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Original Research Paper

Neurology

RARE CASE REPORT -AUTOIMMUNE LGI1 LIMBIC ENCEPHALITIS IN ELDERLY

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KEYWORDS :

BACKGROUND

Autoimmune encephalitis is one of the main causes of noninfectious encephalitis. Can be broadly classified into non-paraneoplastic, paraneoplastic and vasculitis associated encephalopathy. It can be triggered by tumors and infections. Autoimmune encephalitis presents with variety of clinical features such as acute onset behavioral changes, psychiatric symptoms, memory loss, movement disorders, dystonia, mutism and seizures. Neuronal antibodies are directed against cell surface Ag(CSAab) ,synaptic antigen (SyAab), intraneuronal Ag(INAab). Anti LG1 and CASPR2 encephalitis are usually non-neoplastic autoimmune encephalopathy where antibodies are directed against proteins associated with Voltage gated k channel. About 50% patients with anti-VGKC encephalitis do not present antibodies against LGI1 or CASPR-2. Anually 1 case is detected amongst 100000 patients. This is a case report of a patient presented to Geriatrics OPD and the series of evaluation which led to diagnosis and treatment outcome.

Case Report

A 66-year-old male patient, a follow-up case of hypertension, compliant to medication came to Geriatrics OPD with complaints of giddiness intermittent in nature,associated with blackouts for a duration of 2 to 3 seconds since 1 month. Patient's relatives gave history of blank stares with loss of response during these episodes, and occurred 4-5 times in a day. Patient did not report involuntary movements, memory loss, bowl bladder incontinence, loss of consciousness, limb weakness, facial weakness, sensory loss and cranial nerve deficits. Initially routine biochemical investigations, were done and patient was evaluated for postural hypotension and peripheral causes of giddiness. No abnormality was found. Cardiac evaluation and MRI Brain imaging was normal.2 months later patient presented with increased episodes (7 to 8 times/day) of blackouts associated with blank stares, right upper limb and lower limb predominant non sustained involuntary movements with hyperextension of fingers, facial contractions and increased tone of back muscles lasting for 3 seconds. Irrelevant talks were reported soon after such episodes. Increased anger and irritability behavior reported by relatives. Patient gave history of loss of memory during such episodes. No history of recent fever , vaccinations or COVID infection. Patient was screened for HIV, thyroid antibodies and ANA. EEG showed abnormal intermittent theta waves and CSF examination mild increase in CSF protein. Patient was started on prophylactic antiepileptic medication but did not respond to therapy. Patient was screened for LGI1 and CASPR2 Antibodies. LGI 1 antibody was detected on immunofluorescence with absence of CASPR2 antibodies and speckled pattern of ANA detected.18 FDG PET scan revealed no abnormal uptake in any tissue. Patient was started on Inj.Methylprednisolone 1g/day and administered for 5 days along with calcium, Vitamin D supplements and blood sugar monitoring. Patient showed complete remission of involuntary activity after 5 days of steroids. He was discharged on oral Tab Prednisolone and no Focal seizure activity has been reported till date.

DISCUSSION

Autoimmune encephalitis presents as an immune response against neuronal autoantigens with production of antibodies. Patients with AIE may present with a variety of movement disorders. Autonomic disturbances are also frequently reported such as sudoresis, hypotension and gastrointestinal manifestations. Diagnostic criteria for limbic encephalitis include working memory deficits, psychiatric symptoms, and often seizures, rapid progression within three months from onset. Definite sero-positive AIE requires typical clinical picture and detection of positive anti-neuronal antibodies in serum and CSF or Bilateral brain abnormalities on MRI T2-weighted FLAIR sequence restricted to the medial temporal lobes. EEG usually shows epileptic or slow-wave activity involving the temporal lobes with CSF pleocytosis .LGI1(leucine rich glioma inactivated protein1) is a secreted synaptic protein that interacts with transmembrane proteins ADAM22 and ADAM23 to form a trans-synaptic complex involving potassium channels. They are expressed mainly in hippocampus. The clinical spectrum of anti-LGI1 encephalitis usually comprises limbic encephalitis, hyponatremia and seizures occurring in an elderly Half of the patients develop fasciobrachial dystonic seizures, which are characterized by brief unilateral contractions of the arm (often evolving into the ipsilateral face or leg) that are shorter than three seconds and occur several times a day. Two-thirds of patients present with brain MRI hyperintensities in the medial temporal lobe. Paraneoplastic anti-LGI1 encephalitis is uncommon. The CASPR-2 is a juxtaparanodal adhesion molecule that interacts with contactin 2 and the cytoskeleton, and is involved in clustering of potassium channels in myelinated axons. Anti-CASPR2 antibodies are associated with peripheral nerve hyperexcitability (myokymia, fasciculations, cramps) and encephalitis.

