ORIGINAL RESEARCH PAPER

General Medicine

UNMASKING SERONEGATIVE AUTOIMMUNE ENCEPHALITIS IN A YOUNG FEMALE

KEY WORDS:

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Autoimmune encephalitis refers to a group of non infectious immune mediated inflammatory disorders affecting brain parenchyma in which antibodies target nervous system. It is rare and can present with a wide range of neurological and psychiatric manifestations including memory impairment, movement disorders, seizures and psychiatric symptoms such as psychosis and hallucinations.

Autoimmune encephalitis is characterized by antibodies formed against neuronal cell surface proteins or antibodies against intracellular neuronal proteins. This can be idiopathic or can be associated with underlying malignancies, Infections or autoimmune diseases. Seronegative autoimmune encephalitis poses a diagnostic challenge due to absence of definitive autoantibodies.

We report a case of 24 year old female presenting with sleep disturbances, altered behavior, later diagnosed as seronegative autoimmune encephalitis.

Case Report

A 24 year old unmarried female who works as software professional presented to ER with history of sleep disturbance and mood swings for the past 3 months and history of behavioral disturbance for one week, and irrelevant speech since 1day. No previous history of seizures, loss of consciousness or weakness. On examination patient was conscious, irritable, no speech disturbance, motor, sensory, cranial nerve examination was normal and no signs of meningeal irritation. No evidence of papilloedema was found, Other systemic examination was unremarkable.

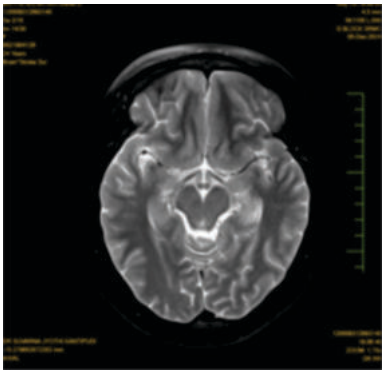
Baseline Investigations Showed:

Hemoglobin	11.5g/dL
WBC	16,850 cells/μL
Platelets	4.76 lakh cells/mm3
BUN	4 mg/dL
Creatinine	0.6 mg/dL
SGOT	21 U/L
SGPT	10 U/L
Sodium	140mEq/L
Potassium	4.2mEq/L
Chloride	103mEq/L
Bicarbonate	23mEq/L
Magnesium	2.3 mg/dL
Phosphorous	3.2mg/dL
Calcium	8.9mg/dL
ESR/CRP	28 mm/hr / 1.0 mg/dL
Urine routine	Normal
Blood and urine culture	Sterile
TVS pelvis	Normal ovaries and uterus.
Viral markers	Negative
ANA	Negative

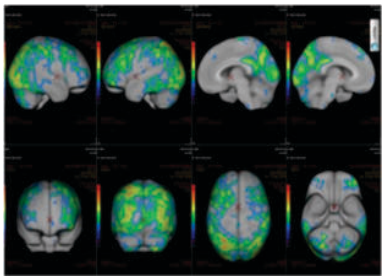
CSF Analysis Showed:

Protein	16 mg/dL
Glucose	72 mg/dL
Chloride	128mEq/L
ADA	4.3 IU/L
WBC	6 cells/mm3
RBC	Nil
CSF-gram stain	Normal
CSF-Culture	Normal

MRI Brain showed T2/FLAIR hyperintensities in the left median temporal lobe-may present limbic encephalitis. No significant stenosis or occlusion in the cerebral, vertebral and basilar arteries.



EEG was normal. Patient was started on Inj.Brivaracetam, Inj. Ceftriaxone and Inj.Acyclovir. During the course in the hospital patient became aggressive and as CSF PCR for HSV1,HSV2 and VZV quantitative assay was negative, hence autoimmune limbic encephalitis was suspected and serum autoimmune encephalitis panel was ordered (NMDA, GABA B, VGKC associated protein, AMP type glutamate receptor antibody) which was negative. PET-CT Brain showed patchy and confluent areas of hypometabolism involving most of bilateral cerebellar hemispheres with relative sparing of medial aspect of bilateral frontal and anterior, superior and inferior aspect of bilateral temporal lobes- findings consistent with autoimmune encephalitis.



