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ENCEPHALOPATHY WITH BEHAVIORAL AND PSYCHIATRIC FEATURES—FIRST ANTIBODY PROVEN CASE OF ANTI-NMDA RECEPTOR ENCEPHALITIS FROM PAKISTAN

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ABSTRACT

Background: Anti-N-methyl-D-aspartate (NMDA) receptor encephalitis is associated with psychiatric symptoms, memory disturbances, seizures, dyskinesia, and catatonia along with other constellation of symptoms. It is more common in females and usually associated with underlying ovarian teratoma. Treatment involves immunosuppression. This is the first antibody proven case from Pakistan. **Case Report:** A 16 year old girl with a short history of sore throat and no other prior illness, presented with 12 day history of behavioral changes (can you please describe some behavioral changes?) and seizures, followed by decreased responsiveness, involuntary limb movements and facial grimacing. She also had intermittent high grade fever for 3 days. On examination she had spontaneous eye opening with continuous involuntary oro buccal and lingual movements. CT/MRI brain was normal. Spinal tap showed increased WBCs with lymphocytic predominance. EEG showed severe diffuse encephalopathy with no clear epileptiform discharges. HSV PCR came out to be negative. She was treated with Ceftriaxone, Acyclovir, Ampicillin, Vancomycin, Phenytoin and Levetiracetam. Acyclovir was later stopped after negative HSV PCR results. On suspicion of non infectious (autoimmune) encephalitis, treatment with IVIg was started and serum anti NMDA receptor antibodies were sent, which came out to be positive. Ultrasound pelvis showed no teratoma. Parents on follow up reported gradual resolution of symptoms and resumption of usual activities. **Conclusion:** Anti NMDA receptor encephalitis is associated with anti NMDA receptor antibodies is responsive to autoimmune treatment.

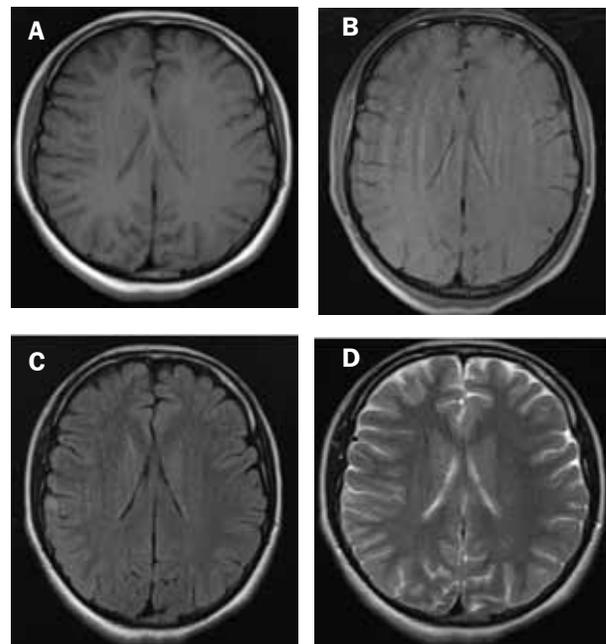
INTRODUCTION

Anti-N-methyl-D-aspartate (NMDA) receptor encephalitis associated with anti NMDA receptor antibodies is more common in females and usually associated with underlying ovarian teratoma⁽¹⁾. Patients may present with a constellation of symptoms including psychiatric symptoms⁽²⁾, memory disturbances, seizures, dyskinesia and catatonia. Treatment involves immuno suppression. A Pub-med search did not reveal any previous case of anti NMDA receptor encephalitis published from Pakistan.

CASE REPORT

We report the case of a previously healthy 16 year old girl with a short history of sore throat preceding the illness and a 12 day history of behavioral changes and seizures, followed by decreased responsiveness, involuntary limb movements, with facial grimacing, and intermittent high grade fever for 3 days. she had received treatment for acute bacterial/viral meningitis with no improvement and was then shifted to our hospital. On examination, she was intubated, had spontaneous eye opening with continuous involuntary oro buccal and

Figure 1. No significant intracranial abnormality noted on MRI brain with no significant contrast enhancement (A. T1WI, B.T1WI post contrast, C. FLAIR, D. T2WI)



lingual movements. Her blood pressure was 120/70 mm of Hg; pulse was 110 beats/min with temperature of 102.0 F. There were no signs of meningeal irritation. workup showed normal chemistries with Na-149, K-3.2, Cr-0.67 and almost normal blood count, with WBCs-11000, Hb-10.17 and platelet count of 223000. ICT malaria and dengue serology were negative. CT/MRI brain was normal (Figure 1). Spinal tap showed increased WBCs with lymphocytic predominance (90%), proteins-25.6 and glucose-69. EEG showed severe diffuse encephalopathy with no clear epileptiform discharges (Figure 2). She was continued on I/V Ceftriaxone 2 gm BD, Acyclovir 750 mg TDS, Ampicillin 2 gm 6 hourly, Vancomycin 1 gm BD, Phenytoin 100 mg TDS and Levetiracetam 750 mg BD. CSF HSV PCR came out to be negative, so Acyclovir was stopped. Autoimmune work up including ANA, AMA, and ASMA came out negative.

