

CASE REPORT

RARE MANIFESTATION OF ANTI-NMDAR ENCEPHALITIS

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N-methyl-d-aspartate receptor (NMDAR) antibody encephalitis is an autoimmune syndrome with the development of antibody production against the NMDAR, affecting synaptic plasticity and cognition. It has a common association with ovarian teratomas with women being affected disproportionately. We present a case of an eight-year-old female child presented with complaints of fever, altered level of consciousness and choreiform movements. Owing to its common occurrence in the developing world, initially, rheumatic fever was kept in the differential diagnosis and was treated accordingly, but through a series of investigations, was diagnosed as a case of N-methyl-d-aspartate receptor (NMDAR) antibody encephalitis. This case report urges the healthcare providers to keep Anti NMDAR encephalitis as a differential in their minds, while dealing with patients, having chorea as their main clinical manifestation. Owing to its rarity, we have primarily reported it here.

Keywords: N-methyl-D-aspartate receptor (NMDAR) encephalitis; Neuronal plasticity; Chorea; Rheumatic fever

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INTRODUCTION

Anti-N-methyl-D-aspartate (NMDA) receptor encephalitis is an immune-mediated disease, in which autoantibodies are formed against N-methyl-D-aspartate (NMDA) receptor, a protein important for synaptic plasticity and memory function, commonly presenting with behaviour and personality disorders or seizures.^{1,2} The pathophysiology of anti-N-methyl-D-aspartate (NMDA) receptor encephalitis includes the formation of antibodies against the NR-1 subunit of the N-methyl-D-aspartate receptor, causing reversible internalization of the receptor within neurons. The annual incidence of anti-NMDAR encephalitis is estimated to be 1 out of 1.5 million people per year, and 65% of cases of anti NMDAR have been reported in people aged ≤ 18 years.^{3,4}

We present herein a case of a patient with anti-NMDAR encephalitis who was managed successfully despite certain atypical and ambiguous clinical features.

CASE REPORT

An eight-year-old healthy female child was presented in the emergency department of Dr. Ruth K.M. Pfau Civil Hospital Karachi with complaints of fever for seven days, altered level of consciousness for four days, and brief episodes of chorea for three days. There was neither history of complicated birth nor of any neurological and psychiatric illness in the family.

On general physical examination, the patient was found to have tachypnoea, tachycardia, hypotension along with a high-grade fever. Anaemica signs, including pallor, angular cheilosis and

koilonychia, were visible in the patient. Neurological exam showed altered level of consciousness, rapid and involuntary jerky movements of both upper and lower limbs, along with reduced power of right limbs. Other systemic examinations were unremarkable.

After admission in the ward, multiple investigations were carried out which showed that the patient had hypochromic anaemia, hypocalcaemia, hypokalaemia, and deranged liver function tests (LFTs). Based on history, physical examination, and investigation, our differential diagnosis included rheumatic chorea, meningoencephalitis, lupus cerebritis, autoimmune encephalitis and, acute demyelinating encephalomyelitis (ADEM). To exclude the differentials, further investigations were carried out. Cerebrospinal fluids (CSF) analysis showed an appropriate picture of encephalitis (Table 1). Moreover, magnetic resonance imaging (MRI) brain with contrast was done, which was unremarkable. ANA and Anti ds DNA antibodies came out to be negative. Vitamin D levels were insufficient; therefore, she was given 600,000 units of vitamin D in injectable form. As a considered aetiology of chorea, thyroid profile, and serum ceruloplasmin workup were also done to rule out the causes, both of which turned out to be within their normal limits. On Electroencephalogram (EEG), diffuse Encephalopathy was shown.

On the second day of admission in the ward, the patients' Glasgow comma scale (GCS) deteriorated to 6/15, so she was immediately shifted to Paediatric Intensive Care Unit (PICU) where she was sedated and intubated. For chorea, haloperidol,

procyclidine, phenobarbital and chlorpromazine were given to the patient, along with IV Dexamethasone, in view of acute demyelinating encephalomyelitis (ADEM). As CSF DR showed a picture of encephalitis; the management was continued for that. She started showing signs of improvement and her condition progressed positively, but chorea remained uncontrolled. CSF DR was repeated after seven days to see the response of treatment which was normal, and the patient was extubated and shifted back to the ward.

On echocardiography, nothing abnormal was seen. Nevertheless, Antistreptolysin O titres (ASOT) were elevated. Owing to the positive association between ASOT and Choreia; an intramuscular Benzylpenicillin injection was started once a week, for three weeks, but choreiform movements were still present. The anti-NMDAR antibody report came out to be positive in CSF. The Child was continued on IV Dexamethasone and four drugs for chorea, i.e., haloperidol, procyclidine, phenobarbital and chlorpromazine. After consultation with neurologists, the child was given Intravenous immunoglobulin (IVIG) for five days after which she was shifted to oral prednisolone, while the rest of the treatment was continued. After the completion of the above-mentioned therapy, her abnormal movements were completely resolved after 14 days.

