personal compensation in the range of $10,000-$49,999 for serving as a Consultant for Alexion. Dr. Bennett has received personal compensation in the range of $10,000-$49,999 for serving as a Consultant for Genentech-Roche. Dr. Bennett has received personal compensation in the range of $500-$4,999 for serving as a Consultant for TG Therapeutics. Dr. Bennett has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Reistone Bio. Dr. Bennett has received personal compensation in the range of $5,000-$9,999 for serving as a Consultant for Abbvie. Dr. Bennett has received personal compensation in the range of $0-$499 for serving as a Consultant for Novartis. Dr. Bennett has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Chugai. Dr. Bennett has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Mitsubishi Tanabe. Dr. Bennett has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Clene Nanomedicine. Dr. Bennett has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Roche. Dr. Bennett has received personal compensation in the range of $500-$4,999 for serving as an Expert Witness for Parker,Whiteford Taylor. Dr. Bennett has received personal compensation in the range of $5,000-$9,999 for serving as an Expert Witness for Podoll. Dr. Bennett has received personal compensation in the range of $5,000-$9,999 for serving as an Expert Witness for Hogan Lovells. The institution of Dr. Bennett has received research support from Novartis. The institution of Dr. Bennett has received research support from Alexion. Dr. Bennett has received intellectual property interests from a discovery or technology relating to health care. Dr. Bennett has received publishing royalties from a publication relating to health care. Dr. Alvarez has received personal compensation in the range of $10,000-$49,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Alexion. Dr. Alvarez has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Bayer. Dr. Alvarez has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for TG Therapeutics. Dr. Alvarez has received personal compensation in the range of $10,000-$49,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Biogen. Dr. Alvarez has received personal compensation in the range of $5,000-$9,999 for serving on a Scientific Advisory or Data Safety Monitoring board for EMD Serono. Dr. Alvarez has received personal compensation in the range of $50,000-$99,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Genentech. Dr. Alvarez has received personal compensation in the range of $50,000-$99,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Novartis. Dr. Alvarez has received personal compensation in the range of $10,000-$49,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Roche. Dr. Alvarez has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Sanofi. Dr. Alvarez has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Celgene. Dr. Alvarez has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for EMD Serono. Dr. Alvarez has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for GCSO. Dr. Gross has received personal compensation in the range of $5,000-$9,999 for serving as an Expert Witness for AP Expert Group. Dr. Shah has nothing to disclose. The institution of Dr. Kammeyer has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Genentech. The institution of Dr. Vollmer has received personal compensation in the range of $5,000-$9,999 for serving as a Consultant for Biogen IDEC. The institution of Dr. Vollmer has received personal compensation in the range of $10,000-$49,999 for serving as a Consultant for Genentech/Roche. The institution of Dr. Vollmer has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Siranax. The institution of Dr. Vollmer has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Celgene. The institution of Dr. Vollmer has received personal compensation in the range of $500-$4,999 for serving as a Consultant for EMD Serono. The institution of Dr. Vollmer has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Bristol Meyers Squib. The institution of Dr. Vollmer has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Viela Bios. The institution of Dr. Vollmer has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Novartis. The institution of Dr. Vollmer has received research support from Rocky Mountain MS Center. The institution of Dr. Vollmer has received research support from Biogen. The institution of Dr. Vollmer has received research support from Actelion. The institution of Dr. Vollmer has received research support from Genentech/Roche. The institution of Dr. Vollmer has received research support from Anokion. The institution of Dr. Vollmer has received research support from TG Therapeutics. Dr. Kedl has received personal compensation in the range of $10,000-$49,999 for serving as an Expert Witness for Vaccine Injury Compensation Program. Dr. Corboy has received personal compensation for serving as an employee of U of Coloado. Dr. Corboy has received personal compensation for serving as an employee of Rocky Mountain MS Center. Dr. Corboy has received personal compensation in the range of $5,000-$9,999 for serving as a Consultant for Mylan. Dr. Corboy has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Bristol Myers Squib. Dr. Corboy has received personal compensation in the range of $10,000-$49,999 for serving as an Editor, Associate Editor, or Editorial Advisory Board Member for AAN. Dr. Corboy has received personal compensation in the range of $10,000-$49,999 for serving as an Editor, Associate Editor, or Editorial Advisory Board Member for American Neurological Association. Dr. Corboy has received personal compensation in the range of $5,000-$9,999 for serving as an Expert Witness for Mylan. The institution of Dr. Corboy has received research support from MedDay. The institution of Dr. Corboy has received research support from Novartis. The institution of Dr. Corboy has received research support from NMSS. The institution of Dr. Corboy has received research support from PCORI. The institution of Dr. Corboy has received research support from EMD Serono. Dr. Hsieh has nothing to disclose. The institution of Dr. Piquet has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Genentech. Dr. Piquet has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Genentech. Dr. Piquet has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Alexion. The institution of Dr. Piquet has received research support from Rocky Mountain MS Center. The institution of Dr. Piquet has received research support from Novartis. The institution of Dr. Piquet has received research support from Abbvie. The institution of Dr. Piquet has received research support from Roche/Genentech. The institution of Dr. Piquet has received research support from NYU. Dr. Piquet has received publishing royalties from a publication relating to health care. 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Creation and Implementation of a Multi-Disciplinary Clinical Workflow Aimed at Earlier Diagnostic Evaluation for Autoimmune Encephalitis for Patients Presenting With Atypical Psychosis: A Pilot Study

Grace Russo, Gad Noy, Konstantin Stojanovic, Kiran Thakur

Objective

To implement a clinical workflow that facilitates earlier diagnostic evaluation for autoimmune encephalitis (AE) among patients presenting with atypical psychosis (AP).

