Background

Management protocols for pediatric NMDARE increasingly recommend anti-CD-20 agents following first-line treatment with high-dose corticosteroids, intravenous immunoglobulin (IVIg), and/or plasma exchange therapy (PLEX). Even with early, aggressive treatment, some patients exhibit refractory disease or recurrences. Identification of clinical predictors for refractory disease course may allow earlier, targeted treatment escalation in these patients.

Design/Methods

We performed IRB-approved retrospective, descriptive review of patients in our institutional NMDARE database (2011-2021). Refractory disease was defined as lack of neurological improvement within 1-3 months, or recurrent relapse, after standardized treatment protocol (steroids, IVIg or PLEX, and two doses of rituximab 500 mg/m^2). Demographics, clinical information, and diagnostic results from refractory patients were collected.

Results

8/73 (10.9%) patients met criteria for refractory NMDARE (median age 10.0 years, IQR 8.3-14.0. 2 male, 6 female). Median days from symptom onset to first treatment was 12.5 (IQR 8.5-18.8), to detection of +NMDA Ab was 20.5 (17.8-24.0), and to rituximab was 27.5 (26.5-31.0). All were critically ill at disease onset, with seizures, encephalopathy, and respiratory failure. 2 (25%) had associated ovarian teratoma. Oligoclonal bands were tested in 6, with 4 resulting positive (67%). 7 had confirmed B-cell depletion after rituximab. Post-rituximab NMDA titers persisted in serum in 5 (63%) and CSF in 8 (100%). Immune therapy escalation was varied, and included repeat rituximab, mycophenolate, cyclophosphamide, and tocilizumab.

Conclusions

Severe initial presentation is a consistent feature among our refractory patients. The contribution of other factors such as oligoclonal bands and time to diagnosis/treatment are less clear, and warrant inter-group comparison with non-refractory patients. Persistence of serum and CSF titers despite B-cell depletion may suggest utility in targeting CD-20-negative mature plasma cells which may continue to produce disease-causing antibodies.

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Clinical Improvement Following Delayed Initiation of Immunotherapy in a Case of LGI1 Antibody Encephalitis Presenting with Faciobrachial Dystonic Seizures Following COVID-19 Vaccination

Kayla Martin, Matthew Creech, Michael Lane, Jacqueline Bernard

Objective

To demonstrate a case of suspected post-vaccine autoimmune encephalitis associated with leucine-rich glioma-inactivated protein (LGI1) antibodies with significant clinical improvement after initiation of immunotherapy nearly a year after symptom onset.

Background

Although the autoimmune encephalitides have overlap in presentation, some have unique manifestations (such as orofacial dyskinesias seen with NMDA encephalitis). These unique associations can serve as a clinical marker of response to treatment and even allow for earlier initiation of immunotherapy while awaiting results from antibody testing. LGI1 encephalitis characteristically presents with faciobrachial dystonic seizures (FBDS) that are refractory to anti-seizure medications (ASMs) but responsive to immunotherapy.

Design/Methods

Case report

Results

A previously healthy and highly independent 89-year-old woman developed what she described as abnormal posturing and spasms of the right shoulder two to three weeks after receiving the J&J COVID-19 vaccine. The abnormal movements progressed to involve the right side of her face and were refractory to multiple ASMs. EEG captured multiple events without epileptiform correlate. Several months later she developed paranoia, delusions, and hallucinations. Autoimmune encephalopathy panel returned positive for the LGI1-antibody around nine months after the onset of FBDS. Upon our initial exam, she had a fluctuating level of arousal, impaired recall of recent events, and was tangential in conversation. There were frequent, brief, repetitive, dystonic movements of the right side of the face consistent with FBDS. Admission was arranged for immunotherapy (intravenous methylprednisolone and intravenous immunoglobulin). Upon follow-up four weeks later, there was significant improvement in arousal and concentration with resolution of FBDS and delusions.

Conclusions

This case highlights a classic case of LGI1 encephalitis after vaccination presenting with FBDS and progressive cognitive changes. Despite immunotherapy being delayed, there was marked clinical improvement. It is important to recognize this entity and that it typically has a favorable outcome.

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Therapeutic Plasma Exchange in the Management of Stiff Person Syndrome Spectrum Disorders: A Case Series and Review of the Literature

Shuvro Roy, Nicolas Mercure-Corriveau, Danielle Obando, Yujie Wang, Laetitia Daou, Aaron Tobian, Evan Bloch, Scott Newsome

Objective

To describe the safety, tolerability, and response to TPE in patients with SPSD.

Background

Stiff person syndrome spectrum disorders (SPSD) are a rare group of disabling neuroimmunological disorders. SPSD often require immune therapies especially in the setting of inadequate response to symptomatic treatments. The safety and efficacy of therapeutic plasma exchange (TPE) in SPSD is unclear.

