are important for early diagnosis of this disorder and appropriate treatment.

Disclosure: Dr. Manrique-Trujillo has nothing to disclose. Dr. Franada has nothing to disclose.

Do Anti-Epileptic Drugs Increase High Risk Comorbidity Amongst Patients With Neuro-Autoimmune Disease?

Mohsen Ahmed, Afaaq Ahmed, Ronak Trivedi, Muhammed Ors, Nabeel Ahmed, Kranthi Mandava, Nizar Souayah

Objective

To investigate the effects of anti-epileptic drugs (AED) on the overall burden of disease in patients with neuro-autoimmune disease (NAD).

Background

AEDs have shown to provide benefits against neurological damage in patients with various neurological illnesses. However, the extent of AEDs role in neuroprotection and the prevention of additional comorbidity in patients with NAD has not been completely characterized.

Design/Methods

A retrospective analysis on 34464 patients hospitalized at a tertiary care center in a major metropolitan area was conducted. 3997 patients were on AED medications, while 30467 patients were not taking any AEDs (nAED). 190 patients had a NAD diagnosis. Patients with NAD were classified according to use of AED or nAED (aAED and anAED). The outcomes compared included prevalence of neurological complications defined as either seizure, blurry vision, delirium, or altered mental status, encephalopathy, length of stay, ICU admission, comorbidity, and death.

Results

There was no significant difference in the prevalence of NAD between patients in AED or nAED (0.75%, 0.52%, $p > 0.05$). Among patients with aAED and anAED, there was no significant difference in length of stay (8.7, 7.8, $p > 0.5$), ICU admission (26.7%, 12.5%, $p > 0.05$), prevalence of comorbidities (56.7%, 52.5%, $p > 0.05$), or mortality (6.7%, 3.1%, $p > 0.3$). 36% of aAED and 16.3% of anAED had high risk comorbidity ($p < 0.05$). The prevalence of overall neurological complications was 37% and 10% among aAED and anAED, respectively ($p < 0.001$). Patients in aAED had significantly higher encephalopathy compared to anAED at 23% and 3.8%, respectively ($p < 0.0001$).

Conclusions

These results suggest that AEDs may be associated with an increase in high-risk comorbidities and neurological complications including encephalopathy among patients with NAD. Work is in progress to assess the contribution of the primary diagnoses for which AEDs were prescribed on the burden of NAD.

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Neuroinflammatory Disease Responsive to MEK-Inhibitor

Vicky Chen, Vijayshree Yadav, Ariane Soldatos, Yoon-Jae Cho, Avindra Nath, Desmond Brown, Eli Diamond, David Solit, Randall Woltjer, Christina Sayama, Jesse Winer, Emily Garavatti, McKinnon Garrett, Dhanalakshmi Angappan, Eugene Nicholson

Objective

Illustrate that some neuroinflammatory diseases may respond best to antiproliferative therapies rather than immunomodulatory therapies.

Background

Genomics are increasingly employed in the diagnostic armamentarium of refractory neuro-inflammatory diseases. Metagenomic next-generation sequencing is used to detect pathogens and germline genetic testing is used to detect inborn errors of the immune system. Genetic testing of tissue can identify somatic mutations for targeted treatment. MEK-inhibitors are an emerging treatment for RAS/MAPK pathway mutated diseases which include some neuro-inflammatory mimics like neuro-histiocytoses.

Design/Methods

NA.

Results

Previously healthy 12-year-old girl presented with 1 month of diplopia and headaches. Her brother has clinically diagnosed NF1 (café-au-lait macules, cutaneous neurofibromas). Exam notable for right third nerve palsy. MRI showed T2/FLAIR hyperintense lesions of the right temporal lobe, basal ganglia, and cervical through thoracic cord, nodular leptomeningeal enhancement along the entire spinal cord, and right middle cerebral artery vessel wall enhancement. CSF: WBC 6/mm^3 (62% lymphocytes 37% monocytes), protein 133 mg/dL. She improved with pulse methylprednisolone and maintenance steroids. At 5 months, she developed malignant elevated intracranial pressure with CSF OP >50 cm water, bradycardia, and encephalopathy requiring weekly LPs. Brain biopsy showed astrocytic and microglial activation without significant inflammation. No histiocytes were noted. There was no evidence of neoplasia or infection. She was tried on anakinra. At 6 months, she developed left third nerve palsy and seizures. For weeks, she required daily LPs for intracranial hypertension despite placement of ventriculoperitoneal shunt. Additional treatments included infliximab, steroids, and siltuximab. NGS from brain biopsy identified 2 NF1 mutations (nonsense, splicing). Allele fractions: 6% and 9%. Her mental status and need for frequent LP improved dramatically with trametinib.

Conclusions

This case illustrates the importance of considering somatic genomic testing of neural tissue even when the neuropathology is not suggestive of a malignancy or histiocytosis as this can inform newer molecularly targeted therapeutic options.

