Research Article

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A Prospective Study to Evaluate Neurological Antibodies in Patients with Autoimmune Encephalitis: An Experience from a Specialised Immunology Laboratory

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Abstract

Objectives: *The objective of this research is to evaluate the incidence of various antibodies against neuronal antigens along with concomitant clinical correlation.*

Materials and Methods: *A prospective study was conducted in the department of immunology with a study duration of 1.8 years (Jan 2021 to August 2022). A total of 330 samples were tested for autoimmune encephalitis panel using indirect cell-based immunofluorescence technique. All cases reported with a positive antibody were discussed with their clinical presentation.*

Results: *A total of 28 cases were reported positive, of which fifteen were females and thirteen males. The age range was 5-78 years with median age of 41.5 yrs. Of these 28 cases, 22 were positive on testing serum while 6 were positive with cerebrospinal fluid (CSF) samples. Out of the total 28 samples, 21 were positive for antibodies against NMDAR, three for CASPR, two for LGI1 and one for AMPA. There were 2 cases with concomitant positivity for both CASPR and LGI1.*

Conclusion: *There is still much need for exploration and research in this fascinating group of entities. Sound clinical approach and a necessity to be on the lookout for unexplained clinical symptoms, multifocal lesions on imaging and behavioural abnormalities in order to suspect and diagnose these patients and provide timely treatment.*

Keywords: Autoimmune Diseases, Encephalitis, Fluorescent Antibody Technique

Key Points

1. Autoimmune encephalitis is a rare and unusual neurological condition with presence of several abnormal antibodies to neuronal antigens.
2. Early detection of these antibodies is pivotal in commencing immunotherapy and improving patient survival.
3. NMDAR antibodies was the most common antibody present in our study with patients presenting with wide variety of clinical symptoms.

Introduction

Autoimmune encephalitis (AE) is a type of encephalopathy mediated by an antigenic immune response in the central nervous system and is the third most common cause of encephalitis followed by infectious encephalitis and acute disseminated encephalomyelitis [1]. AE is a serious disease characterised by seizures, mental disorders, and clinical cognitive decline [2]. Recent epidemiological studies suggest that AE is possibly as common as infectious encephalitis with an estimated prevalence rate of 13.7/100,000 [3].

Materials and Methods

A prospective study was conducted in our department of immunology with a study duration of 1.8 years (Jan 2021 to August 2022). A total of 330 samples were tested for autoimmune encephalitis panel using indirect cell-based immunofluorescence technique which uses specific transfected cells (EU 90) as standard substrates for the monospecific detection of neuronal antibodies. The kit used for evaluation is manufactured by EUROIMMUN which provides detection of antibodies against glutamate receptors (type NMDAR, AMPA1, AMPA2, AMPA1/2), contactin-associated protein 2 (CASPR2), leucine-rich glioma-inactivated protein 1 (LGI1), dipeptidyl aminopeptidase-like protein 6 (DPPX) and GABAB receptor (GABARB1/B2).

Clinical correlation for all positive cases where information was available on the Test Request Form (TRF) was done and the results were evaluated using standard statistical measures. Consent was taken for all samples tested at our laboratory and approved by ethical committee.

Results

A total of 28 cases were reported positive, an incidence of 8.4% (28 out of 330 cases), of which fifteen were females and thirteen males. The age range was 5-78 years with median age of 41.5 yrs. Of these 28 cases, 22 were positive on testing serum while 6 were positive with cerebrospinal fluid (CSF) samples. Out of the total 28 samples, 21 were positive for antibodies against NMDAR, three for CASPR, two for LGI1 and one for AMPA antibodies. (Figure 1) There were 2 cases with concomitant positivity for both CASPR and LGI1 antigen. We did not experience any samples with GABA and DPP6 positivity.

