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NMDA ENCEPHALITIS IN AN ELDERLY WITH POOR PROGNOSIS

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ABSTRACT

We present a case of a 65 years old man from Islamabad who presented with six months history of psychiatric and behavioural symptoms, significant weight loss. Later on he developed difficulty swallowing and altered sensorium. This was followed by an episode of shortness of breath leading to respiratory arrest, followed by ICU stay on ventilator support, then developed focal deficit in form of left sided weakness, dysautonomia, bradycardia leading to cardiac arrest and another cardiopulmonary resuscitation, myoclonic jerks, orofacial dyskinesias, status epilepticus, coma ultimately resulting in death of the patient. Patient was found to be NMDA receptor antibody positive. CT chest and abdomen did not reveal any hidden malignancy. Patient was given intravenous pulse steroids for 5 days followed by five sessions of plasmapheresis but did not respond. He stayed on ventilator support for 40 days and did not improve. This is the second case of antibody proven NMDA encephalitis from Pakistan, the first being from Islamabad as well and published in this journal.

Key words:

NMDA encephalitis, status epilepticus, dysautonomia

INTRODUCTION

NMDARs basically are ligand-gated ion channels which are major mediators of excitatory neurotransmission. Antibodies to the NMDAR (the main target being the NR1 subunit) were initially described in a paraneoplastic encephalitis associated with ovarian teratomata, with neurological symptoms presented prior to tumour diagnosis (range, 1–380 weeks).^{1,2}

The first symptoms are usually psychiatric, behavioural disturbances and seizures, with clinical worsening over 10–20 days to generate dyskinesias (orofacial grimacing, dystonic posturing and choreoathetoid movements), autonomic instability and reduced consciousness, often requiring ventilatory support.^{3,4} The two-stage progression of these symptoms may involve cortical and subcortical functions.^{3,4}

We report a case of an elderly male with similar classical presentation of neuropsychiatric manifestations followed by hypoventilation, respiratory and bulbar

paralysis, focal deficit and refractory seizures.

CASE REPORT

A 66 years old male presented with history of depressive and behavioural symptoms for six months for which various antidepressants were given. There was history of significant weight loss in past six months with decreased appetite and reduced oral intake. He also used some unknown homeopathic medications during this period. He was brought to emergency with one week history of depressed conscious level, difficulty in breathing, difficulty in swallowing. On examination he was found to be dehydrated, low BP, GCS was 8/15, gag reflex was absent but there was no focal neurological deficit. Initial investigations showed low Sodium and Potassium. He was intubated and Potassium was replaced. Thiamine and glucose was also given. His CT scan brain was normal. His MRI brain could not be done as he was on ventilatory support. His CSF examination showed increased proteins of 72mg/dl with normal cells. His echocardiogram was normal. His EEG showed

diffuse encephalopathy as shown in figure 1. Autoimmune vs Paraneoplastic encephalitis was suspected. His CT chest abdomen and pelvis was done to rule out malignancy but were unremarkable

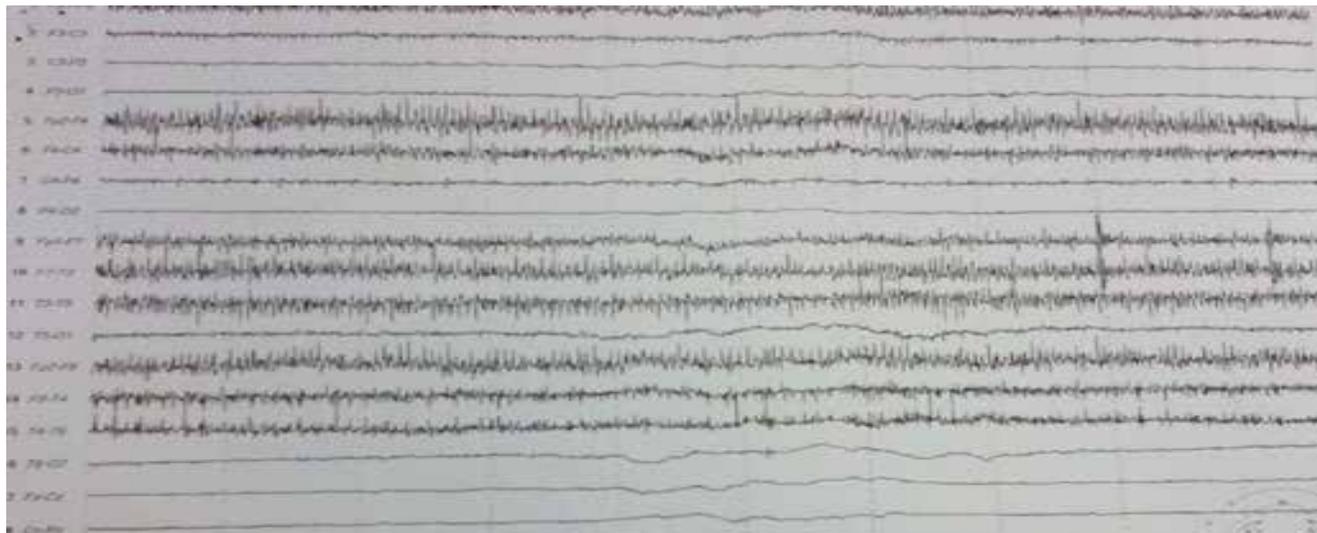


Figure 1. EEG of of the patient suggestive of diffuse encephalopathy.

