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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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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Treatment-Refractory Autoimmune Glial Fibrillary Acidic Protein Meningoencephalomyelitis in a Young Adult Female

Janetta Arellano, Michael Sy

Objective

To describe a case of autoimmune glial fibrillary acidic protein (GFAP) astrocytopathy refractory to immunotherapy without evidence of malignancy or coexisting autoimmunity.

Background

Autoimmune GFAP astrocytopathy is an autoimmune disease of the central nervous system associated with the presence of GFAP-IgG in the CSF. Patients may present with acute or subacute onset of headache, encephalopathy, seizures, abnormal vision, weakness or numbness, postural tremor and cerebellar ataxia. GFAP astrocytopathy is usually corticocorticosteroid-responsive in the acute setting but may rarely require maintenance immunotherapy to prevent relapse. Treatment refractory cases should trigger work up for coexisting autoimmunity or malignancy.

Design/Methods

A 35-year-old female patient presented with subacute meningoencephalomyelitis with prodromal symptoms.

Results

Her cerebrospinal fluid revealed lymphocytic pleocytosis and elevated protein. Brain magnetic resonance imaging (MRI) with and without contrast showed perivascular radial enhancement and periventricular T2 FLAIR hyperintensity. Spinal MRI with and without contrast demonstrated longitudinal T2 FLAIR hyperintensity from T1-T2 to T7-T8. Despite high dose steroid treatment, her disease progressed with an enlarging periventricular lesion and worsening visual acuity. Biopsy of the enhancing periventricular lesion showed perivascular inflammation. After five cycles of plasma exchange along with a five-day course of intravenous methylprednisolone 1 gram daily, her symptoms stabilized. The CSF autoimmune encephalopathy panel (Mayo Clinic Laboratories) came back positive for GFAP-IgG antibody on tissue immunofluorescence assay, and was confirmed positive by GFAP cell-based assay. No neoplastic disease was identified using high resolution PET/CT scans. Based on the aggressiveness of her disease, she received one cycle of cyclophosphamide, and was discharged home on an oral corticosteroid taper. Even one year after addition of both mycophenolate mofetil and rituximab, MRI imaging continued to reveal new enhancing lesions.

Conclusions

Autoimmune GFAP astrocytopathy may sometimes require long-term immunosuppression even without presence of malignancy or other coexisting autoimmune disease.

Disclosure: Dr. Arellano has nothing to disclose. The institution of Dr. Sy has received research support from NIH. Dr. Sy has received intellectual property interests from a discovery or technology relating to health care.

Autoimmune Encephalitis Misdiagnosis in Adults; A Multicenter Observational Study of Outpatient Subspecialty Clinics

Michael Geschwind, A. Sebastian Lopez-Chiriboga, Kyle Blackburn, Sanchit Turaga, Sophie Binks, Jennifer Zitser, Jeffrey Gelfand, Gregory Day, Steven Dunham, Stefanie Rodenbeck, Stacey Clardy, Andrew Solomon, Sean Pittock, Andrew McKeon, Divyanshu Dubey, Anastasia Zekeridou, Michel Toledano, Lindsey Turner, Steven Vernino, Sarosh Irani, Eoin Flanagan

Objective

To determine the diseases misdiagnosed as AE and potential reasons for misdiagnosis.

Background

Misdiagnosis of autoimmune encephalitis (AE) may harm patients.

Design/Methods

Patients with AE misdiagnosis were identified (1/1/2014-12/31/2020) from outpatient AE subspecialty clinics including: Mayo Clinic (n = 44); Oxford (n = 18); UT Southwestern (n = 18); UCSF (n = 17); Washington University (n = 6); University of Utah (n = 4). Inclusion criteria were adults (=18 years) with: 1) A prior diagnosis of AE; and 2) An alternative diagnosis made at a participating center. We collected data on clinical features, investigations, fulfillment of possible AE criteria, alternative diagnoses, and potential contributors to misdiagnosis.

Results

We identified 107 patients misdiagnosed with AE. Thirty (28%) fulfilled diagnostic criteria for "possible AE". Median onset age was 48 years (inter-quartile range, 35.5-60.5) and 65 (61%) were female. Correct diagnoses included: functional neurologic disorder, 27 (25%); neurodegenerative disease, 22 (21%); primary psychiatric disease, 19 (18%); cognitive deficits from comorbidities, 11 (10%); cerebral neoplasm, 10 (9%); and other, 18 (17%). Onset was insidious (>3 months) in 51 (48%). MRI brain was suggestive of encephalitis in 19/104 (18%) and CSF pleocytosis occurred in 16/84 (19%). Thyroid-peroxidase antibodies were elevated in 24/62 (39%). Positive neural autoantibodies were more frequent in serum (48/105[46%]) than CSF (7/91[8%]; p<0.001) and serum antibodies included: GAD65, 14; voltage-gated-potassium-channel-complex [LGI1, CASPR2 negative], 10; NMDA-receptor by cell-based assay only, 10 (6 negative in CSF); and other, 18. Immunotherapy adverse effects were observed in 17/84 (20%). Potential contributors to misdiagnosis included: over-interpretation of a non-specific positive serum antibody, 53 (50%); misinterpretation of functional, psychiatric, or non-specific cognitive dysfunction as encephalopathy, 41 (38%).

Conclusions

Red flags suggesting alternative diagnoses to AE include lack of fulfillment of "possible autoimmune encephalitis" criteria, positive non-specific serum antibody, and insidious onset. Avoiding AE misdiagnosis will prevent morbidity from unnecessary immunotherapies and delayed treatment of the correct diagnosis.

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