

The transient appearance of anti-GAD antibody in a type 2 diabetic patient with empyema

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The Transient Appearance of Anti-GAD Antibody in a Type 2 Diabetic Patient with Empyema

Key words: anti-GAD antibody, diabetes mellitus, *Streptococcus pneumoniae*, infection, false positive

Glutamic acid decarboxylase (GAD) catalyzes the synthesis of the neurotransmitter GABA (γ -aminobutyric acid) and exists in two isoforms, GAD65 and GAD67. These proteins are 65% homologous, differing primarily in the amino terminal third of the protein, and can be found in brain and islet. GAD65 is predominantly expressed in human pancreatic β -cells and the presence of the anti-GAD65 antibody (GAD-Ab) is a predictor of the development of β -cell destruction. GAD-Ab has been detected in 70–80% of recently diagnosed type 1 diabetic patients and is a useful diagnostic marker of type 1 diabetes mellitus. Although type 1 diabetic patients remain positive for GAD-Ab for a long time (1), in type 2 diabetic patients it is rare for GAD-Ab to transiently convert to positive.

The present patient, a fisherman, was diagnosed with diabetes mellitus at the age of 20, but he was unable to come to our hospital on a regular basis. He was admitted to our hospital when he was 24 because of an injury to the right foot, at which time, his glycosylated hemoglobin level (Hb_{A1c}) was 12.8%. The patient's maternal grandmother, but not his parents, had diabetes mellitus. GAD-Ab was negative and urinary excretion of C-peptide (u-CPR) was 42.6 $\mu\text{g}/\text{day}$. Results of both thyroid and microsome tests were negative. The patient was diagnosed with type 2 diabetes mellitus and was given 2.5 mg per day of glibenclamide. However, glycemic control was poor with Hb_{A1c} remaining above 10% for the following 3 years. On October 2, 2001, at the age of 27, he was admitted to our hospital again for high fever and right chest pain. There were moist rales and knock pain upon the right lower lung field. Neurological examinations produced no abnormal findings. The radiograph of the patient's chest showed an infiltrative shadow in the right lower lung field and right pleural effusion. The white blood cell count was 21,400/ mm^3 (neutrophils 97.0%, monocytes 1.0%, lymphocytes 2.0%) and the C-reactive protein level was 34.1 mg/dl. The pleural fluid was exudative and the culture showed the presence of *Streptococcus pneumoniae*. The right lung was drained with a chest tube, and he was treated with intravenous injection of imipenem-cilastatin sodium (1.0 g/day) and gentamycin sulfate (80 mg/day). On admission, Hb_{A1c} , ketone body, amylase and GAD-Ab ("Cosmic", Tokyo, Japan) were 12.6%; 902 $\mu\text{mol}/\text{l}$, 16 IU/l and 4.8 U/ml (reference range: less than 1.3 U/ml), respectively. Since

there was a possibility of progression to insulin-requiring diabetes because of GAD-Ab converting to positive, he was also treated with multiple subcutaneous insulin injections to provide adequate glycemic control. On November 14, 2001, Hb_{A1c} was 8.2% and u-CPR, 53.9 $\mu\text{g}/\text{day}$. Laboratory data after he was discharged from our hospital showed that GAD-Ab was less than 1.3 U/ml, insulin antibody level 4.6% (reference range: less than 10%), islet cell antibody level negative and IA-2 antibody level less than 1.0 U/ml.

There are a few cases in which GAD-Ab became positive after interferon treatment for hepatitis C virus chronic infection, and some of them showed a decrease in insulin secretion (2). In addition, it has been reported that viral infections such as rotavirus and coxsackie virus, may be associated with a risk for development of type 1 diabetes mellitus (3). Viral induction of autoimmunity is thought to occur by either bystander T-cell activation or molecular mimicry. It has been reported that *Streptococcus pneumoniae* type 3 encodes a protein highly similar to GAD65 (4), so that pneumococcal infection may be associated with the induction of GAD-Ab.

GAD-Ab disappeared after the treatment for empyema, while u-CPR did not decrease in the present patient. The transient appearance of GAD-Ab in our case may not be associated with the development of β -cell destruction. GAD-Ab can be found in other autoimmune diseases such as stiff-man syndrome, autoimmune thyroid disease, in 6–10% of patients classified with type 2 diabetes, as well as in 1–2% of the healthy population (5). The GAD-Ab radioimmunoassay by "Cosmic" also showed a false-positive level of 1.2%. Cases positive for GAD-Ab thus need to be carefully followed up with an eye on the changes in this titer and for evaluation of insulin requirement.

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