

A successful validation of the ability of anti-GAGA4 IgM antibody assay to differentiate multiple sclerosis patients from other neurological diseases patients in a German cohort: a cross-sectional retrospective analysis

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Background: Previous studies (Israeli, Canadian-Belgian cohorts) demonstrated that anti-Glc(α1,4)Glc(α) (anti-GAGA4) IgM antibody levels are higher in diagnosed and first presentation multiple sclerosis (MS) patients than other neurological disease (OND) patients, thus enabling the identification of a subgroup of MS patients. Corrections for total IgM and age were shown to improve the performance of this assay.

Objective: To validate the ability of anti-GAGA4 IgM EIA assay to differentiate between relapsing-remitting MS (RRMS) and OND patients in a German cohort.

Methods: Retrospective analysis of frozen sera from a German cohort of 126 patients (age between 18 and 65 years): 83 RRMS patients (age: mean ± SD, 37.4 ± 10.0 years; 65% female), 8 primary progressive MS (PPMS) patients (age: mean ± SD, 42.5 ± 12.2 years; 50% female) and 35 OND patients (15 other inflammatory neurological disorders (OIND), 20 other noninflammatory neurological disease (ONIND), age: mean ± SD, 53.5 ± 10.2 years; 37% female). Sera were diluted 1:1200 and levels of anti-GAGA4 IgM antibodies were measured by gMS®Dx immunoassay, normalized by dividing by the square root of total IgM levels (mg IgM/ml serum). Based on results from a former study, correction for patients' age was done by adding 0.455 (EU/(mg/ml)^{0.5}) per year from the age of 20 years. Anti-GAGA4 cutoff level for determining antibody status (positive or negative) was set at 57 EU/(mg IgM/ml serum)^{0.5}.

Results: Significantly higher levels of anti-GAGA4 IgM antibodies were observed in RRMS patients (median: 48.0 EU/(mg/ml)^{0.5}, p=0.0001, Mann-Whitney U test) compared with OND patients (median: 33.3 EU/(mg/ml)^{0.5}). Receiver operating characteristic (ROC) curve analysis demonstrated that anti-GAGA4 can differentiate between RRMS and OND patients (area under the curve (AUC): 0.812). Anti-GAGA4 was positive in 29/87 RRMS patients (sensitivity: 33.3%, 95% confidence interval: 23.6-44.3%); negative in 33/35 OND patients, (specificity: 94.3%, 95% confidence interval: 80.8-99.1%). PPMS patients had relatively low levels anti-GAGA4 IgM antibodies (median: 39.1 EU/(mg/ml)^{0.5}) and only one of the eight patients had a value above the cutoff.

Conclusions: The ability of anti-GAGA4 to differentiate between RRMS and OND patients was further validated.