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ANTI-CASPR 2 ANTIBODY ENCEPHALITIS: A CASE REPORT

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ABSTRACT

Encephalitis is a term denoted to Inflammation in the brain which can be due to infection, autoimmunity, or can be a part of a paraneoplastic phenomenon with malignancy. Anti-CASPR 2 antibody encephalitis is a rare form of encephalitis that can be associated with malignancy, paraneoplastic phenomenon or can be an autoimmune disease.

We present a case of a young boy who presented with new onset seizures and altered sensorium and was diagnosed with anti-CASPR 2 antibody encephalitis. Anti-CASPR 2 Antibody Encephalitis is a rare form of encephalitis which due to its great diverse presentation should be kept in the differential diagnosis of conditions like limbic encephalitis.

Key Words: CASPR 2; autoimmune encephalitis; KV1; autoimmunity;

INTRODUCTION

CASPR-2 (contactin-associated protein-like 2) is a protein that's part of neurexin family. It is a cellular adhesion molecule that acts as membrane scaffold to anchor the KV1 channels in the unmyelinated regions of nodes of Ranvier. It is most located in neurons of the basal ganglia, limbic system, motor area, sensory pathways, and temporal lobe.[1]

The antibody to CASPR2 acts by blocking its scaffolding and anchor action for KV1 channels which in turn leads to membrane hyperexcitability. It can manifest as limbic encephalitis, as Morvan syndrome, where presenting features include neuromyotonia, memory disturbances, altered conscious state, sleep disorders, and autonomic dysfunction.[2] It affects mostly older males with a median age of 65 years but is rarely reported in the pediatric age group. Its presentation and disease course are slower than other autoimmune disorders. This disorder is not usually associated with neoplasm.[3]

CASE PRESENTATION

Fourteen years of age, male, having no previous co-morbidities, presented in ER of Pakistan Institute of Medical Sciences with a history of low-grade fever with generalized body aches for five days, and irrelevant talk, irritability for three days. Then he developed altered conscious state with generalized tonic-clonic fits for one day. No history of headache, vomiting, flu like symptoms, diarrhea, weight loss, night sweats or change in bowel habits, memory disturbances, and sleep disorders.

At the time of presentation, his vitals were blood pressure of 100/70mHg, pulse 124 beats/min, respiratory rate of 28 breaths/min, temperature of 102 degree F, and O2 saturation of 76% at room air with random blood glucose level of 127mg/dl. He was intubated, pupils were bilaterally equal but sluggishly reactive to light, and plantars were bilateral upgoing. On chest auscultation, there were bilateral coarse crepitations and the abdominal examination was unremarkable. A non-contrast CT scan of brain showed no abnormality. Treatment started on the lines of meningoencephalitis with empirical antibiotics i.e. ceftriaxone 2 gram twice a day and Vancomycin according to body weight, and anti-seizure medicines. These antibiotics were later stopped as the treatment progressed and work up showed evidence of autoimmunity rather than infection. He was shifted to the medical Intensive Care Unit and put on mechanical ventilatory support.

Complete blood count showed mild leukocytosis with a neutrophilic predominance and normal hemoglobin and platelet count. Serum electrolytes, liver enzymes and serum urea and creatinine were within normal range. COVID-19 PCR from a nasopharyngeal swab was negative. Cerebrospinal fluid routine examination showed a total leukocyte count of 08/ uL, 70% neutrophils and 30% lymphocytes, and glucose of 90 mg/dl and protein of 29.1mg/dl. Anti-nuclear antibody was negative, and the serum Erythrocyte sedimentation rate was 80mm/hr. CSF Herpes Simplex Virus PCR HSV 1 and HSV 2 were negative. Serum autoimmune encephalitis antibodies profile test by Indirect Immunofluorescence came positive for Contactin-associated protein 2 (CASPR2 antibodies).

A plain Computed tomography scan brain was unremarkable. Magnetic resonance imaging of the brain with contrast was unremarkable. Electroencephalography with 19 channel awake recording with International 10/20 electrode placements showed diffuse slowing. The workup for occult malignancy was negative. The following Table 1 summarizes the laboratory workup.