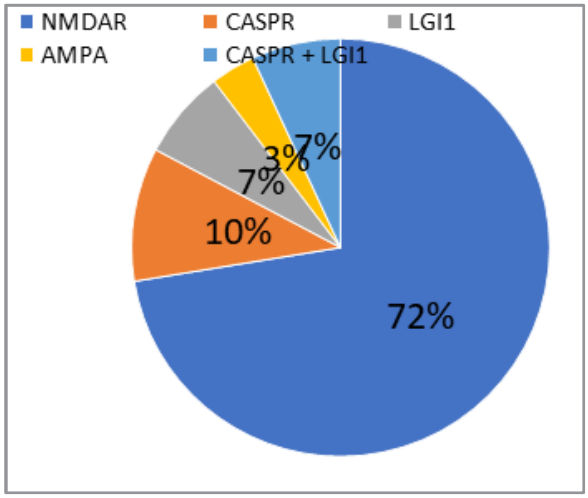

Figure 1: Pie-diagram showing distribution of antibodies against various antigens in our patient samples

NMDAR Positivity- Antibodies against NMDAR antigen was the most common finding in our setting (Figure 2). Patients with positive status had varied and overlapping symptoms which ranged from fever, refractory and non-refractory seizure disorders including status epileptics, behavioural abnormalities, headaches, altered sensorium, motor aphasias, dystonia along with confusion and even unusual and unreported rapidly progressive dementia and ataxia were noted.

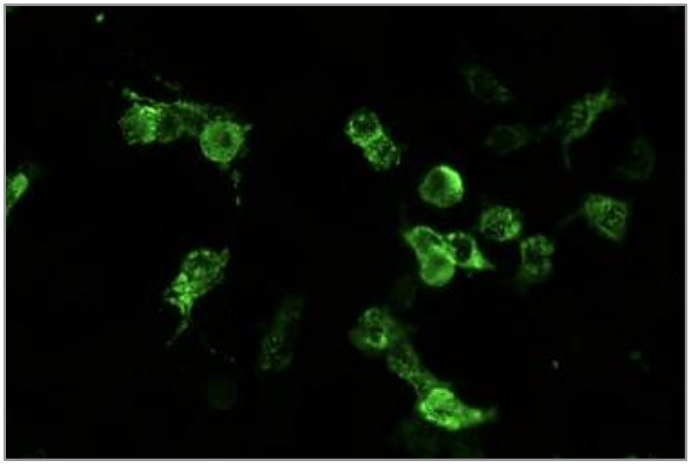

Figure 2: Immunofluoresence microscopic photograph, 400x magnification- Positive NMDAR antibodies with strong staining of transfected cells and its cell processes.

On the contrary, of the two cases that were positive for CASPR, patient had lumbar spondylosis and bilateral periventricular and subcortical leukoaraiosis respectively.

LGI1 Positivity- Antibodies against LGI1 was seen in 2 cases wherein one patient was a suspected case of viral encephalitis with an unremarkable CSF analysis.

Patient with AMPA positivity had normal CSF findings, was on acyclovir and antibiotics with history of SARS-Cov-2 infection 6 months ago. Patient also had hyponatremia and residual lung disease due to long standing history of smoking. He presented with an ischaemic stroke in the right hippocampus region with GCS of 8.

Discussion

Clinical presentation has mainly been classified by type; types include mental symptoms, epileptic seizures, motor disorders, language disorders, sleep disorders, autonomic nervous dysfunction and ventilation disorders [4]. The duration of the disease could be several months or more, which is costly, and the lesions often involve the limbic system, mainly the cingulate gyrus, hippocampus and frontal lobe. The pathogenesis of AE is not clear. Previous studies have shown that AE is associated with viral infections, tumours or autoimmunity [5].

The patients with anti-NMDAR encephalitis are mostly women with an average age of onset of 21 years. Approximately, 70% of the patients had presymptomatic headaches, fever, vomiting, diarrhea, and upper respiratory tract infections. The typical manifestation is the neuropsychiatric symptoms in the early stage, followed by progressive worsening of cognitive dysfunction and confusion. There was presence of partial or complete seizures during the disease (even status epilepticus), which might be refractory epilepsy, and the antiepileptic drugs were generally ineffective but the response improved after receiving immunotherapy [6].

Elevated IL-6 which is known as a common feature of the disease during the inflammatory phase can be a linking factor due to its role in facilitating autoantibody production in anti-NMDAR encephalitis. Overproduction of inflammatory cytokines seems to affect blood-brain-barrier (BBB) integrity, increase its permeability, and lead to viral transmission through BBB [7].

