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Responsive Neurostimulation Therapy for Super-Refractory Autoimmune Epilepsy

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Background: Immunotherapy remains the cornerstone for treatment of autoimmune epilepsy; however, some remain super-refractory despite immunotherapy and anti-seizure medications (ASMs).

Methods: Case-series study of two patients with super-refractory AE treated with bilateral hippocampal responsive neurostimulation (RNS).

Results: Case 1: A 37 year-old woman presented with frequent (5-8/day) focal seizures with flushing and disabling chest pain of 4 years. Seizures are refractory to intravenous methylprednisolone and immunoglobulin and 9 ASMs. Serum autoimmune epilepsy panel was positive for Glutamic acid decarboxylase 65 (GAD65) antibody (250mg/dL). Brain MRI showed left mesial temporal sclerosis (MTS) and fluorodeoxyglucose positron emission tomography (fdg-PET) showed bitemporal hypometabolism. Evaluation for occult malignancy was negative. Bilateral independent temporal seizures were recorded. She was treated with RNS utilizing bi-hippocampal electrodes. Right hippocampal onset seizures were aborted within 8 weeks, however left hippocampal onset seizures were only reduced by 25%. At 18 months, she continued to experience seizures, albeit at reduced frequency.

Case 2: A 39 year-old woman presented with frequent focal and bilateral tonic clonic seizures. CSF was inflammatory but neuroimmunology panel was negative. Seizures are refractory to intravenous methylprednisolone and immunoglobulin, plasma exchange, Rituximab, Cyclophosphamide, and Azathioprine, 11 ASMs, and vagus nerve stimulation therapy. Brain MRI showed bilateral MTS. Screening for occult was unrevealing. Bilateral independent temporal seizures were recorded, and she was implanted with bi-hippocampal RNS electrodes. Within 8 weeks, seizure frequency was reduced by over 50%. Further, the RNS data disclosed catamenial clustering and led to the initiation of progesterone. At 6 months follow-up, she reported significant seizure reduction.

Conclusions: RNS has a role in the treatment of super-refractory autoimmune epilepsy. RNS helps track seizure burden objectively and may inform anti-seizure medication optimization in this patient population.

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Updated Data on the Tocilizumab Treatment in New Onset Refractory Status Epilepticus

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Background: New onset refractory status epilepticus (NORSE) is defined by new onset status epilepticus (SE), showing no response to at least 2 anti-epileptic drugs (AEDs) without evidence of other structural, toxic, or metabolic causes in patients who have been otherwise previously healthy. As no clear etiology has been established for NORSE, autoimmune or paraneoplastic causes account for the majority of NORSE cases with an identifiable cause. Even though immunotherapies including steroid, immunoglobulin, and rituximab have been tried to treat NORSE, approximately 60% of the patients had poor functional outcomes, suggesting need of the next line of immunotherapy. With updated data on the tocilizumab treatment in NORSE patients, we investigated the therapeutic potential of the tocilizumab, interleukin-6 receptor inhibitor, as new candidate of immunotherapy for NORSE.

Methods: In this study, updated data on two additional NORSE patients were analyzed to the previous data published. In a prospective cohort for autoimmune encephalitis since June 1, 2012, of which patients who have been admitted to Seoul National University, the patients who were diagnosed with NORSE with poor response to conventional immune therapy including steroid, immunoglobulin, and rituximab and treated with tocilizumab from August 2015 to November 2018 were subjected to further analysis.

Results: Compared to the previous data of 7 SE patients, 7 out of 9 SE patients showed cessation of SE with a median interval of 5 days from the initiation of treatment. According to our data, patients who responded to tocilizumab tended to show either clinical or electrophysiological improvement at most within the second cycle of treatment, which means early response to treatment. Two patients experienced infection as adverse event after tocilizumab treatment, and one patient on updated data showed no response to tocilizumab even after two cycles of treatment.

Conclusions: Tocilizumab treatment resulted in cessation of SE in 7 out of 9 patients according to our results. Therapeutic effects of tocilizumab on SE patients who do not show definite response to conventional immunotherapy are to be further studied with alternative immunologic pathway, and further prospective study with larger number of patients is warranted.

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Combination therapy of immunoglobulin, Rituximab, and Tocilizumab in treating acute autoimmune encephalitis

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Background: A considerable portion of autoimmune encephalitis (AE) does not respond to conventional immunotherapies and subsequently have poor outcomes. Tocilizumab, an anti- interleukin-6 antibody, has some effect on treating AE refractory to first-line immunotherapies and Rituximab. We aimed to determine the efficacy of the combination therapy of immunoglobulin (±steroid), Rituximab, and Tocilizumab (IsRT) in treating acute AE over conventional treatment options.

Methods: This institutional cohort included seventy-nine consecutive patients with antibody-proven AE. Acute treatment regimens were categorized as IsRT, IsR, and Is. Patients' clinical severity was assessed at every two weeks for the first three months, at every month for the next