Anti-GABA$_B$ Receptor Limbic Encephalitis

Case Report and Literature Review

Dhungana S, Nunez-Wallace KR, Van Hook C, Tarakad A, Abers MS, Kass JS
Baylor College of Medicine, Houston, TX

BACKGROUND

Anti-GABA$_B$ receptor limbic encephalitis is an uncommon cause of limbic encephalitis that presents with early and prominent seizures along with typical features of limbic encephalitis such as memory impairment and behavioral changes.[1] Antibodies targeted against the GABA$_B$ receptor were first identified in patients with limbic encephalitis by Lancaster *et al* in 2009. In this case series, 7 of 15 patients had an underlying neoplasm.[1] Frequent co-occurrence of other antibody types in these patients likely suggest a tendency to autoimmunity and possibly an anti-tumor immune response in those cases with an underlying neoplasm.[2]

CASE REPORT

A 29 year-old male was admitted with a two week history of new onset multiple generalized tonic-clonic seizures, headache, and cognitive and behavioral disturbances. He denied other neurologic or systemic symptoms. He had no significant past medical history, including no history of seizures. On exam, there were no meningeal signs. He was alert but confused and agitated and had difficulty cooperating. Cranial nerve function was intact. He had full strength in all muscle groups and sensation was normal throughout. Deep tendon reflexes were 3+ and symmetrical. Coordination and gait were normal.

Basic laboratory studies, including a complete blood count, metabolic panel, and ESR were normal. MRI of the brain showed FLAIR hyperintensity in the limbic region along with subtle leptomeningeal enhancement in the parieto-occipital region (Fig 1) . Diffusely slow background was noted on EEG. Cerebrospinal fluid (CSF) analysis demonstrated 37 WBC/mm^3 with 90% lymphocytes and protein 48 mg/dl. Glucose was normal and viral studies were negative.

Serum and CSF samples were sent for a limbic encephalitis work-up. High titers of antibody against the GABA$_B$ receptor was detected in both the serum and the CSF. CT chest, abdomen and pelvis and testicular ultrasound did not reveal an underlying neoplasm. PET scan was attempted on multiple occasions but was not possible because of patient's severe agitation.

Patient was initially treated with high dose intravenous steroids and plasma exchange, but showed no response to either. Subsequently, two doses of Rituximab (second dose at 2 weeks) were administered. He remained encephalopathic 3 months after initial presentation.

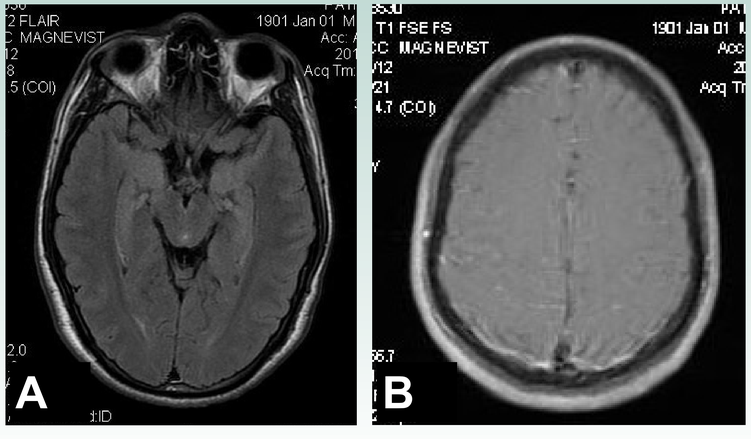

Figure 1. MRI brain.

A. T2 FLAIR sequence demonstrates ilateral limbic hyperintensities.
B. T1 sequence demonstrates parieto-occipital leptomeningeal enhancement.

DISCUSSION

CSF studies in limbic encephalitis usually show a lymphocytic pleocytosis and antibodies to either intracellular antigens (Hu, Ma2, CV2/CRMP5) or cell surface antigens (NMDA, AMPA, GABAB, LGI1, Caspr2).[2] Anti-GABA$_B$ receptor antibodies are found in only 5% of limbic encephalitis cases. These patients present with early and prominent seizures, and MRI is reported to be abnormal in 66% of cases, most with FLAIR hyperintensities in the medial temporal lobes.[2]

Our patient's clinical presentation and high titer of anti-GABA$_B$ receptor antibodies in the serum and CSF strongly suggest anti-GABA$_B$ receptor encephalitis. Leptomeningeal enhancement on MRI in our patient is atypical, although it has been reported in a recently published report.[3] We were unable to find an underlying neoplasm. In one series, an underlying malignancy was detected in one-third of patents, mostly small cell lung cancer.[2] Another recent study identified small cell lung cancer in 8 of 10 patients.[4] Given the frequent association of underlying malignancy, an exhaustive search for a neoplasm should be undertaken.

Anti-GABA$_B$ receptor limbic encephalitis that is managed with immunotherapy in addition to treatment of the underlying tumor often results in improvement. In a series of 15 patients, 7 of which had an underlying tumor, 9 patients responded to immunotherapy and/or treatment of the underlying tumor whereas 4 patients who received no treatment showed not improvement.[2] Although there are no guidelines on treatment of limbic encephalitis, high dose steroids, IVIG, and plasmapheresis are usually the first line agents with rituximab and other immunosuppressants reserved for patients who remain unresponsive.

CONCLUSION

Anti-GABA$_B$ receptor limbic encephalitis is uncommon. However, recognition of this condition as well as the other types of limbic encephalitis is important as prompt and aggressive treatment with immunotherapy and treatment of the underlying tumor can be effective. Further studies are required to help construct useful guidelines on treatment of the condition.

REFERENCES

[1] Lancaster et al. Antibodies to the GABA(B) receptor in limbic encephalitis with seizures: case series and characterization of the antigen. *Lancet Neurol* 2010; 9: 67-76.

[2] Lancaster E, Martinez-Hernandez E, Dalmau J. Encephalitis and antibodies to synaptic and neuronal surface proteins. *Neurology* 2011; 77:179-89.

[3] Goldenholz et al. Treatment of γ-aminobutyricacidB receptor-antibody autoimmune encephalitis with oral corticosteroids. *Arch Neurol* 2012; 69: 1061-3.

[4] Boronat A, Sabater L, Saiz A, et al. GABAB receptor antibodies in limbic encephalitis and anti-GAD associated neurological disorders. *Neurology* 2011; 76: 795-800.