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RESEARCH ARTICLE

AUTOIMMUNE ENCEPHALITIS: A POTENTIALLY TREATABLE CAUSE OF ACUTE PSYCHOSIS.

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Abstract

Autoimmune encephalitis is a difficult clinical diagnosis due to predominance of psychiatric symptoms and the similarities in the clinical, imaging and laboratory findings of many forms of encephalitis especially infective encephalitis. Patients generally develop impaired memory and cognition over a period of days or weeks. There may be clues to specific causes on history or physical examination, but often these specific signs are absent. A broad approach to testing for infectious diseases and various neuronal autoantibodies can lead to the correct diagnosis. Here we present the case study of a 22 year-old male patient who presented with symptoms of psychosis following his father illness but upon investigations was diagnosed to be a case of autoimmune encephalitis.

Introduction:-

Encephalitis i.e. brain inflammation is often thought to be mediated by infections (e.g. viral). Herpes simplex encephalitis (HSE) is the most common viral encephalitis with 2000 cases per year in the USA, the majority of cases being HSV-1 infection.[1] Encephalitis is a common medical emergency. With the advances in molecular diagnostics, new immunological markers (antibodies) are being discovered in patients presenting with encephalitic syndromes. Thus, research has evoked interest in the '*immune theory*' of encephalitis. This group of disorders is appealing to clinicians because of the favourable response to immunotherapy as compared to infectious encephalitis where limited pharmacotherapy is available for most of the viral agents[2]. Despite a growing knowledge of autoimmune encephalitis (AE), this area remains poorly understood. Diagnosis in such cases is often considered late or not at all, resulting in poor outcomes.[3]

The Case:

22 year old male, resident of Rewari, postgraduate student, presented with chief complaints of Social withdrawn behavior since 4 months, restlessness and decreased sleep since 3 months, forgetfulness since 2 months, visual hallucinations since 2 months and intermittent lip smacking movements since 1 month. History dated back to June, 2018 when his father was unwell due to congestive heart failure. After that he started staying at home most of the times and would talk less to family members. He tried to study his commerce books but could not concentrate and grasp anything. On 20th June, his mother noticed that midway through dinner, he stopped eating, becomes still and the food remained in his hands. He was also unable to sleep at night. He was taken to a local psychiatrist, where he

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was diagnosed to be having catatonia and was put on antipsychotics. His condition continued to remain the same despite the treatment. In July, his father expired of congestive heart failure. In due course, he also started having visual hallucinations like seeing rats in his bed. He started forgetting things like last meal, last conversation but could recollect his school or events of remote memory. Also there were on and off crying spells and lip smacking episodes.

He was brought to psychiatry department, PGIMS, Rohtak and was put on antipsychotics and Benzodiazepines. As his condition didn't improve in one month following treatment, he was referred to medicine department for opinion. On examination, Mini mental status examination (MMSE) of the patient was found to be 12/30. Complete hemogram, Liver function tests and renal function tests of the patient were found to be within normal limits. Cerebrospinal fluid (CSF) tap of the patient was also done to rule any organic cause in the case. CSF examination revealed acellular picture, normal sugar and protein levels. Serological tests for Herpes simplex virus were found to be negative in CSF. EEG of the patient was done (Figure 1) which showed generalized slowing in all the head regions. MRI Brain of the patient showed slight prominence of sulci, ventricular system and basal cisterns s/o early diffuse cerebral atrophy (Figure 2).

