Results

She was diagnosed with autoimmune encephalitis and treated with IV methylprednisolone and IVIG. She rapidly improved clinically, and her imaging findings resolved.

Conclusions

We demonstrated prominent cerebellar imaging findings and good recovery in a patient with anti-GQ1b and mild anti-GAD65 seropositive autoimmune encephalitis. Our case is the first reported double positive autoimmune encephalitis with features of BBE and direct cerebellar involvement

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Active Immunization Against NMDA NR1 Subunit as a Model of Autoimmune Encephalitis

Grace Jachimiec, Negin Jalali Motlagh, Chih-Chung Lin, Enrico Kuellenberg, Jesús Planagumà, Gregory Wojtkiewicz, John Chen, Jenny Linnoila

Objective

To identify and develop the optimal active immunization induction method for NMDAR encephalitis in rodents.

Background

Encephalitis is a devastating neurologic disorder with high morbidity and mortality. Many cases are autoimmune. N-Methyl-D-aspartic acid receptor (NMDAR) encephalitis (NMDARE), characterized by antibodies against the NMDAR in the blood and spinal fluid of patients, is the most common form of autoimmune encephalitis (AE). A translational rodent model of NMDARE would allow for in-depth studies into AE pathophysiology, leading to advances in the diagnosis and treatment of this debilitating neuropsychiatric disorder.

Design/Methods

7-week-old female C57BL/6J mice were injected subcutaneously with an emulsion of complete Freund's adjuvant, attenuated Mycobacterium tuberculosis (TB), and a 30 amino acid peptide flanking the NMDAR NR1 subunit N368/G369 residue targeted by antibodies in NMDARE patients. Three different induction methods were tested by varying the amount and injection method of pertussis toxin, subcutaneous injection sites, reimmunization, and amounts of TB. Mice were bled biweekly and sacrificed at 2, 4, 6, 8, and 14 weeks. Serum and CSF NMDAR antibody titer; mouse behavior; hippocampal NMDAR protein and cluster density; and brain immune cell entry and cytokine content were examined.

Results

Immunized mice had serum and CSF NMDAR antibodies. Mice exhibited behavioral changes, altered hippocampal NMDAR protein, brain immune cell entry, and elevated cytokines in their brains. Titers were higher and changes were sustained in reimmunized mice.

Conclusions

Active immunization against the portion of the NMDAR targeted in patients with NMDARE resulted in robust production of NMDAR antibodies in the blood and spinal fluid, changes in hippocampal NMDAR protein, elevations in brain immune cells and cytokines, and behavioral changes in mice. Reimmunization was needed to sustain the responses. Active immunization therefore holds potential as a translational model of NMDARE, allowing for the creation of a novel generation of diagnostics and therapeutics.

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The Texas Children's Hospital Experience With Pediatric Anti-NMDAR Encephalitis: 2010-2021

Alexander Sandweiss, Yike Jiang, Tim Erickson, Timothy Lotze, Eyal Muscal, Kristy Murray

Objective

Our objective was to characterize the patients with anti-NMDAR encephalitis and identify the most common presenting symptoms and etiologies.

Background

Anti N-methyl-d-aspartate receptor (NMDAR) encephalitis is a specific autoimmune CNS disorder that decouples electrochemical synapses from their neuronal network, causing seizures, neuropsychiatric symptoms, movement problems, and autonomic dysfunction. Although well studied in the adult population, the clinical characteristics and potential triggers in pediatric cases of anti-NMDAR encephalitis are not well understood.

Design/Methods

We retrospectively analyzed patients with anti-NMDAR at Texas Children's Hospital (TCH) between 2010 and 2021, characterizing the demographics, presenting symptoms, and underlying etiologies.

Results

Of the 65 pediatric cases at TCH, our cohort is 65% female and 62% Hispanic, which is 1.6 times higher than the demographics of our TCH patient population and that of the Houston Metropolitan area at large (Harris County, 39% Hispanic). The average age of onset in our pediatric cohort was 7.2 years (range 3 months to 17.9 years). Post-herpetic NMDAR encephalitis and ovarian teratoma associated encephalitis made

up 12.8% and 4.2% respectively. Among the idiopathic NMDAR encephalitis group, the most common presenting symptom was focal weakness associated with altered gait and speech regression (39.6%), while 12% presented with isolated psychiatric symptoms. Within our cohort, 100% had behavioral/cognitive symptoms, 79% had seizures, 73% had speech problems, 67% had movement disorder, and 61% had memory deficits.