Patient was started on Inj.Methylprednisolone500mg IV OD pulsing was given for 7 days, which was later switched to oral prednisolone1mg/kg body weight. Patient's sensorium improved and during the course in the hospital patient did not have any behavioural disturbances or altered mentation. On follow up patient has made a full recovery.

DISCUSSION

Autoimmune encephalitis is increasingly recognized as a major cause of subacute psychiatric and cognitive dysfunction, especially in young individuals[1]. Incidence of Autoimmune Encephalitis was estimated at 1.2 per 100,000 person-years[2]. Etiologically it can be paraneoplastic or non paraneoplastic. Serologically autoimmune encephalitis is divided into seropositive and seronegative based on presence of auto antibodies. Commonly associated Auto antibodiesare anti-NMDAR(N-Methyl D-Aspartate receptor), LGI 1(Leucine rich Glioma1), CASPR2(Anti- contactin associated Protein like2),GABA B and AMPAR (alpha amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor) etc. However few patients can be seronegative, especially if the disease is in early state or unidentified antigens are involved. Limbic encephalitis is an anatomical sub type, typically involving medical part of temporal lobe, amygdala and hippocampus, hence usually present with amnesia, behavioural disturbance, psychiatric symptoms, seizures and altered consciousness.The clinical and radiological features do not reliably differentiate seropositive from seronegative autoimmune encephalitis, or paraneoplastic from non-paraneoplastic encephalitis. However, certain features have been found to be more commonly associated with one or the other autoantibodies: N-Methyl D-Aspartate receptor-associated (NMDA-R)Limbic encephalitis usually presents with seizures and psychiatric symptoms in association with ovarian teratoma in young women, Voltage Gated potassium channel complex(VGKC) antibody-positive Limbic encephalitis presents with hyponatremia, faciobrachial dystonic seizures, amnesia and autonomic symptoms in middle-aged men, and GABA-B receptor encephalitis usually presents with psychosis, sleep disturbance and seizures in older men[3].Seronegative autoimmune encephalitis is a diagnostic challenge, According to the Graus criteria (2016)[4], a diagnosis of probable autoimmune encephalitis can be made when the patient has: Subacute onset (less than 3 months) of memory loss, behavioral abnormalities, or seizures,Plus at least one of the following:Abnormal brain MRI (hyperintensities involving medial part of temporal lobe in limbic area)[5,6]. Abnormal EEG (such as diffuse slowing or epileptiform activity), CSF findings showing inflammation (pleocytosis or elevated protein), And no evidence of alternative diagnoses (like infections, metabolic causes, or tumors.PET CT also plays a important role when neuroimaging is inconclusive [7].In our case, the patient's initial presentation was suggestive of a psychiatric illness. However, MRI showed left medial temporal lobe hyperintensities and PET-CT findings also supported the diagnosis of Autoimmune encephalitis.

Treatment of Autoimmune encephalitis involves early first line immunotherapy with corticosteroids, IVIG and plasma exchange. Second line therapy includes Rituximab or Cyclophsphamide in refractory or relapsing cases[8,9]. Our patient responded well to steroids and had a full recovery by the time of discharge.

CONCLUSION

This case emphasizes the need for a high index of suspicion for autoimmune encephalitis, even in the absence of detectable antibodies. Imaging and early immunotherapy are key to favorable outcomes. Early treatment is crucial to prevent long term neurological complications such as epilepsy ,dystonia, cognitive impairment. Seronegativity should not delay immunosuppressive therapy if diagnostic criteria are fulfilled.

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