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Protective Association of HLA-DRB1*04 Subtypes in Neurodegenerative Diseases Implicates Acetylated Tau PHF6 Sequences

Guo Luo, Yann Le Guen, Adityasai Ambati, Selina Yogeshwar, Vicente Peris-Sempere, Jean-Charles Lambert, Michael Greicius, Emmanuel Mignot, AD/PD Collaborators

Objective

To explore genetic association between human leukocyte antigen (HLA) and neurodegenerative diseases and investigate mechanisms behind the association.

Background

Pathophysiology of Alzheimer's disease (AD), Parkinson's disease (PD) and amyotrophic lateral sclerosis (ALS) involves accumulation of tau (neurofibrillary tangles) and amyloid-ß-rich (amyloid plaques) aggregates in AD, a-synuclein-rich aggregates (Lewy bodies) in PD and TDP-43 aggregates in ALS, although these aggregates may also co-occur. Likewise, consensus is growing that tau may play a key role in PD and ALS as well.

Design/Methods

We analyzed HLA associations in ~176,000 individuals with PD or AD versus controls across ancestry groups. Pursuing this, we also compared postmortem brain density of neurofibrillary tangles and amyloid plaques in brain, tau and Aß42 levels in cerebrospinal fluid (CSF) of ~8,000 individuals (controls and AD), and examined association of HLA in ~2,500 patient with pathologically demonstrated Lewy Body Dementia. This was followed by HLA binding and tetramer T cell studies.

Results

A shared genetic association was observed across AD and PD at rs601945 (PD: odds ratio (OR) = 0.84; 95% confidence interval, [0.80; 0.88]; p = 2.2 x 10-13; AD: OR = 0.91[0.89; 0.93]; p = 1.8 x 10-22) and with a protective HLA association recently reported in ALS. Hierarchical protective effects of HLA-DRB1*04 subtypes best accounted for the association, strongest with HLA-DRB1*04:04 and HLA-DRB1*04:07, intermediary with HLA-DRB1*04:01 and HLA-DRB1*04:03 and absent for HLA-DRB1*04:05. The same signal was associated with decreased neurofibrillary tangle (but not neuritic plaque) density postmortem and was more associated with lower tau levels than Aß42 level changes in CSF. Furthermore, protective HLA-DRB1*04 subtypes strongly bound the aggregation-prone tau PHF6 sequence, but only when acetylated at K311, a modification central to aggregation. T cells recognizing this epitope were identified, showing relevance of this immune response in patients with neurodegenerative disorders.

Conclusions

An HLA-DRB1*04-mediated adaptive immune response, potentially against tau, decreases PD, AD and ALS risk, offering the possibility of new therapeutic avenues.

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Real-World Resource Utilization and Productivity Loss Among Patients With Myasthenia Gravis in Sweden: A Nationwide Population-Based Study

Qiaoyi Zhang, Qian Cai, Nurgul Batyrbekova, Lilla Di Scala, Shane Kavanagh

Objective

To assess annual healthcare resource utilization including inpatient admission and outpatient visits, employment status, and sickness absence associated with myasthenia gravis (MG).

Background

MG is a rare, chronic and debilitating autoimmune neuromuscular disease characterized by muscle weakness and fatigue that leads to hallmark symptoms including ptosis, dysphagia, dyspnea and limb weakness. Nearly 10% of patients are estimated to have treatment-refractory MG.

Design/Methods

Data were linked from four longitudinal nationwide population-based registries in Sweden. Patients with = 1 diagnosis of MG (ICD-10 G70.0) from 01/01/2001 to 12/30/2017 were selected. Date of 1st MG diagnosis in the national patient register was designated as index date. The healthcare resource use, employment status, and sickness absence for all cause and associated with MG within 1-year post-index period were evaluated.

Results

A total of 4,339 patients with newly diagnosed MG were identified from 2001 and 2017. Mean (±SD) age at index date was 59.8 (±19.5) years; 54% were female. During the first year post-MG diagnosis, 50.6% of patients) had = 1 MG-related inpatient admission and 23.6% spent >1 month as an inpatient. Most patients (89.3%, n = 3,875) had = 1 specialist visits for MG and 16.1% had >5 visits during 1-year post-index period. 58.9% of patients had = 1 all-cause inpatient admission and 97.5% of patients used = 1 outpatient specialist services in the same period. Among patients of working age with =1-year follow-up (n = 2,006), 37.3% of them were not employed; among those in employment (n = 1,250), 44.6% reported = 1 sickness absences within 1-year post-index period.

Conclusions

Patients with MG require considerable care both for MG and comorbidities over a period of years. An important sub-population of patients (e.g., those with MG crisis) may be the intensive users of both inpatient and outpatient care. Future research needs to detail treatment pattern and outcomes in this population.

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Anti-myelin Oligodendrocyte Glycoprotein Antibody-Associated Disorder (MOGAD) in a Pediatric Patient with Rare Presentation of a Cerebellar Tumefactive Lesion

Avni Sanghi, Grace Gombolay, Tuba Khan

Objective

NA.

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