



BMH Medical Journal 2014;1(2):33-36 **Case Report**

## **Anti GAD65 Encephalopathy Presenting with Reversible Encephalopathy and Orofacial Dyskinesias**

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### **Abstract**

Anti GAD65 antibodies have been implicated predominantly in limbic encephalitis in addition to systemic disorders like Type 1 diabetes mellitus. Here a patient presenting with seizures, behavior disturbances, memory and gait abnormalities and peculiar orofacial dyskinesias is reported, who was found to have high titre positivity of Anti-GAD 65 and excellent therapeutic response to steroids, suggesting that this could be an additional phenotype for the encephalopathy caused by this antibody.

**Key Words:** Anti GAD65 Encephalopathy, Orofacial Dyskinesias, Reversible Encephalopathy

### **Introduction**

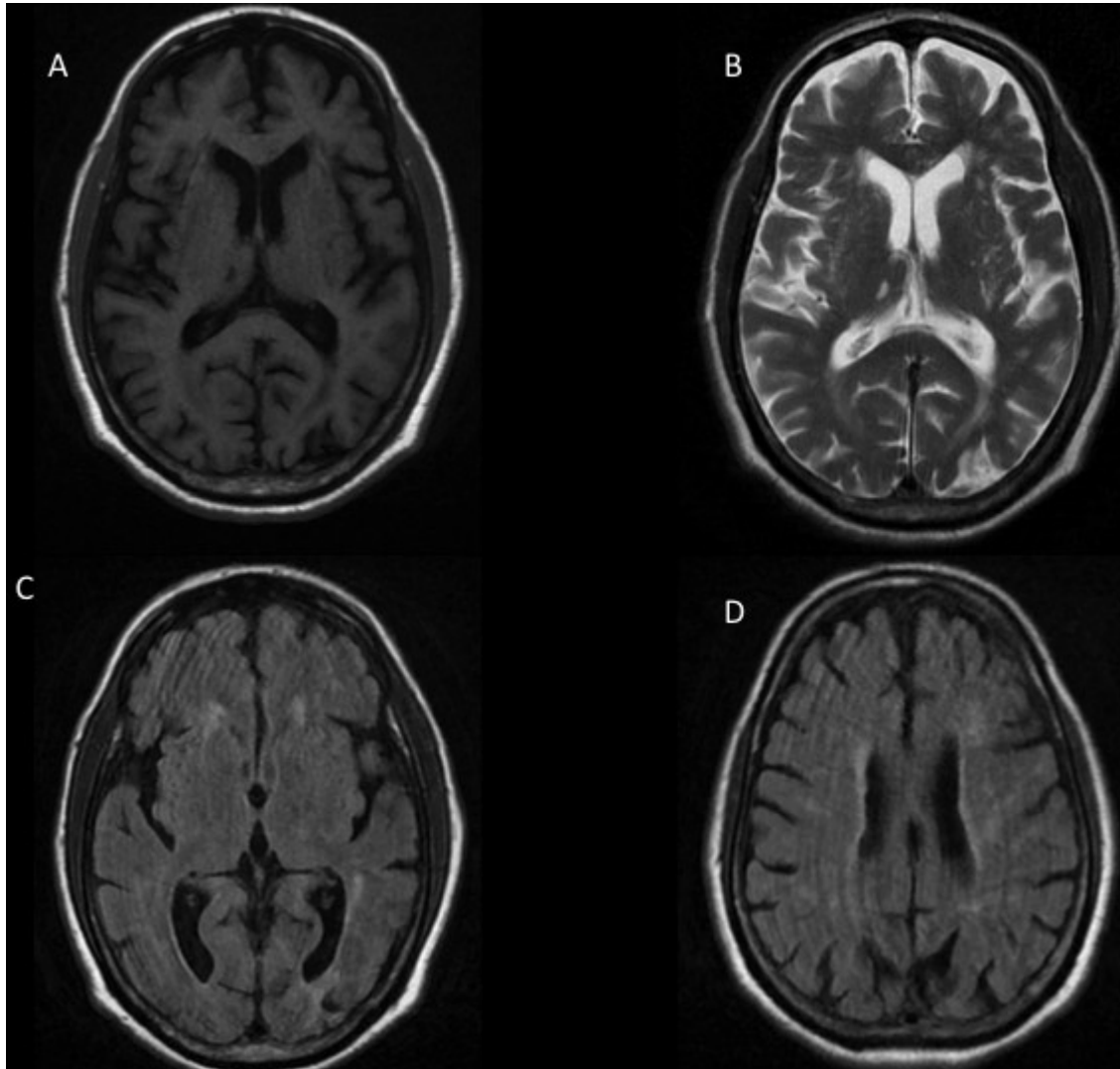
Antibodies to the 65 kilo-dalton variant of Glutamic Acid Decarboxylase (GAD-65) have been described in association with a variety of neurological [1,2] as well as systemic auto-immune disease including Type 1 Diabetes Mellitus [3], Stiff Person Syndrome [3,8], brain stem syndromes including nystagmus [4], cerebellar ataxia [5] and Limbic Encephalopathy [1,3,5-7]. It may be considered as part of the spectrum of non para neoplastic autoimmune encephalopathy syndromes [9]. Here a patient presenting with subacute encephalopathy and peculiar orofacial dyskinesias with high titre positivity of Anti-GAD 65 antibodies in serum and good response to steroid therapy is reported, a phenotype that is not so far described in the available literature.