Conclusions

Our study describes the clinical characteristics which help define the presenting symptoms and potential etiologies in a heterogenous population from the largest single center pediatric cohort of anti-NMDAR encephalitis to date.

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A Case of Bilateral Sequential Optic Neuropathies With Pachymeningitis and Aortitis: Difficulty in Differentiating Erdheim-Chester Disease From IgG4-Related Disease

Tefani Perera, Erica McKenzie, Katayoun Alikhani

Objective

We describe a case of bilateral sequential optic neuropathies with pachymeningitis and aortitis, with findings that raised suspicion of Erdheim-Chester disease versus IgG-4 related disease.

Background

Erdheim-Chester disease (ECD) is a rare histiocytic neoplasm characterized by tissue infiltration by foamy histiocytes, and chronic, uncontrolled inflammation. IgG4-related disease (IgG4-RD) is an insidiously progressive immune-mediated fibrotic disease typified by tumour-like mass formation in many affected organs. Neurologic manifestations are diverse.

Design/Methods

A 58-year-old male was transferred to our centre for acute onset sequential optic neuropathies. His visual acuity was light perception for the right eye and 20/50 in the left eye.

Results

Enhanced MRI of the brain and orbits showed focal pachymeningeal thickening and enhancement in the anterior cranial fossa and over the left frontal lobe with eccentric enhancement of the right optic nerve sheath. CRP was elevated (23 mmol/L to 62 mmol/L); extensive CSF and serum infectious and inflammatory investigations were unrevealing. PET body demonstrated aortitis and CT angiography suggested coronary artery vasculitis. Bone scan showed symmetric involvement of the long bones. Dural biopsy was delayed due to the Covid-19 pandemic and was completed following a protracted steroid course and a 15 mg/kg dose of cyclophosphamide. Pathology showed mixed inflammatory infiltrate and increased expression of IgG4 neutrophils. Clusters of CD68+, CD1a, and S100-negative macrophages were seen in all layers of dura. No BRAF mutation was identified.

Conclusions

This case demonstrates classic imaging findings of ECD including pachymeningitis, symmetric long bone involvement and aortitis. Pathology in ECD may show characteristic foamy histiocytes, that were absent in this case. This case demonstrates the challenge of biopsy interpretation following immunosuppressive and cytotoxic therapy and the difficulty of differentiating ECD from IgG4-RD.

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Clinical Characteristics of Double SeroPositive Myasthenia Gravis

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Objective

This study aims to delineate the clinical phenotype of DSP-MG and assess the histopathological correlation with thymoma.

Background

Double SeroPositive Myasthenia Gravis (DSP-MG), a rare autoimmune disease that affects neuromuscular transmission, is characterized by antibodies against both AChR and MuSK receptors. This is the second study to be conducted in the world which attempts to define the clinical phenotype of DSP-MG patients.

Design/Methods

This is a retrospective case series conducted at a tertiary care hospital in South India conducted between February 2018 and October 2021. All patients who were diagnosed with DSP-MG based on typical clinical presentation and positive titres of both Anti- AChR and Anti-MuSK antibodies were included in the study.

Results

This study consisted of 13 DSP-MG patients (7 Females, Mean age-60.77 +/-14.24). The presentation was generalized in 9 patients, bulbar in 3 and ocular in 1 patient. Severity of the disease was assessed using the Modified Osserman System wherein 5 patients were Grade 4, 4 patients in grade 3, 3 patients in grade 2 while 1 patient was grade 1. The muscle groups affected first were the limbs (n = 6), ocular (n = 5), bulbar (n = 3) and respiratory (n = 1). MDCT done in 11 patients showed thymoma in five and thymic hyperplasia in 1. Four patients underwent thymectomy whose histopathology showed Type A, B2 (n = 2) and AB thymomas. Four patients had associated thyroid dysfunction and 3 patients were found to have developed MG post stroke. All 13 patients improved with Anticholinesterases, 9 patients were administered immunosuppressants, 3 patients were given IVIg and a single patient underwent plasmapheresis.

Conclusions

Our study shows that DSP MG is more similar to the clinical phenotype of AChR-MG, rather than MuSK-MG that has been previously defined in literature.

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