Autoimmune epilepsy: clinical features, management and outcomes

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Background
• Despite increased recent research interest, no clear guidelines exist for the diagnosis or management of autoimmune epilepsy.
• Autoantibodies associated with encephalitides, as well as with epilepsy, include those directed against
  • Membrane antigens: anti-VGKC, anti-NMDA and anti-AMPA, anti-P/Q type VGCC and anti-GABA,  
  • Intracellular neuronal antigens: anti-Hu, anti-Ma2, anti-CPRM-5, etc.
• For the intracellular antigens, the pathophysiology of autoimmunity is T-cell mediated, rather than antibody-mediated as with surface antigen-related autoimmunity. Mechanism for encephalitides among patients with anti-GAD and anti-thyroid antibodies remain unclear.

Objective
• We hypothesized, earlier diagnosis as well as earlier treatment initiation would lead to better Responder Rate for autoimmune epilepsy patients.
• Additionally we evaluated the response to immunomodulatory therapy among patients with or without underlying malignancy.

Methods
• Retrospective chart review using data from two teaching hospitals (Parkland Memorial Hospital (PMH) and UT Southwestern University Hospital (UTSW) from January 2008 through December 2013.
• Cases included in the study were patients presenting with new onset seizure activity, plus at least two of the following:
  • Presence of CSF with inflammatory or infilterate of brain parenchyma (lymphocytic pleocytosis or elevated CSF protein > 50)
  • MR imaging showing signal changes consistent with encephalitis (mesial temporal FLAIR signal changes)
  • Presence of autoimmune/paraneoplastic antibodies in serum or CSF which have been associated with autoimmune encephalitides in previous studies (Hu, CRMP, VGKC, NMDA, AMPH, GABA, glycine, ANNA-1, 2, striatal, ACi, P/Q type calcium channel antibody).
• To respond to immunomodulatory therapies.
  • Cases were excluded if there was evidence of another identified cause of the patient's symptoms.
  • Presence of CSF viral/bacterial/fungal antigens or antibodies or DNA PCR which could explain underlying acute inflammatory brain parenchymal changes.
  • Presence of metastatic lesions which might have precipitated seizures (severe renal or hepatic failure, malignant hypertension, severe hyper/hypoglycemia).
  • Presence of brain structural lesions such as stroke, tumor, traumatic lesions, hypertensive mets, vascular malformation, infarct or infectious lesions which could have precipitated the present seizures.
• Cases selected based on inclusion and exclusion criteria that did not have a pre-specified antibody were further divided based on the presence or absence of high titers of TPO antibodies (>100 IU/ml).
• Clinical data was analyzed using SPSS 21 software. Categorical variables were analyzed using Chi Square.

Results
• 34 patients were included in the study. Mean age of patients was 44.94 years and 64.7% (22) of the patients were males.
• Electrographic seizures were documented in 64.7% (22) of patients in our institution. Twelve patients had clinical or electrographic evidence of seizures at an outside hospital.
• 22 had unilateral or 4 had bilateral temporal lobe onset, while 8 had extra-temporal onset/multiple ictal foci.
• 29.4% (10) patients had only electrographic seizures, without clinical correlate, while 44.1% (15) patients were discovered to have focal status epilepticus on VEEG monitoring.
• Median number of seizures during initial prolonged VEEG monitoring was 8 (range 0 to 48)
• Median number of anti-seizure medications used was 2 (range 1 to 5)
• 94.1% (31) patients received immunomodulatory therapies, including high dose corticosteroids (96.8%), plasmapheresis (62.5%), IVIG (34.4%), Rituximab (21.8%), mycophenolate (15.6%), cyclophosphamide (12.5%).
• Median time to clinic follow-up post discharge was 53.50 days (19 to 101 days).
• 63.3% (19) of patients had 50% reduction in seizure frequency at the first clinic visit following initial management of acute episode.
• 16 (17.6%) patients had complete resolution of seizures on initial clinical follow up.
• Patients without an underlying malignancy had a better RR (p>0.05).
• Time from symptom onset to EEG (U=56.00, p<0.05), symptom onset to CSF (U=56.50, p<0.05) and symptom onset to MRI (U=41.00, p<0.005) was significantly lower among patients who had a favorable Responder Rate.
• Duration of symptom onset to diagnosis (U=48.00, p<0.005) and duration of symptom onset to immunomodulatory therapy (U=43.00, p<0.005) was also significantly lower among patients who had a 50% reduction of seizures.
• Even following adjustment of baseline characteristics (age, gender, race, type of antibody) time from symptom onset to diagnosis (U=0.82-0.98, p<0.05) and time from symptom onset to immunomodulation (U=0.83-0.99, p<0.05) continued to be significantly lower in group showing clinical improvement.
• Patients with the VGKC antibody more commonly had MRI changes (78%) consistent with encephalitis, compared to those with NMDA-R antibody (28.5%) patients; this difference was statistically significant (p < 0.02).
• The type of autoimmune antibody (VGKC or NMDA) was not associated with a difference in RR.

Conclusions
• This study highlights important clinical aspects of autoimmune epilepsy.
• Early diagnosis is likely the most critical step for affected individuals, and the summarization of the common clinical and electrographic presentations provided herein may aid in that diagnosis.
• Our study demonstrates that timely initiation of immunomodulatory agents helps reduce seizure frequency.
• The patients without an underlying malignancy tend to respond better to such therapy.
• Future prospective studies will be necessary to determine the ideal immunomodulatory treatment regimen for patients based on clinical presentation and antibody type.

References