After 03 days of ICU stay he developed sudden asystole, became pulseless and BP less, CPR was done for eight minutes. He revived. He started to improve GCS improved to 11/15 but he developed left sided weakness along with some focal fits on right side and orofacial dyskinesias. CT scan brain was repeated which again was unremarkable as shown in figure 2.

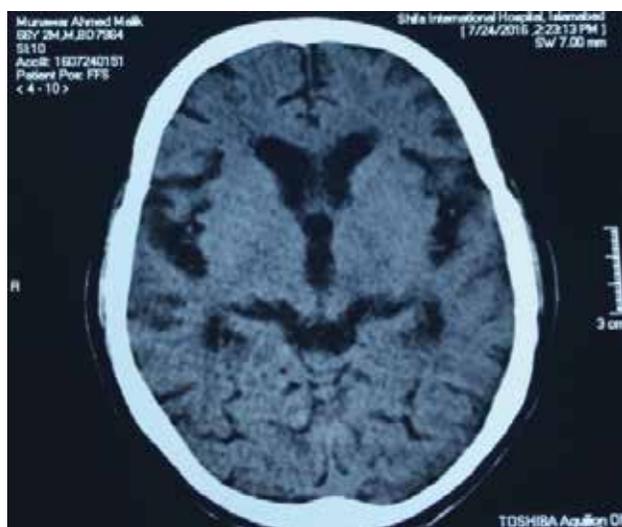


Figure 2. CT scan brain of the patient which was normal.

He started having seizures. He was loaded with Phenytoin, injectable valproate and levetiracetam were

also given in appropriate doses but fits continue to increase, meanwhile he was started on midazolam infusion for refractory status epilepticus. During this period further workup was done including anti neuronal antibodies, autoimmune profile, anti GAD antibodies. His NMDA receptor antibodies came back positive and was given pulse steroids for 05 days. He did not show any improvement and was started on plasmapheresis. He had another episode of bradycardia leading to asystole and another CPR was done for 10 min. He revived but GCS remained 3/15 post CPR and there was high suspicion of hypoxic ischemic brain damage post CPR. He was however given complete five sessions of plasma exchange with no improvement. He stayed on ventilator support for around 40 days in vegetative state. Weaning off trials from ventilator support were attempted but were not successful. Finally, support was withdrawn on wishes of family and patient died.

DISCUSSION

This syndrome is a severe encephalopathy that generally follows a characteristic temporal sequence of features³ as was seen in our patient. Patients may present with a constellation of symptoms including psychiatric symptoms⁵, memory disturbances, seizures, dyskinesia and catatonia⁵

In adults, the neuropsychiatric features almost always precede presentation of movement disorders, autonomic dysfunction, or reduced consciousness by about 10 days or more³, same was the case in our patient.

Brain MRI is unremarkable in 50% of the cases¹. If abnormal, it usually shows increased signals in FLAIR and T2 sequences in cerebral, cerebellar or medial temporal lobes¹

If abnormalities are present, they are either seen cortically (usually in the limbic mediotemporal cortex)^{1,6,7} or subcortically in the brainstem, the basal ganglia, or the cerebellum.^{2,3} Rarely, T2 and FLAIR hyperintensities or contrast enhancement (in cortical meninges or basal ganglia) are detected²

MRI brain could not be done in our patient as he stayed on ventilator support throughout the hospital stay. CT scan brain done twice in our patient was normal. CSF usually reveals nonspecific changes⁸ as seen in our patient. EEG often reveals diffuse delta slowing without paroxysmal discharges,^{5,9}

Paraneoplastic cases are infrequent in children^{3,4,10} and are very unusual in men³. All paraneoplastic workup was negative in our patient.

In previous studies it has been that patients do seem to benefit from aggressive immunotherapy^{3,4}. Patients may recover completely or be left with residual cognitive impairment and usually all have amnesia for the events of the acute illness^{3,4}. Our patient however did not improve and died.

CONCLUSION

NMDA encephalitis has a recognizable pattern of presentation but can have a lethal course and poor prognosis especially in elderly.

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Author's contribution:

Farheen Niazi; Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review

Abdul Hameed; Study concept and design, data collection, data analysis, manuscript writing, manuscript review

Tariq Hussain; Study concept and design, data collection, data analysis, manuscript writing, manuscript review

Sarah Faiz; Study concept and design, data collection, data analysis, manuscript writing, manuscript review

Hassan Atique; Study concept and design, data collection, data analysis, manuscript writing, manuscript review