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AN ADOLESCENT CASE OF AUTOIMMUNE ENCEPHALITIS – FROM SUSPICIOUS TO DIAGNOSIS

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Abstract

Autoimmune encephalitis defines as brain inflammation caused by misdirected immune response against self-antigens expressed in the central nervous system. Second most common cause of Auto Immune Encephalitis is anti-NMDAR (N-Methyl D-aspartate receptor) encephalitis. Most commonly occur in female. It comprises a group of Non – infectious Immune Mediated Inflammatory disorders of the brain parenchyma, involving the cortical or deep grey matter with or without involvement of the white matter, meninges or spinal cord. Child usually present with psychiatric symptoms, seizure & abnormal movements. CSF analysis is the diagnostic confirmation of autoimmune encephalitis. Management includes symptomatic treatment & immunotherapy. Early identification and treatment can improve the patient outcome, when identified and treated early, patient may have shown less hippocampal damage. We present a 15-year-old female child who was initially diagnosed and treated as psychiatric like illness and later on diagnosed as anti-NMDAR autoimmune encephalitis.

Keywords: Anti-NMDAR, Autoimmune Encephalitis, Hippocampus, CSF Analysis, Immunotherapy.

INTRODUCTION

Anti- NMDAR encephalitis is a form of autoimmune encephalitis. It is a rare autoimmune disease, that is frequently underdiagnosed. Due to variability in the initial presentation, it is not only underdiagnosed but also can be misdiagnosed as psychiatric illness or other pathologies. Most patients with anti- NMDAR encephalitis develops a multistage illness that progresses from psychosis, memory deficits, language disintegration into a state of unresponsiveness, seizure, with catatonic features, associated with abnormal movements, autonomic and breathing difficulty [1].

Predominantly affects children and young adults, most commonly in female. It can occur with or without association with tumour, most commonly ovarian teratoma [2] and it is dependent on age, sex, and ethnicity, being more frequent in women older than 18 years, slightly more predominant in black women than in white women. In case of clinical suspicion, electroencephalogram and MRI are useful for diagnosis, but lumbar puncture for cerebrospinal fluid analysis confirms the diagnosis.

Treatment is symptomatic management, if tumour presents treated with tumour resection and first line management is corticosteroids, intravenous immunoglobulin, or plasma exchange and less frequently some patient need second-line immunotherapy like cyclophosphamide or rituximab. Early diagnosis and treatment can prevent further progression.

Case report:

An adolescent developmentally normal child who was admitted with complaints of abnormal behaviour for 3 days, hyper religiosity and inability to sleep. Child was apparently normal 7 days back when she had flu like illness for 2 days following an asymptomatic period for 3 days, then she suddenly had involuntary movements, for

that she was treated symptomatically. After 4 days child had hallucinations, psychotic behaviour, decreased verbal output, seizure like activity and did not sleep properly for 3 days, before she was presenting to hospital. There was no history of any drug intake, dog bite or stressful event. At the time of admission child was oriented to person but not with place and time. She was having inappropriate speech and was restless and agitated. No significant examination findings noted. Initially misdiagnosed as psychiatric illness. Over next 2 days, child had seizure like activity, did not sleep properly. She stopped interacting with parents and decreased verbal output with abnormal behaviour.

As the day progresses, she had seizures with fall in Glassgow Coma Scale (12/15). In view of initial presentation with psychiatric symptoms child was misdiagnosed as psychiatric disorder followed by development of seizure, encephalopathy with abnormal movements child was evaluated and diagnosed as autoimmune encephalitis. Initial baseline blood investigations were normal. Electroencephalogram showed diffuse slowing suggestive of bilateral cerebral dysfunction. MRI brain showed prominent sulcal space with no cerebral oedema. Lumbar puncture for Cerebrospinal fluid analysis was done and positive for Anti-N-methyl-D-aspartate receptor antibodies. Initially started with Pulse methyl prednisolone, once diagnosis was confirmed IV immunoglobulin was given. Child was poorly responsive then started on IV monoclonal antibody rituximab, after that child started to improve. Child improved clinically better and she is going school, return to her normal daily activities. Child was on regular follow up with 6month interval period.

DISCUSSION

Autoimmune encephalitis comprises a group of non-infectious immune mediated inflammatory disorders of brain parenchyma, involving the cortical or deep grey matter with or without involvement of the white matter, meninges or spinal cord. Pathogenesis is N-methyl-D-aspartate receptor antibodies ligand gated cation channel involved in synaptic transmission by 2 heteromers that is Glutamate N1 and Glutamate N2. N-methyl-D-aspartate receptor antibodies binding to N-methyl-D-aspartate receptor, internalization of the receptors by the cell, decreasing the synaptic transmission of N-methyl-D-aspartate clusters. N-methyl-D-aspartate receptor antibodies inhibit the GABAergic neurons leading to a disintegration of the excitatory pathways and increase extra cellular glutamate. Hence hyperkinetic movement disorder will occur. Ovarian teratoma express Glutamate N1.

Anti-NMDAR encephalitis constituted 4% of all the cases of encephalitis [3]. About 80% of cases occur in females and more frequently affected age group is young teenagers and children. Most commonly associated tumour is with ovarian teratoma, other than teratoma are uncommon only 2% [4]. There are 5 clinical stages of autoimmune encephalitis – initial prodromal phase comprises flu like illness, fever, malaise and headache. Then progress to psychotic phase that comprises delusions, hallucinations, paranoia and agitation. Later on, phase 3 (alteration of sensorium, seizures and autonomic instability), phase 4 (hyperkinetic phase comprises orofacial dyskinesia, bruxism, stereotyped movements), phase 5 (recovery phase – gradual return of awareness and responsiveness) [5].

Diagnosis of the disorder mainly established by demonstrating N-methyl-D-aspartate receptor antibodies in CSF and serum. In most of the patient CSF analysis shows pleocytosis, normal or increase in proteins, oligoclonal bands. EEG findings is non-specific and shows slow and disorganised activity. Treatment is first line immunotherapy includes IV pulse steroid or IV immunoglobulin or plasma exchange. If there is no improvement is noted then start on second line therapy like IV rituximab or IV cyclophosphamide. If it is associated with ovarian tumour, treat the tumour by resection. 75% of patients show complete recovery. Relapses occur in 20-25% of patients [4,6,7].

CONCLUSION

Anti-NMDAR encephalitis is one of the common causes of encephalitis, has distinctive clinical features and is potential reversible if diagnosis early and treated appropriately. Proper diagnosis is important for autoimmune encephalitis from psychiatric like illness, history taking with proper order of event is mandatory for diagnosis. Proper medication with regular follow up is mandatory. Early diagnosis and proper treatment can prevent the further damage. It is frequently associated with underlying malignancy and need for appropriate screening.

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