### **Case Report**

A 75 year old gentle man presented to the outpatient clinic of Neurology Department at Baby Memorial Hospital with history of recent onset of rather peculiar constellation of neurological symptoms since past 4-6 months. He had worsening of gait, memory impairment, lack of interest in activities which he used to do, and abnormal involuntary orofacial movements involving grimacing, chewing and biting. He had retired from government service 20 years ago and was fine except for type 2 diabetes mellitus and essential hypertension, for which he was on regular treatment since the past 10 years. He also gave history of seizures since 2 years, for which he had been evaluated with EEG and MR imaging and had been started on anti-epileptic medication (phenytoin) and was well controlled at the time of presentation. The MR Imaging done for seizures 2 years ago was unremarkable except for small vessel ischemic changes and age related cerebral atrophy.

When examined, he was alert, speech was dysarthria, he had dyskinesias of face, jaw and tongue. Communication was poor, and he took several minutes to answer simple questions like his name. Formal cognitive testing was impossible. His MMSE score was around 11, limited by the impaired communication. There were no pyramidal signs, and tendon reflexes were normal. He performed the finger nose test without difficulty but his gait was slow, broad based.

MR Imaging of the brain was repeated and was again unremarkable except for small vessel ischemic changes and atrophy (**Figure 1**)



**Figure 1:** T1 (A) T2 (B) and FLAIR (C &D) MR Images of the brain showing age related cerebral atrophy and small vessel ischemia

Biochemical tests including blood counts, electrolytes, renal, liver and thyroid functions, including thyroperoxidase antibodies were normal. Chest Radiograph and ultrasound scan of the abdomen were also negative.

Lumbar CSF showed no pleocytosis (cell count of 2 lymphocytes/HPF), but elevated protein (65mg %) and normal glucose (85mg%). Electroencephalography could not be obtained satisfactorily due to artifacts caused by the severe orofacial movements.

Considering the possibility of autoimmune encephalopathy, serum was sent for autoimmune and paraneoplastic antibodies. Anti-neuronal nuclear antibodies (types 1,2&3), Purkinjee cell antibodies (types 1&2), Anti-Tr, Anti-glial/neuronal nuclear antibody type 1, Anti-amphiphysin, Anti-collapsin

response mediator protein-5, Anti Ma, Anti Ta, N-Methyl D-Aspartate (NMDA) receptor antibody, and voltage gated potassium channel(VGKC) antibodies were negative. However Anti GAD-65 was positive in high titres (1:85, normal up to 1:5).

Though the phenotype was unusual, anti GAD-65 related autoimmune encephalopathy was considered a strong possibility and he was treated with five days of intravenous infusion of Methyl Prednisolone (1g/day) followed by oral prednisolone at 1mg/kg/day. Improvement was slow, but definite and by the 10th day, the abnormal movements completely stopped, his gait became normal and his memory and behavior returned to near normal levels. He continues to be under follow up.

## Discussion

Anti GAD-65 has been associated predominantly with stiff person syndrome, limbic encephalitis, brain stem signs including nystagmus, in adults. The enzyme GAD 65 is located predominantly in the presynaptic regions and is involved in the conversion of glutamate to the inhibitory neurotransmitter - Gamma Amino Butyric Acid (GABA). Antibodies to the enzyme could impair GABA production and thus cause neurological syndromes. Since GABA has a predominantly inhibitory role, neuronal excitation could be expected in this situation, leading to symptoms like seizures and dyskinesias. However, literature is dominated with reports of rapid and fluctuating confusional states and behavioral abnormalities consistent with limbic encephalopathy. The symptoms in the patient reported here represent a logically possible but so far unreported presentation of Anti-GAD 65 related encephalopathy.

## References

1. Malter MP, Helmstaedter C, Urbach H, Vincent A, Bien CG. Antibodies to Glutamic Acid Decarboxylase define a form of Limbic Encephalitis *Ann Neurol* 2010;67:470-478.
2. Meinck H, Faber L, Morgenthaler N, Seissler J, Maile S, Butler M, Solimena M, DeCamilli P, and Scherbaum W. Antibodies against glutamic acid decarboxylase: prevalence in neurological diseases. *J Neurol Neurosurg Psychiatry*. 2001; 71: 100-103.
3. Gilliam LK, Binder KA, Banga JP, Madec A-M, Ortqvist E, Kockum I, Luo D, Hampe CS. Multiplicity of the antibody response to GAD65 in Type I diabetes. *Clin Exp Immunol*. 2004; 138(2): 337-341.
4. Antonini G, Nemni R, Giubilei F, Gragnani F, Ceschin V, Morino S, Bucci E, Accornero N. Autoantibodies to glutamic acid decarboxylase in downbeat nystagmus. *J Neurol Neurosurg Psychiatry*. 2003; 74: 998-999.
5. Mirabelli-Badenier M, Morana G, Pinto F, Uccelli A, Veneselli E, Battaglia FM, Biancheri R, Baglietto MG, Vincent A, Mancardi MM.. Anti Glutamic Acid Decarboxylase Limbic Encephalitis Without Epilepsy Evolving Into Dementia with cerebellar ataxia. *Arch Neurol* 2012;69: 1064-66.
6. Sharma A, Dubey D, Sawhney A, Janga K. GAD65 positive autoimmune limbic encephalitis: A case report and review of literature. *J Clin Med Res*. 2012; 4:424-428.
7. Finelli PF. Autoimmune Limbic Encephalitis with GAD Antibodies. *The Neurohospitalist* 2011;1:178-179.
8. Burn DJ, Ball J, Lees AJ, Behan PO, Morgan-Hughes JA. A case of progressive encephalomyelitis with rigidity and positive antiglutamic acid decarboxylase antibodies. *J Neurol Neurosurg*

Psychiatry. 1991; 54: 449-451.

9. Sudheeran Kannooh. Paraneoplastic neurologic syndrome: A practical approach Ann Indian Acad Neurol. 2012; 15: 6-12.