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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.

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

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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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