Table 1: Workup and laboratory investigations

Laboratory Investigations		
	Patient Lab results	Normal Reference Ranges
TLC	140000 / microliter	4000-11000 / microliter
Hemoglobin	13.7 g/dl	13.2-16.6 g/dl
Platelets	225000	150000-400000 / microliter
Serum Urea	11 mg/dl	5 – 20 mg/dl
Serum Creatinine	0.8 mg/dl	0.5-1.1 mg/dl
Serum Sodium	138 mEq/L	135-145 mEq/L
Serum Potassium	3.9 mEq/L	3.5-4.5 mEq/L
ALT	35	35 – 45
Serum Bilirubin	0.6 mg/dl	0.2 – 1.2 mg/dl
Covid 19 PCR	Negative	Negative
ESR	80 mm/Hour	< 15 mm/Hour

CSF analysis		
	Patient Value	Reference
White blood Cell count	08 /ul	< 5/ul
Protein	29.1 mg/dl	15 – 45 mg/dl
Glucose	90 mg/dl	> 60% serum glucose
Xanthochromia	Absent	Absent
RBC's	< 5/ul	< 5/ul
Gram stain	Negative	Negative
Auto antibodies		
Anti NMDAR antibody	Negative	Negative
Anti CASPR 2 antibody	Positive	Negative
Anti VGKC antibody	Negative	Negative
Anti LGI1 antibody	Negative	Negative
Anti-GAD antibody	Negative	Negative

Abbreviations: TLC –Total leukocyte count, ALT- alanine amino transferase, ESR- erythrocyte sedimentation rate, HIV- human immunodeficiency virus, TSH-thyroid stimulating hormone, RBC-Red blood cells, WBC- white blood cells, Hpf-high power field, VGKC-voltage gated potassium channel, GAD-glutamic acid decarboxylase, NMDA- N-methyl-D-aspartate, CASPR-Contactin-associated protein-like, LGI1- Leucine-rich glioma-inactivated 1)

He was extubated after three days and was stepped down to the neurology ward. His GCS improved with no focal neurological deficit. Pulse Therapy was started in the form of intravenous methylprednisolone one gram for five days and he showed marked recovery. Patient was then shifted to oral steroids with bone protective agents. He was discharged on oral anti-seizure medication and oral steroids with the plan of long-term immunosuppression therapy, At the time of discharge he had a Modified Rankin Scale of 0 and Mini-Mental State Examination score (MMSE) of 30.

DISCUSSION

Anti –CASPR2 Encephalitis is a rare autoimmune encephalitis with approximately 150–200 patients reported in total in all. It has a male predominance of around 90% with the age of onset between 60-70 years of age but can be earlier in women.[5] Anti –CASPR2 Encephalitis presents with insidious onset of symptoms that can include psychiatric symptoms, memory and speech disturbances, seizures, abnormal movements, altered consciousness. The major causes of mortality are autonomic instability, and central hypoventilation. It can also present as Morvan syndrome with hyperexcitable peripheral nerves (paresthesias, fasciculations limb twitch), rarely seen in other autoimmuneencephalitis.[4]

Core symptoms include cerebral symptoms (cognition 80%, epilepsy 50%), autonomic dysfunction (45%), and peripheral nerve hyperexcitability (55%), cerebellar symptoms (35%), weight loss (60%), insomnia (55%) and neuropathic pain (60%).[5]

Standard laboratory studies are normal in patients. CSF analysis can show mild exocytosis and raised proteins but is normal in 75% of patients, MRI of the brain is also mostly normal but can show medial temporal lobe high signal abnormalities bilaterally, and EEG shows nonspecific abnormalities.[6] Diagnosis is confirmed via CSF analysis for antibodies.

There is no randomized trial of treatment to date due to the rarity of the disease. But most reports suggest treatment with immune therapy including steroids, and IVIGs with some patients requiring additional therapies such as cyclophosphamide or rituximab.[6] The decision to start further immune therapy is decided on case-to-case basis depending on factors like response to steroids, functional status and presence or absence of relapse. Studies have shown that if promptly diagnosed anti-CASPR2 antibody encephalitis and treated with immune therapy, the patient shows good recovery and has good long term prognosis.[3,6] Although additional data is required for long-term prognosis.

CONCLUSION

Despite its rarity, due to its great diverse presentation, anti-CASPR 2 antibody encephalitis should be kept in the differential diagnosis of certain conditions like limbic encephalitis, epilepsy, new onset psychiatric symptoms and ataxia.

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Amina Saddiqa; case management, manuscript revision
Bushra Khalid; case management, manuscript revision
Soban Khan; case management, manuscript revision
All the authors have approved the final version of the article, and agree to be accountable for all aspects of the work.