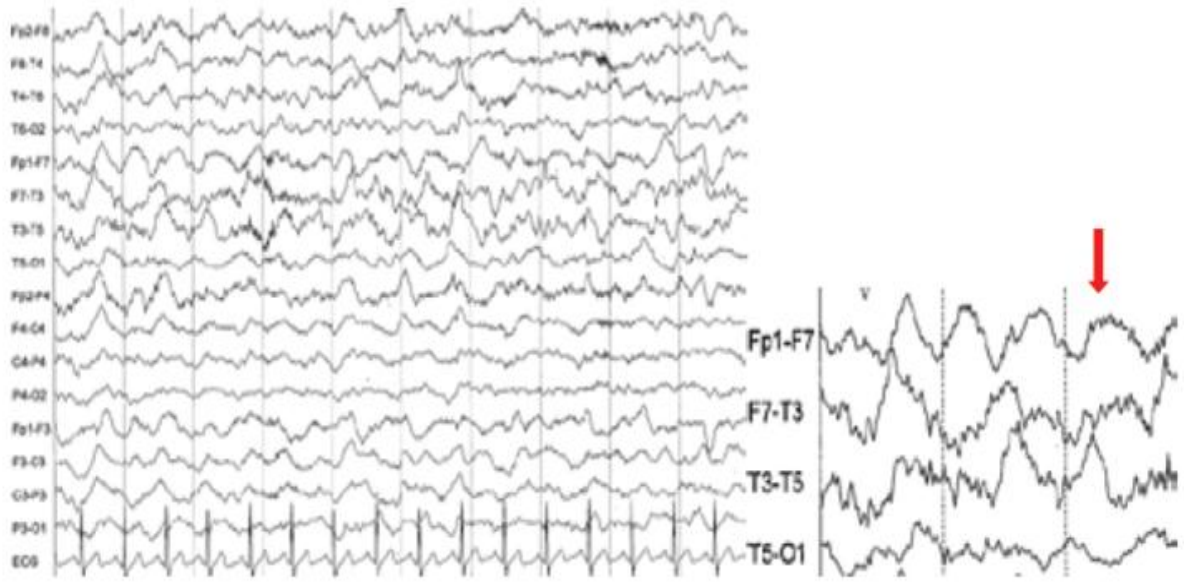

Figure 1:- EEG showing generalised theta-delta range slowing with serrated appearance of delta waves (due to overriding fast beta activity) in frontal area (red arrow); representing extreme delta brush

In view of the young age of the patient, subacute psychotic symptoms, oral dyskinesias, slowing pattern in EEG and no history of fever, possibility of autoimmune encephalitis was kept and autoimmune encephalitis panel (Figure 3) was ordered from CSF. Anti NMDA (N-methyl D-aspartate) receptor antibody came out to be *positive*. Other autoantibodies like anti GABA-B (gamma-aminobutyric acid) receptor antibody, anti LG1 (Leucine-rich glioma inactivated) receptor antibody, anti CASPR2 (Contactin-associated protein-2) receptor antibody were not detected.

The Patient was put on injection Methylprednisolone 1g IV for 5 days. After that, he was given intravenous immunoglobulins (IVIG), 2g/kg divided into 5 days. There is significant improvement in patient general condition. Visual hallucinations, orolingualdyskinesias, crying spells are resolved. Recent memory has also improved. He has been put on tab prednisolone 80 mg 1 OD and Azathioprine 25 mg 1OD. Plan is to taper off steroids over 6-8 wks and increase the dose of Azathioprine.

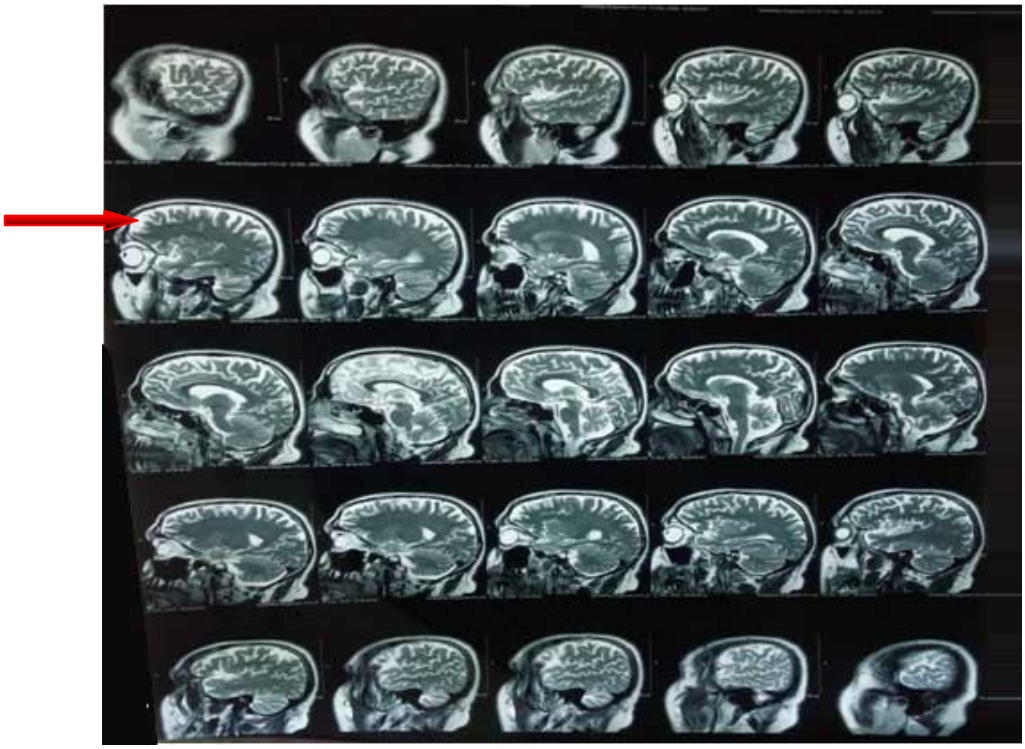

Figure 2:- T2 weighted sagittal section images of brain showing prominence of cortical sulci (red arrow).

