Evaluation of The Association of Glutamic Acid Decarboxylase Antibody and Limbic Encephalitis in Children with Type 1 Diabetes Mellitus

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INTRODUCTION

Glutamic acid decarboxylase (GAD) is the enzyme that catalyzes the conversion of L-glutamat into GABA, one of the classical neurotransmitters with neuroinhibitory function. GAD is present in GABAergic neurons and also in pancreatic beta cells. It is remarkable that Anti-GAD antibody can have widely different disease manifestations, i.e., Type 1 Diabetes Mellitus (DM), Stiff-Person Syndrome , limbic encephalitis, epilepsy. Cooccurence of type 1 diabetes mellitus and limbic encephalitis is reported in the literature.

There is no study in the literature about the presence of limbic encephalitis in patients with Type 1 diabetes mellitus.

METHOD

Anti-GAD antibody high positive (> 100 IU / ml), Anti-GAD low positive (10-100 IU / ml) and Anti-GAD negative (≤10 IU / ml), 34 cases with type 1 DM were included in Gazi University Faculty of Medicine Pediatric Endocrinology Department. Anti-GAD levels of the patients were evaluated retrospectively. Physical examination and electroencephalography (EEG) were performed in the pediatric neurology department. Cranial Magnetic Resonance was planned for cases with positive findings in terms of neurological examination and / or limbic encephalitis in EEG. All EEGs were ordered with sleep deprivation.

Table: Demographic and clinical data of the patients**.**

Parameter		Value
Gender (M/F)	Male	14(41.2%)
	Female	20(58.8%)
Age (on diagnosis)		6.8±2.9
Age (Study)		10.6±3.8
Follow-up duration (Years)		3.8±3.0
Anti GAD (on diagnosis)		387.5±773.9
HbA1c (Mean, %)		8.8±2.0
Anti GAD Level	≤10	8(23.5%)
	>10, ≤100	11(32.4%)
	>100	15(44.1%)
HbA1c (%) Level	≤7	2(5.9%)
	>7	32(94.1%)
Epileptic Activity	Absent	24(70.6%)
	Present	10(29.4%)

Values are given as number of cases (percent) or mean ± standard deviation

RESULTS

The general characteristics of the patients are given in the table. Anti-GAD levels were correlated with HbA1c averages ($p < 0.05$). The mean HbA1c of the Anti-GAD antibody negative cases was 8.2%, the mean HbA1c of the Anti-GAD antibody low positive cases was 9.4%, and the mean HbA1c of the Anti-GAD antibody high positive cases was 8.7%. A total of 34 EEG records were identified. Of the total number of records, 24(70.6%)were normal and 10 (29.4%) abnormal. There was no significant relationship between anti-GAD levels and epileptic activity.

DISCUSSION

Our study shows that especially sleep deprived EEG may be used as an indicator of limbic encephalitis or autoimmune epilepsy in children with GAD autoimmunity. These patients are going to be followed for long term for the development of limbic encephalitis or autoimmune epilepsy in the future. Our hypothesis is tha GAD autoimmunity, even after many years, can spread to the CNS. As early treatment of GAD antibody-associated CNS disorders has a better prognosis, vigilance for electroencephalographic findings indicating GAD antibody-associated CNS autoimmunity is mandatory in patients with GAD antibody-associated endocrine dysfunction.