatoid Arthritis[5,6]. Though they shared similar MG manifestations, they were atypical of either sporadic early- or late-onset MG. Both had the A26, B60, CW7 and DR4 antigens but did not share the usual antigens found in Chinese or Caucasian MG. A literature search did not reveal any articles on the HLA associated with Chinese FAMG. A larger study may show that HLA antigens in Chinese FAMG is different from that reported in sporadic MG.

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