Design/Methods

This retrospective, single-center (AIMS, Kochi, India) cohort study included 60 adult patients with autoimmune encephalitis who were first admitted from August 2016 till November 2021. We used a univariate binary logistic regression for the entire cohort (n = 60) or the cohort of seronegative cases (n = 54) and a two-tailed Fisher's exact test for a small group of seropositive cases (n = 6). A Chi-square test was performed to describe the results in rare cases if logistic regression failed to work.

Results

In the entire cohort (n = 60) a statistically significant association was found between a good fast treatment response and a total count of cells in the CSF more than 4 cells/mm^3 (OR 4.571, 95% CI 1.31–15.956, p = 0.017), IgG Local Synthesis (OR 7.273, 95% CI 1.562–33.863, p = 0.011), and Integrative Parameter of Local IgG Synthesis proposed by Ziadie M. et al. (OR 5.318, 95% CI 1.271–22.250, p = 0.022). Good fast response was defined as an improvement with single agent from the first line therapy by mRS-9Q of at least 3 points in case of severe disease and at least 2 points in case of moderately severe disease at the time of discharge. Higher Albumin Index values associated with higher odds of having poor GCS Score (OR 1.165, 95% CI 1.011–1.343, p = 0.035). In the cohort of seronegative cases (n = 54) we obtained similar results. In the cohort of seropositive cases (n = 6), none of the patients had a good fast response.

Conclusions

In our research, evidence of Local IgG Synthesis in CNS and CSF total cell count more than 4 cells/mm^3 showed association with a good and fast treatment response in patients with autoimmune encephalitis.

Disclosure: Miss Popova has nothing to disclose. Mr. Nair has nothing to disclose. Dr. Mathai has nothing to disclose. Ms. Sasikumar has nothing to disclose. Siby Gopinath has nothing to disclose. Dr. Nambiar has nothing to disclose. Dr. Kumar has nothing to disclose. Dr. Saraf has nothing to disclose. Mrs. Leelamaniamma has nothing to disclose. The institution of Dr. Kannoth has received research support from Novartiz.

Recurrent Acute Necrotizing Encephalopathy with underlying RANBP2 mutation

Dhanalakshmi Angappan, Christopher Hollen

Objective

N/A.

Background

Acute necrotizing encephalopathy (ANE) is a rapidly progressive encephalopathy that can occur in otherwise healthy children after common viral infections such as influenza and parainfluenza. Most ANE is sporadic and nonrecurrent (isolated ANE). We report a case of recurrent acute necrotizing encephalitis in a boy with an identified RANBP2 mutation, which is known to account for the majority of recurrent ANE cases.

Design/Methods

CASE REPORT Our patient is a 13-year-old boy with no significant medical or developmental history and no family history of neurodevelopmental disorders.He had his first episode at 15 months of age-which manifested as irritability, non-responsiveness and was diagnosed as acute disseminated encephalomyelitis (ADEM) and subsequently had 4 additional episodes of ANE at ages 4,4.5,5, and 10. After his third episode, testing for RANBP2 was performed and found to be positive. His typical presentation includes fever, staring spells, nystagmus and altered sensorium during these episodes typically within 24 hours of febrile-illness. He has had multiple triggering viral infections identified including adenovirus, influenza A and parainfluenza. Ultimately his ANE episodes were managed with iv pulse steroid therapy and IVIG.With treatment he has had a slow but nearcomplete recovery, including radiological resolution. He does have mild cognitive impairment and learning difficulties which have persisted.

Results

N/A.

Conclusions

This patient has had numerous episodes of ANE triggered by infection that have responded well to acute management without prophylactic immunomodulation. This is, to our knowledge, themost non-fatal recurrences that have been reported with this condition. Our case suggests that multiple relapses are possible in patients with ANE and early diagnosis and treatment of the episodic encephalopathy would result in improved outcomes. Our case raises the consideration of prophylactic immunotherapy but also demonstrates a relatively positive outcome with a watchful management approach. Keywords: acute necrotizing encephalopathy.

Disclosure: Dr. Angappan has nothing to disclose. Dr. Hollen has nothing to disclose.

Primary Immune Dysregulation in Subacute Sclerosing Panencephalitis: A Case-Control Study

Vijay Varman, Vinay Suresh, Hardeep Malhotra, Neeraj Kumar, Ravindra Garg

Objective

The primary objective was to study the pattern of immune dysregulation in cases with subacute sclerosing panencephalitis (SSPE). The secondary objective was to assess the correlation between the measured immunological variables and disability/death at 6 months,

Background

SSPE is a chronic progressive neurological condition caused by a defective measles virus. It is postulated that immune-dysregulation might result in persistent infection (immune evasion) as well as initiation of autoimmune phenomenon (via natural killer cells) leading to panencephalitis.

Design/Methods

This was a prospective observational study conducted at a tertiary-case referral-facility from January 2020 to September 2021. Thirty consecutive patients fulfilling the Dyken's criteria for SSPE and 30 age-and-sex-matched healthy controls were enrolled. Immunological profile constituted by lymphocyte subset analysis, immunoglobulin levels and complement levels were done in all cases and controls. Cases were staged as per Jabbour's system; disability was assessed using the modified Rankin Scale (mRS).

Results

Patients with SSPE had a mean age of 14.76 years (± 6.9 years). There were 25 males and 5 females; 6.7% cases belonged to Jabbour's first stage, 40% to second stage and 53.3% to third stage. Levels of absolute lymphocyte count, B-cells, T cells, helper T-cells and cytotoxic T-cells were significantly higher in cases. IgG, IgM and IgE levels were significantly higher while IgD levels were significantly lower in cases. At baseline, 13.3% of cases had a mRS score of 0-2 and 86.7% had a score of 3-6; at 6 months 10% had a mRS score 0-2 (favorable outcome) while 90% had a mRS score 3-6 (poor outcome). No correlation of immunological parameters with outcome was found.