Most individuals affected are male and one-third of them present with paraneoplastic manifestations, usually associated with thymoma, lung cancer or endometrial carcinoma. About half of patients with anti-VGKC encephalitis do not present antibodies against LGI1 or CASPR.Differential diagnosis in anti-neuronal AIE includes, Hashimoto's encephalopathy , other steroid-responsive encephalopathies, acute disseminated encephalomyelitis, neuromyelitis optica spectrum disorders, central nervous system vasculitis, neuropsychiatric lupus, angiocentric lymphoma, Rasmussen's encephalitis and febrile infection related epilepsy syndrome.Serological panel for autoimmune disorders should be evaluated along with routine serum investigations. It is important to rule out HIV and HHV6-

associated encephalitis in immuno-compromised patients. Due to the low frequency of tumor association in patients with anti-LGI1 and patient screening should be considered at disease onset, with no need for periodic screenings. The nature of the antibody and the clinical syndrome, determines the risk and type of an underlying malignancy. Fluorodeoxyglucose positron emission tomography (FDG-PET) is indicated as it increases cancer detection.Evidence suggests that early immunotherapy improves outcome thus treatment for AIE should not be delayed. 1st line treatment approaches includes corticosteroids, intravenous immunoglobulin and plasma exchange .Patients are treated with methylprednisolone 1 g IV for 3–5 days and intravenous immunoglobulin (0.4 g/kg/day for five days) or methylprednisolone and plasmapheresis. Plasmapheresis is recommended in patients with refractory seizures and severe dysautonomia, although there is no compelling evidence of superiority of any approach. If an associated tumor is detected, oncologic management is important for improvement. Autoimmune encephalitis patients who fail to improve after 10–14 days should receive second-line therapies such as rituximab or cyclophosphamide, or both. Relapses may occur in 31% of patients with anti-LGI1 encephalitis and 10% of those with anti-CASPR2 encephalitis, sometimes years after the first episode. About 33% of the patients with anti-LGI1 encephalitis are left disabled, mostly due to memory problems.

Diagnosis of Autoimmune encephalopathy should always be considered in a case presenting with acute onset involuntary activity with behavioral changes and memory impairment even with normal radiological studies. Tumor workup should be ideally carried out in all cases as it affects prognosis. Early initiation of therapy is likely to improve outcome. Exclusion of other diseases mimicking autoimmune encephalitis is important as it has its own therapeutic implications.

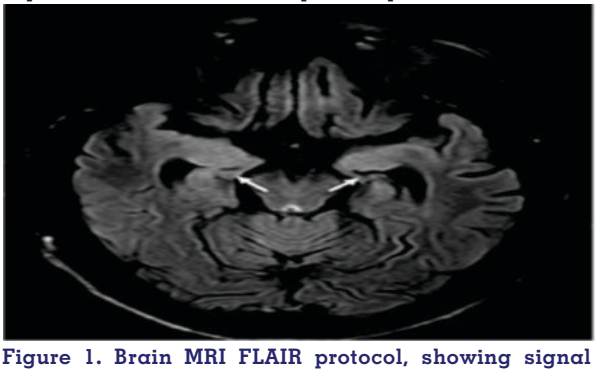

Figure 1. Brain MRI FLAIR protocol, showing signal hyperintensity and atrophy at the mesial temporal level and bilateral hippocampi.

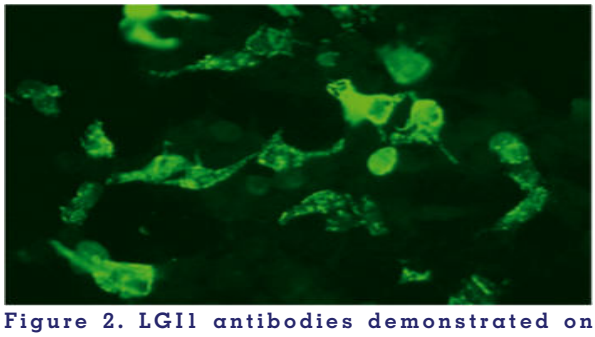

Figure 2. LGI1 antibodies demonstrated on Immunofluorescence

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