Background

Clinical features found to have positive predictive value for AE were recently identified.[1] Early identification of "red flag" features was associated with a 58% reduction in time from symptom onset to AE diagnosis.[2] "Yellow flag" features, while less specific, were also associated with AE, especially when multiple were present simultaneously.[3] A workflow that utilizes these features would be of clinical significance.

Design/Methods

We created a standardized workflow to triage patients presenting to the psychiatric emergency department with AP using red/yellow flag features. The presence of one or more yellow flags (hyponatremia, first psychotic symptoms at age >40, systemic/infectious prodrome, refractory symptoms, and malignancy history) results in neurology consultation. Following the consultation, there may be a recommendation for more involved testing such as CSF studies, imaging, and/or EEG. The presence of a red flag (seizure, dysautonomia, movement disorder, or focal finding on neurologic exam) results in admission to the neurology service.

Results

Since the implementation of the workflow in February 2022, 5 patients have been identified. All patients received neurology consultation within 24 hours of presentation, after which 3 underwent diagnostic evaluation for AE.

Conclusions

The implementation of a multi-disciplinary clinical workflow to triage patients presenting with AP is feasible. Preliminary evidence suggests a significant decrease in time from presentation to diagnostic evaluation for AE compared to the time prior to its implementation.

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3. Herken, et al. (2017).

Two Cases of Isolated Neurofilament Heavy Chain Antibody Syndrome

Alexander Mirzoev

Objective

Novel clinical and laboratory findings in anti-neurofilament heavy chain encephalitis

Background

Antibodies to mature components of neuronal intermediate filament (NIF) have been implicated in several neurological disorders, including multiple sclerosis, amyotrophic lateral sclerosis, and more recently, various autoimmune encephalitides. The components include a-internexin, light chain and heavy chain. In the largest case series of anti-NIF syndromes (McKeon et al, 2021), patients' cell-based assays revealed antibodies to one, two or all three components. Heavy chain antibodies (anti-NfH) were present in most, including three out of four patients with encephalopathy and cerebellar involvement. One was due to a paraneoplastic phenomenon. Anti-NfH was also elevated in two cases of encephalopathy with spasticity. It was the lone autoantibody in one of the six aforementioned cases.

Design/Methods

N/A.

Results

Case 1: 37-year old female with a history of ovarian carcinoma, treated in 2016. Cognitive impairment started in fall 2019, with significant worsening to the point of catatonia and coma in October 2020. Though encephalopathy improved, severe ataxia and nystagmus persisted. Two MRI brain studies and an EEG were unremarkable, and no radiological evidence of cancer recurrence. Oligoclonal bands (in both CSF and serum) and serum anti-NfH were elevated. Case 2: 59 year-old female with gradual cognitive decline since March 2018, followed by rapid cognitive deterioration in Oct 2020. There was limb weakness, severe rigidity, clonus and a witnessed seizure. EEG showed intermittent rhythmic delta activity. MRI brain indicated severe bilateral hippocampal atrophy. CSF Protein and CSF anti-NfH were elevated.

Conclusions

This case series contains the first reported paraneoplastic encephalopathy with cerebellar involvement from isolated anti-NfH. Also presented is the first reported case of PERMS from any NIF antibody. Further research is needed on quantitative and qualitative factors of anti-NIF syndromes. Specifically, the clinical relevance of the number of antibodies, and associations between phenotype and specific antibody combination.

Disclosure: Dr. Mirzoev has nothing to disclose.

False Positive Cerebrospinal Fluid NMDA Receptor Antibodies: A Single Center Case Series

Rumyar Ardakani, Steven Vernino, Kyle Blackburn

Objective

To report the presence of CSF NMDA receptor antibodies in four patients without NMDA receptor encephalitis encountered at a single tertiary care center.

Background

The diagnosis and confirmation of anti-NMDA encephalitis relies heavily on detection of IgG antibodies to the NR1 subunit of the NMDA receptor in cerebrospinal fluid. While this is generally considered a highly specific test for anti-NMDA encephalitis, there have been rare reports of false positive testing.

Design/Methods

A retrospective chart review of medical records for patients with positive CSF NMDA receptor antibody testing at University of Texas Southwestern Medical Center between 2011 to 2021 was performed.

Results

40 patients were identified who had positive CSF NMDA receptor antibodies. Of these 40 patients, 4 (10%) were concluded to have false positive results. The false positive results consisted of 1 patient with refractory status epilepticus from suspected synthetic cannabinoid use, 1 patient with an anaplastic astrocytoma, 1 patient with fungal meningitis from Candida dubliniensis, and 1 patient with bifrontal cerebritis of suspected infectious etiology. Of the 4 patients with false positive antibody testing, 3 were immediately recognized as likely false positives while 1 patient was misdiagnosed and treated for an autoimmune encephalitis prior to a final diagnosis with tissue biopsy.

Conclusions

Although uncommon, false positive CSF NMDA receptor antibodies pose significant diagnostic and therapeutic challenges for clinicians. In our case series, false positive tests occurred in patients with apparent central nervous system disorders, including seizure, infection, and neoplasm. While antibody testing is an essential tool for the diagnosis of NMDA receptor encephalitis, caution should be exercised in interpreting positive results when the clinical and paraclinical data are not consistent with the well characterized phenotype of NMDA receptor encephalitis.

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