Myasthenia Gravis Antibody Panel Testing: Prevalence of Acetylcholinesterase, Striated Muscle and Titin Antibodies

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ABSTRACT

Myasthenia gravis (MG) is an autoimmune disease characterized by fluctuating and fatigable muscle weakness. While diagnosis is based on clinical presentation and disease progression, MG patients may also be classified by their serologic antibody profile. The most prevalent muscle-targeted autoantibody (55% or more) MG patients with thyromegaly have autoantibodies against acetylcholine receptor (AChR); however, striated muscle antibodies are not specific for myasthenia gravis or thymoma. A variety of muscle antibodies serve as antigenic epitopes for anti-AChR autoantibodies, including acetylcholine, acrylamide, ryanodine receptor, and ryanodine receptor. Titin is the largest identified protein with a molecular mass of 3,000 kD, which is the third most abundant protein in the skeletal and cardiac sarcomere, and is responsible for the elasticity of striated muscle. The prevalence of titin or STMR antibodies in older MG patient populations (< 60), without thymoma restricts the clinical utility of this marker. In younger MG patients; however, titin antibodies are as significant as AChR antibodies.

MATERIALS and METHODS

Clinical Samples: 759 serum samples submitted to ARUP Laboratories for myasthenia gravis antibody panel testing (ARUP Catalog # 2005639) over a four-month period were evaluated in this study. Consecutively received specimens were studied except for four specimens where gender and age of patient were not provided.

Methods: Patient sera were tested for myasthenia gravis antibody receptor binding antibody by a laboratory-developed radioimmunoassay precipitation assay. STMR antibodies were detected using a commercial FDA-cleared IFA assay (Mardis, Carlsbad, CA; Prod # 10-5808) and titin antibody by enzyme linked immunosorbant assay (ELISA). Conssecutively received specimens were reacted with the only exclusion criteria being lack of patient gender or age; only four sera were excluded from statistical analysis. This study was conducted in compliance with ARUP policies and Health Insurance Portability and Accountability Act guidelines under the University of Utah Institutional Review Board approved protocol 7275. Statistical analysis for equality of percentages was evaluated by arcsine transformation of proportions; p values less than 0.05 were considered significant.

RESULTS

The proportion of ACHR antibody positive sera (N = 84; 11.1%) was equivalent to the historical average for specimens submitted to ARUP previously evaluated over a three year period (12.0%; p > 0.05). Titin and striated muscle antibody assay results qualitatively agreed in 95.0% (72/755) of our patient sera; however, STMR antibody assay agreements were statistically significant differences between ACHR antibody positive (59/84; 70.2%) and ACHR antibody negative (66/757; 8.0%) sera. Titin antibody was significantly more prevalent in both ACHR antibody positive sera (47/84; 56.0%) and ACHR antibody negative sera (15/757; 2.0%) compared to striated muscle antibody; which was detected in 35.7% (30/84) of ACHR antibody positive sera and 0.3% (2/675) of ACHR antibody negative sera. The overall Titin STMR agreement statistic (70.2%) was similar to that previously observed in acetylcholine receptor binding antibody assays.

Conclusion: MG patients may be immunologically sub-categorized according to the presence or absence of numerous autoantibodies; thus combinational (i.e. panel) testing assists in identifying low prevalence subsets of patients with disease. The presence of either striated muscle antibody or titin antibody is prognostic for thyromegaly in early-onset MG patients; although these antibodies are often detected in late-onset MG (> 60 years) of patients without thyromegaly. The proportion of ACHR antibody positive sera in our patient population suggests that this panel is used to screen patients with muscle weakness to rule out rather than confirm the diagnosis of MG. Titin and STMR antibody were rarely observed in ACHR receptor antibody negative sera and significantly higher proportions of titin and STMR antibody were observed in acetylcholine receptor antibody positive sera, in agreement with previous reports. ELISA testing was more sensitive than IFA testing for the detection of striatal muscle antibody with the majority of discordant results observed in patients over 60 years of age (32/38; 84.2%).

REFERENCES

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