Since there is an assertive association between ovarian teratoma and anti NMDAR encephalitis, ultrasonography of the abdomen and pelvis was carried to rule out any ovarian teratoma. The result of it was negative. The patient was also followed in the outpatient department up to 6 months after being successfully managed. The patient showed no signs of relapse. Along with follow-up, a series of USG was also performed on every visit to rule out the suspicion of teratoma.

This case was written after taking consent from the patients' guardians.

Table-1: Patient's Cerebrospinal fluid analysis report

CSF Analysis	Patient's value	Normal range
Appearance	Clear	Clear, Colourless
Protein	34.8 mg/dL	15-45 mg/dL
Glucose	84 mg/dL	50-80 mg/dL
RBC	Nil	<1 RBC/mm ³
WBC	19/mm ³	0-8 leukocytes/mm ³
Polymorph	5%	Nil
Lymphocytes	95%	<5%
Anti-NMDA antibody	Positive	

CSF; cerebrospinal fluid, RBC; red blood cells, WBC; white blood cells

DISCUSSION

Anti N-methyl-d-aspartate receptor (NMDAR) encephalitis was first described in young women,

having an association with ovarian teratoma, in 2007.^{5,6} It is an immune-mediated disease, developing auto-antibodies against NMDAR, a protein important for neuronal plasticity and memory function.¹ Gable *et al* described in their study that 65% of cases of Anti-NMDAR occur in ≤ 18 years.³

Anti-NMDAR encephalitis commonly presents with behaviour and personality disorders or seizures.² In less than 12 years of children, it presents as polysymptomatic, with predominant symptoms being neurological, while in adults, it presents conspicuously with psychiatric symptoms. However, it can manifest as oligosymptomatic.^{5,6}

Pathophysiology of anti-NMDAR encephalitis includes targeting NR1 subunit and receptor internalization. Also, these antibodies can cause encephalitis-lethargica, immune-mediated chorea encephalopathy syndrome, as well as encephalopathy of obscure origin.⁶

Rheumatic chorea, meningoencephalitis, lupus cerebritis, autoimmune encephalitis, acute demyelinating encephalomyelitis (ADEM) were kept among the main differential diagnosis. Initially, we suspected a case of rheumatic fever because the incidence of rheumatic fever in countries with lower socioeconomic status is 300,000–500,000 new cases per annum. Moreover, without treatment, nearly 230,000 deaths occur because of its high mortality.⁷ Keeping in mind other differentials, such as autoimmune encephalitis, we also started off the patient with 'steroid therapy', but she showed minimal response to it. Then after the neurologist's opinion, we commenced intravenous immunoglobulin (IVIG) along with other steroid and anti-epileptic drugs (AEDs), to which the patient responded rigorously. After the anti-NMDAR antibody result, which came out to be positive, the patient was firmly diagnosed as having anti-NMDAR encephalitis. From works of literature, it expounded that Anti-NMDAR encephalitis presents with many neurological complaints at a time. In contradistinction to this, our case presented conspicuously with features of chorea alone.

Anti-NMDAR encephalitis is associated with certain malignancies. It has been described in different surveys that ovarian teratoma has a significant relation with NMDAR encephalitis. This association points to the fact that ovarian teratomas are responsible for the formation of anti NMDAR antibodies leading to encephalitis. Surgical removal of the tumour in such patients gives a promising result of clinical betterment.⁸ To rule out this association, an ultrasound of the abdomen and pelvis was performed, which was inconclusive for such diagnosis.

In conclusion, since rheumatic fever is a common health problem encountered in the developing world and choreiform movements are mostly associated with it in our setup, this peculiar occurrence of Anti-NMDAR encephalitis with chorea being the main clinical manifestation, owing to its rarity, has been reported here.

In literature, some cases have partial manifestations. Such cases remain undiagnosed and, as a result, can increase the risk of mortality in patients who have presented with partial features or some isolated feature, i.e., chorea, just as is in this case.

Therefore, it is high time for physicians to keep this rare feature of anti-NMDAR encephalitis in mind for prompt diagnosis and early as well as an effective treatment of such patients. Surely, immediate diagnosis and management of Anti-NMDAR encephalitis can decrease the mortality rate of patients to a greater extent.

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AUTHORS' CONTRIBUTION

All the authors had full access to data and contributed to the treatment and management of the patient. All authors contributed to the design and concept, literature review, manuscript drafting and revision of the case study. All the authors read and approved the final version of the manuscript and agrees to be accountable for all aspects in ensuring that questions

related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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