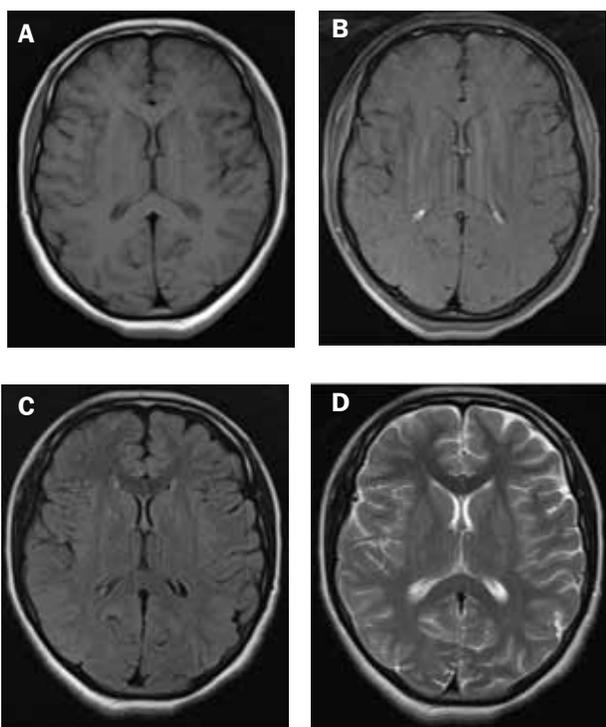


Figure 2. No significant intracranial abnormality noted on MRI brain with no significant contrast enhancement (A. T1WI, B.T1WI post contrast, C. FLAIR, D. T2WI)

On suspicion of non herpetic (autoimmune) encephalitis, she was given IVIg for 5 days and serum anti NMDA receptor antibodies were sent, which came out. Ultrasound pelvis showed no teratoma. She was discharged and advised proper nursing care and rehabilitation. Parents on telephonic follow up reported that her symptoms had resolved gradually and she had resumed usual activities.

DISCUSSION

Anti-NMDA receptor encephalitis is a neuroimmune syndrome with autoantibodies recognizing extracellular epitopes in NR1/NR2 heteromers of NMDA receptor⁽³⁾, and attenuating NMDA receptor function through its internalization⁽⁴⁾. Reduction in NMDA receptor activity results in inactivation of GABAergic neurons, causing disinhibition of excitatory pathways leading to frontostriatal syndrome which may manifest as psychosis, catatonia, mutism, rigidity and dystonia or affecting the brainstem that may cause semi-rhythmic limb, trunk and bulbar movements. Autonomic instability, with hyperthermia, hypoventilation, blood pressure fluctuations, tachycardia, bradycardia, constipation or ileus may also occur due to involvement of dopaminergic, noradrenergic and cholinergic systems^(5, 7).

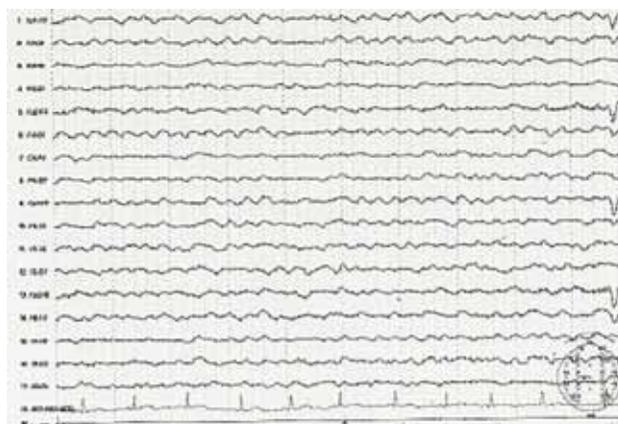


Figure 2. EEG showing severe diffuse encephalopathy

Anti-NMDA receptor encephalitis is more common in females (80%) with 23 years as median age of presentation and association with underlying ovarian teratoma in approximately half of the cases. Patients present with schizophrenia like psychiatric symptoms, usually preceded by fever, headache, or viral infection-like illness. After reaching the peak of psychosis, most patients develop memory problems, seizures, unresponsive/ catatonic state, decreased consciousness, orofacial-limb dyskinesias, autonomic instability and hypoventilation, with 88% of patients requiring intensive care support usually^(5, 8, 9). This disorder is usually severe and can be fatal, but it is potentially reversible. Once patients recover from the hyperkinetic phase, gradual improvement is expected within months with full recovery over 3 or more years. Recognition of symptom complex is the key to diagnosis. Brain MRI is unremarkable in 50% of the cases. If abnormal, it usually shows increased signals in FLAIR and T2 sequences in cerebral, cerebellar or medial temporal lobes⁽⁹⁾. CSF reveals nonspecific

changes ⁽¹¹⁾. EEG often reveals diffuse delta slowing without paroxysmal discharges ^(1, 2). Detection of NMDA receptor antibody in CSF or serum is helpful in making the diagnosis ⁽³⁾. Treatment is focused on tumor resection and immunotherapy (corticosteroids, plasma exchange, intravenous immunoglobulin). In non-responders, second-line immunotherapy (rituximab or cyclophosphamide or combined) is required. Recovery may also occur spontaneously. More than 75% of the patients recover completely or have mild sequelae, while remaining end up with disability or death ^(12, 13).

CONCLUSION

Anti-NMDA receptor encephalitis has a recognizable pattern of presentation that may mimic psychiatric and infective diseases and if diagnosed correctly can be effectively treated.

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Author's contribution:

Rabel Khalid Memon: Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review

Maimoona Siddiqi: Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review

Rizwanullah Khan: Data collection, data analysis, manuscript writing, manuscript review