Conclusions

Significant immune dysregulation in terms of lymphocyte subsets and immunoglobulin levels seem to exist in SSPE. These findings may pave way for targeted immunomodulator therapy that can be targeted in a larger cohort of patients.

Disclosure: Mr. Varman has nothing to disclose. Mr. Suresh has nothing to disclose. Dr. Malhotra has nothing to disclose. Dr. Kumar has nothing to disclose.

Dr. Garg has received intellectual property interests from a discovery or technology relating to health care. Dr. Garg has received intellectual property interests from a discovery or technology relating to health care.

Rank Wise Effect of HLA-DQ5 Explains Risk for the Development of Anti-IgLON5 Disease

Selina Yogeshwar, Vicente Peris-Sempere, Sergio Muñiz-Castrillo, Guo Luo, Carsten Finke, Jerome Honnorat, Emmanuel Mignot, Anti-IgLON5 Disease Collaborators

Objective

To better characterize the genetic association between human leukocyte antigen (HLA) and anti-IgLON5 disease and to explore auto-antigen binding to associated HLA molecules and their functional involvement in pathophysiology.

Background

Anti-IgLON5 disease is a rare, but likely underdiagnosed type of autoantibody encephalitis with a heterogeneous clinical phenotype, including sleep, movement and brainstem dysfunction. Its pathophysiology remains elusive, although dominant association with HLA-DRB1*10:01-DQB1*05:01 strongly supports an autoimmune basis.

Design/Methods

A multicentric cohort of 62 patients and 433 controls matched by principal component analysis was included. Genome-wide association analysis was performed with 4-digit resolution HLA imputation and selected 8-digit resolution validation typing. A generalized logistic model was used to determine the association with individual alleles and haplotype counts to establish haplotype associations. Furthermore, we computationally predicted binding of IgLON5-derived peptides to risk-associated HLA-molecules.

Results

Our results indicate a rank wise effect of HLA-DQA1*01:05~DQB1*05:01 (heterozygotes: OR 46.6), HLA-DQA1*01:01~DQB1*05:01 (homozygotes: OR 26.9; heterozygotes: OR 2.5) and HLA-DQA1*01:04~DQB1*05:03 (homozygotes: OR 30.9; heterozygotes: OR 5.6), in order of descending relative risk predisposition. Differences between encoded heterodimers are minimal (a few amino acids outside the main HLA sequence binding region), suggesting a common function. Computational binding predictions support similar, high binding affinity for IgLON5275-283 in a post-translationally modified (N-deglycosylated) form by all three of these HLA-DQ molecules and other common binders. In contrast, association analysis suggests that effects of HLA-DR are likely explained by linkage disequilibrium.

Conclusions

This study is the, so far, largest genetic study on anti-IgLON5 disease. Our results strongly suggest HLA-DQ over HLA-DR association, with higher reactivity against post-translationally modified versus physiological peptides, in line with reduced T cell priming against these epitopes. Further studies should address the functional implications of these HLA associations.

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Cohort Study of Autoimmune Encephalitis (AIE) in Pediatric and Adult Population from India-A Single Tertiary Centre Experience

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Objective

Study and compare clinico-epidemiological data and long-term outcomes in pediatric (<18 yrs) and adult AIE patients based on serostatus.

Background

India is a burgeoning hub for autoimmune diseases. Studies on AIE comparing seropositive and seronegative outcomes in pediatric and adult population are lacking. We highlight age and serostatus specific approach in low resource country settings.

Design/Methods

Retro-prospective study from Narayana Institute of Neurosciences, Bangalore (2016-2021) included AIE patients as per Autoimmune Encephalitis International Working Group and Autoimmune Encephalitis Alliance Clinicians Network. Serum and CSF autoimmune encephalitis panels, CSF meningitis panel was incorporated to exclude infections and other demyelinating disorders. With phone calls and outpatient follow ups (1-4 yrs), results were statistically analyzed and compared based on age and serostatus.

Results

Adult AIE was commoner than pediatric (75% vs 25%,n = 60) and seronegative than seropositive (56.7% vs43.3%) with overall male preponderance. NMDAR (11.7%), MOG (8.3%), LGI1 and GAD65 (5% each) were common antibodies (MOG commoner than NMDAR in children; NMDAR, LGI1 and GAD 65 equally predominant in adults). Common presentations included seizures (75%) and memory disturbances (66.7%) independent of serostatus. There were no differences in MRI and EEG parameters based on age or serostatus. Methylprednisolone mono-therapy (46.6%) was multitude than add on rescue immunosuppressants [IVIG (28.3%),rituximab (10%), PLEX & cyclophosphamide (3.3% each)]. Pediatric age, specific antibodies, status epilepticus and dysautonomia were markers requiring aggressive immunotherapy. Oral steroids (61.7%),mycophenolate (8.3%)and azathioprine (6.7%) were maintenance immunosuppressants. 10% patients (mostly seropositive) had poor outcome with Modified Rankin Scale (MRS) >3. Deaths (all adults) though rare was slightly preponderant in seronegative type owing to lack of consent for aggressive immunosuppression. Clinical relapse was noted in 10% (mostly seropositive). 86% patients were weaned off maintenance immunosuppression (earlier in seronegative).

Conclusions

Seronegative and pediatric AIE had better long term outcomes. Methylprednisolone mono-therapy is efficacious in majority of the cases when started early. Early recognition and aggressive management in high risk groups has pivotal role. Further multi-centric studies are needed to confirm these findings.

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