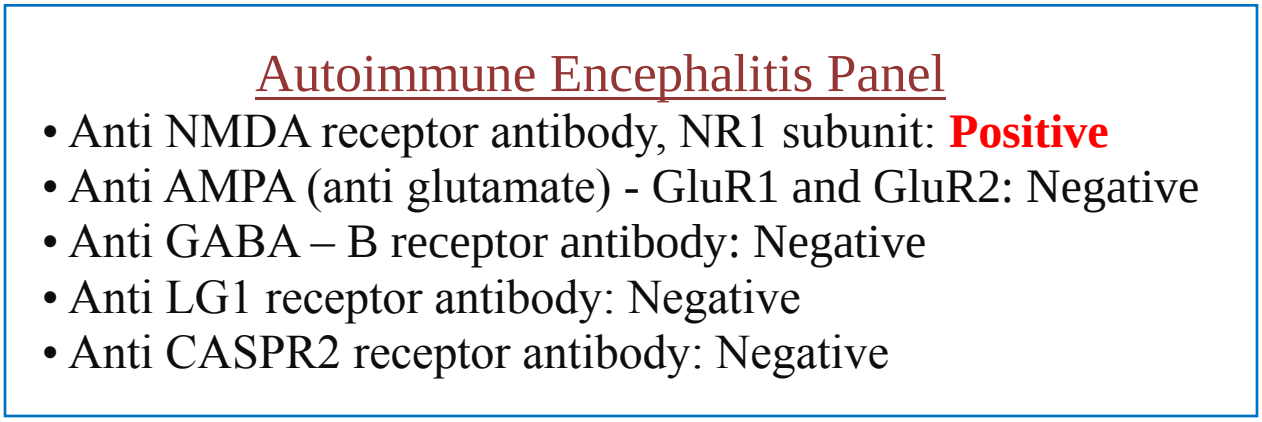

Figure 3:- Autoimmune encephalitis panel: NR-1 subunit of anti NMDA receptor antibody is positive.

Discussion:-

Autoimmune conditions are not a common cause of encephalitis. However, with recognition of newer antibodies, diagnostic serology is becoming increasingly available[3]. Since its discovery, anti-NMDA receptor antibody encephalitis has been found to be one of the most common forms of autoimmune encephalitis, surpassing several viral etiologies (Granerodet al[4], 2010). In contrast to patients with VGKC-complex antibody encephalitis, which mainly occurs in men older than 50 years of age (male to female ratio 2:1), anti-NMDA receptor antibody encephalitis mainly affects women younger than 50 years of age (male to female ratio 1:4). Anti-NMDA receptor antibody encephalitis has been described to occur in a multistage process (Iraniet al[5], 2010), although this may not always be the case in all patients. The disorder can start with a 'flu like' illness but is generally followed by psychiatric symptoms (particularly psychosis, mood disorder and personality change), amnesia, confusion or seizures. The next stage occurs 2–3 weeks later and is characterised by movement disorders including dystonia, chorea, rigidity and catatonia (including posturing and echopraxia). In children, orofacialdyskinesias are often the first symptom. The syndrome classically culminates in autonomic disturbance (e.g. cardiac dysrhythmia, hyperthermia, unstable blood pressure, hyperhidrosis and sialorrhoea), reduced conscious levels and can lead to

death. It is important to note that psychiatric symptoms, predominantly psychosis, are the most common presenting symptoms of anti-NMDA receptor antibody encephalitis in adults, with the first large case series on autoimmune encephalitis, including 100 patients, reporting 80% patients presenting to psychiatric services (Dalmau et al[6], 2008), and recently a larger series has reported similar high levels of 65% (Titulaer et al[7], 2013). Although psychiatric symptoms become less frequent with decreasing age at onset, they are still a common presenting feature in children.

It is vital to know the relevant signs, symptoms and investigations that may guide the clinician to a positive diagnosis of autoimmune encephalitis. Initial investigation in an encephalitic patient would commonly include CT scan of the brain with contrast, lumber puncture with cell count, protein, glucose (and serum glucose), viral screening, acid fast bacilli (AFB) smear, bacterial and mycobacterial culture. An MRI of brain is mandatory and an EEG should also be performed. Some of the results from these investigations in the cases of infective and autoimmune encephalitis may overlap. However, it is imperative that a diagnosis of autoimmune encephalitis be considered by treating physicians when other more common causes have been excluded or when there are certain diagnostic indicators for autoimmune encephalitis like oropharangeal dyskinesias, catatonia, and delta slowing in EEG etc. Early diagnosis and prompt start of specific therapy (IV immunoglobulins and/or plasmapheresis) form the mainstay of treatment in the cases of autoimmune encephalitis.

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