Design/Methods

A retrospective review of medical records for patients with SPSD seen at Johns Hopkins Hospital was performed. Patient characteristics, exam

findings, diagnostic studies, treatment response and TPE-related complications were recorded. We also conducted linear regression models to assess for possible predictive factors for TPE response. Literature review of SPSD and TPE was also conducted.

Results

Thirty-six SPSD patients were treated with TPE; mean age was 48 years, 81% female, and average anti-GAD65 antibody titer was 42352 U/mL (range, 0-309,902). Twenty-two patients had classic SPS, 10 had SPS-plus, and 3 had other phenotypes. Thirty-three patients were treated for acute exacerbations, and 3 were on maintenance TPE. There were 4 (11.1%) TPE-related complications (catheter infection, catheter thrombosis, hemorrhage), but no deaths or anaphylaxis. Twenty patients (55.6%) reported improvement in symptoms after TPE, 13 reported no change, and 3 reported worsening of symptoms. Of the 36 total patients who received TPE, 21 received TPE at Johns Hopkins Hospital for an acute exacerbation of their condition, with 12 requiring fewer anti-spasmodic medications 3 months after TPE treatment. There were no predictive factors in a positive treatment response to TPE. Literature review identified 42 more patients; 69% of these patients reported a temporary improvement in their condition.

Conclusions

We describe the safety and tolerability of TPE in patients with SPSD and show that TPE-related complications are uncommon and manageable. Additionally, many patients with SPSD derived improvement with TPE. Further studies could help inform clinicians when to use TPE in SPSD.

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Clinical and Paraclinical Features of Non-Paraneoplastic NIF-Mediated Disease Associated With Concurrent SARS-CoV-2 Infection

Lauren Schmidt, Jon Karel, Stefanie Rodenbeck

Objective

To describe clinical and paraclinical features of non-paraneoplastic NIF-mediated disease associated with concurrent SARS-CoV-2 infection.

Background

Neurologic syndromes associated with neuronal intermediate filament (NIF) immunoglobulin G (IgG) most often are characterized by encephalopathy, cerebellar ataxia, or myelopathy. NIF-IgG has been strongly correlated with the presence of an underlying malignancy, with neuroendocrine tumors being most prevalent. Despite the intracellular target of this antibody, patients with NIF-IgG mediated disease tend to improve clinically with immunotherapy. While some cases have been described in a parainfectious context, this is the first such case in the context of a SARS-CoV-2 infection.

Design/Methods

NA.

Results

We reported a case of non-paraneoplastic NIF-mediated disease in the setting of SARS-CoV-2 infection. The patient presented with first time seizure. He was found to have frequent left temporal lobe spikes then two left temporal lobe seizures on neurotelemetry. Brain MRI displayed abnormal signal throughout the left hippocampus and mesial temporal lobe, without contrast enhancement. LP was subsequently performed. CSF showed elevated protein, 14-3-3, T-tau, interleukin 13, interleukin 2 receptor, and interleukin 6. The meningitis/encephalitis panel, and HSV-1/2 IgG were negative. Serum autoimmune encephalitis panel revealed a high-positive titer for anti-NIF 1:960, with concurrent NIF heavy chain cell-based assay positive. He improved with three days of IV steroids and treatment with levetiracetam and lacosamide. He has since been seizure free.

Conclusions

NIF-mediated diseases usually present with encephalopathy, cerebellar ataxia, or myelopathy and are generally seen in the setting of malignancy. Our case illustrated an example of NIF-mediated disease presenting as seizure in the setting of infection. This highlights the importance of consideration of parainfectious autoimmunity.

Disclosure: Dr. Schmidt has nothing to disclose. Dr. Karel has nothing to disclose. Dr. Rodenbeck has nothing to disclose.

Real-World Utilization Patterns of Intravenous Immunoglobulin in Adults With Generalized Myasthenia Gravis in the United States

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Objective

To evaluate real-world utilization patterns of intravenous immunoglobulin (IVIg) among patients with generalized myasthenia gravis (gMG) over 3 years post-IVIg initiation.

Background

gMG is a rare autoimmune neuromuscular disorder with no known cure. Although IVIg is the most commonly used add-on therapy after standard of care treatments in gMG, it is currently unclear whether it is more commonly used as a "one-off" treatment to manage exacerbations, or as maintenance therapy aimed at reducing or replacing steroid use.

Design/Methods

Patients with gMG who initiated IVIg treatment were identified from a US claims database (Symphony Health, an ICON plc Company, Integrated Dataverse [IDV]®, January 1, 2014-December 31, 2019). The

Clinical and Paraclinical Features of Non-Paraneoplastic NIF-Mediated Disease Associated With Concurrent SARS-CoV-2 Infection

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