**Case Report**

**Anti GAD65 Antibody associated Autoimmune Encephalitis with Seizures responding to IVIG and Rituximab: A Case Report**

**Abstract**

The glutamic acid decarboxylase 65-kilodalton isoform (GAD65) antibody is a biomarker of autoimmune central nervous system (CNS) disorders and, more commonly, non-neurological autoimmune diseases. Type 1 diabetes, autoimmune thyroid disease, and pernicious anaemia are the most frequent GAD65 autoimmune associations. One or more of these disorders coexists in approximately 70% of patients with GAD65 neurological autoimmunity. Neurological phenotypes have CNS localization and include limbic encephalitis, epilepsy, cerebellar ataxia, and stiff-person syndrome (SPS), among others. For all phenotypes, responses to immunotherapy are variable (approximately 50% improve). GAD65 autoimmunity is important to recognize for both coexisting non-neurological autoimmune associations and potential immunotherapy-response. Timely initiation of appropriate therapy can avoid serious complications in the patient. Therefore, high clinical suspicion should be there if the initial workup doesn’t lead to a diagnosis.

**Key Words:** Anti GAD65 antibody, Autoimmune encephalitis, Seizure.

**Categories:** Neurology, Autoimmune.

**Introduction**

Anti-glutamic acid decarboxylase 65 antibodies target the intracellular enzyme necessary to synthesize gamma aminobutyric acid (GABA). Glutamic acid decarboxylase (GAD) 65 catalyzes the production of γ-aminobutyric acid (γ-GABA), the most important inhibitory neurotransmitter in CNS(10). Anti-GAD65 is one of the antibodies to the antigen in intracellular cytoplasmic of neuron. Patients may present with stiff man syndrome or cerebellar ataxia (11). Additional clinical presentations include temporal lobe epilepsy with cognitive behavioural features and type I diabetes. MR imaging demonstrates signal abnormality and swelling in the amygdala and hippocampus typical of limbic encephalitis (9). Multifocal CNS abnormalities are seen in a minority of cases (1). Anti GAD65 antibodies are also used in confirming the diagnosis of stiff-man syndrome, autoimmune encephalitis, autoimmune ataxia, brain stem encephalitis, autoimmune epilepsy, autoimmune myelopathy (2)

**Case Presentation**

This is a case of 24 Years old male patient who presented with complaints of high-grade fever(102-104oF) for 2 days and 1 episode of GTCS (generalised tonic clonic seizure) with post ictal drowsiness. Considering as infective etiology all the relevant investigations were done and patient was intubated as general condition of the patient was poor. Blood investigations and imaging of the brain did not reveal any abnormality apart from mild thrombocytopenia. Neurologist opinion was taken and CSF (cerebrospinal fluid) was drained through lumbar puncture. To our surprise apart from mildly increased protein all other parameters of CSF were within normal range. Patient was on ventilatory support for some time. Developed fever with new infiltrates on chest Xray – VAP (Ventilatory associated Pneumoniae). The blood culture grew Klebsiella - CRE. Responded to Ceftazidime-Avibactam & Aztreonam. The patient gradually regained consciousness and was extubated after 2 days.

The patient again had an episode of GTCS while he was on multiple antiepileptic medication, it was then that the suspicion of autoimmune disorder was considered and the relevant investigations were done. Anti GAD65 antibody came positive confirming the underlying autoimmune pathology (2). Meanwhile patient blood culture grew Klebsiella pneumoniae which was treated accordingly. Apart from positive Anti GAD65 antibody, no other investigation pertaining to diagnosis of fever with seizure was positive.

The patient was treated with Methylprednisolone (3), IVIG (Intravenous Immunoglobulin) (4) and Rituximab (Anti CD20 antibody) (5), to which the patient responded dramatically. Gradually the seizure episodes subsided and the antiepileptic medications were also cut down.

**Investigations**

**CSF (Cerebrospinal fluid)**

|  |  |  |
| --- | --- | --- |
| **Test description** | **Observed value** | **Reference limits** |
| Protein | **79** mg/dl | 10-40 mg/dl |
| Sugar | **84** mg/dl | 50-80 mg/dl |

**Discussion**

GAD65 is a crucial enzyme involved in the production of a neurotransmitter named GABA (Gamma-Aminobutyric Acid). GABA is the major inhibitory neurotransmitter in the CNS. There still is a lot unknown as to the role GAD65 antibodies play in neuroinflammation and their pathogenic role remains controversial; in addition, T-cell mediated immune response seem to be important in the pathogenesis of GAD65 encephalitis (6). Anti-GAD Ab is one of the most frequently detected antibodies in patients presenting with idiopathic drug-resistant epilepsy. Anti-GAD65 Ab titre in neurological condition often 100 times higher than type 1 diabetes (7).

While steroids, IV immunoglobulins, and plasmapheresis have been used to treat autoimmune encephalitis, comprehensive data regarding the efficacy of various treatment modalities are lacking, making treatment dependent not only on the clinician's expertise, but also on the patient's comorbidities (8).

**Conclusion**

Early diagnosis and timely initiation of immunotherapy are crucial for improving clinical symptoms and reducing the likelihood of relapses

**Consent**

Written informed consent was obtained from the patients for publication of this manuscript and accompanying images.

**COMPETING INTERESTS DISCLAIMER:**

**Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.**

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