A detailed history and examination is the first and most important step in AE diagnosis. The immune reaction in AE often results in acute or subacute presentation of a duration less than 3 months. Chronic presentations are only seen in some of these conditions, especially LGI1, CASPR2 & DPPX. A preceding viral infection, fever or viral-like prodrome is common [8].

Conclusion

Antibody-mediated neurological diseases are a rapidly growing group of variable clinical entities with multifaceted manifestation and often profound response to treatment. The underlying autoantibodies directly confer pathogenicity by targeting single ion channels or receptors responsible for brain function. The diverse mechanisms of disease include antibody-mediated receptor internalisation, complement activation, disrupted protein–protein interaction and signaling. The far-reaching clinical and scientific implications relate to emerging evidence that humoral autoimmunity participates in a much larger spectrum of neurological diseases [9].

There is still much need for exploration and research in this fascinating group of entities. Sound clinical approach and necessity to be on the lookout for unexplained clinical symptoms, multifocal lesions on imaging and behavioural abnormalities in order to suspect and diagnose these patients and provide timely treatment.

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References

1. Rutatangwa, A., Mittal, N., Francisco, C., Nash, K., & Waubant, E. (2020). Autoimmune Encephalitis in Children: A Case Series at a Tertiary Care Center. Journal of child neurology, 35(9), 591–599. https://doi.org/10.1177/0883073820923834
2. Dalmau, J., Tüzün, E., Wu, H. Y., Masjuan, J., Rossi, J. E., Voloschin, A., Baehring, J. M., Shimazaki, H., Koide, R., King, D., Mason, W., Sansing, L. H., Dichter, M. A., Rosenfeld, M. R., & Lynch, D. R. (2007). Paraneoplastic anti-N-methyl-D-aspartate receptor encephalitis associated with ovarian teratoma. Annals of neurology, 61(1), 25–36. https://doi.org/10.1002/ana.21050
3. Heine, J., Prüss, H., Bartsch, T., Ploner, C. J., Paul, F., & Finke, C. (2015). Imaging of autoimmune encephalitis--Relevance for clinical practice and hippocampal function. Neuroscience, 309, 68–83. https://doi.org/10.1016/j.neuroscience.2015.05.037
4. Seniaray, N., Verma, R., Ranjan, R., Belho, E., & Mahajan, H. (2021). 18F-FDG PET/CT in Initial Diagnosis and Treatment Response Evaluation of Anti-NMDAr and Anti-GAD Dual Antibody Autoimmune Encephalitis. Clinical nuclear medicine, 46(1), e63–e64. https://doi.org/10.1097/RLU.0000000000003379
5. Barbagallo, M., Vitaliti, G., Pavone, P., Romano, C., Lubrano, R., & Falsaperla, R. (2017). Pediatric Autoimmune Encephalitis. Journal of pediatric neurosciences, 12(2), 130–134. https://doi.org/10.4103/jpn.JPN_185_16
6. Sarosh, R. Irani., Katarzyna B., Patrick W., Luigi Z., Susan M., Michael, S. Zandi., & Angela, V., (2010)“ N-methyl-d-aspartate antibody encephalitis: temporal progression of clinical and paraclinical observations in a

predominantly non-paraneoplastic disorder of both sexes. Brain, 133(6), 1655–1667.
7. Achar, A., & Ghosh, C. (2020). COVID-19-Associated Neurological Disorders: The Potential Route of CNS Invasion and Blood-Brain Relevance. Cells, 9(11), 2360. https://doi.org/10.3390/cells9112360
8. López-Chiriboga, A. S., & Clardy, S. L. (2017). Emerging Subspecialties in Neurology: Autoimmune neurology. Neurology, 89(11), e129–e133. https://doi.org/10.1212/WNL.0000000000004356
9. Haselmann, H., Mannara, F., Werner, C., Planagumà, J., Miguez-Cabello, F., Schmidl, L., Grünewald, B., Petit-Pedrol, M., Kirmse, K., Classen, J., Demir, F., Klöcker, N., Soto, D., Doose, S., Dalmau, J., Hallermann, S., & Geis, C. (2018). Human Autoantibodies against the AMPA Receptor Subunit GluA2 Induce Receptor Reorganization and Memory Dysfunction. Neuron, 100(1), 91–105.e9. https://doi.org/10.1016/j.neuron.2018.07.048