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VGKC ANTIBODY (ANTI LG1) ASSOCIATED LIMBIC ENCEPHALITIS IN A YOUNG ADULT WITH FULL RECOVERY

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ABSTRACT

A young boy with no premorbids was admitted with fever, fits and psychosis. His initial investigations including cerebrospinal fluid (CSF) routine examination, electroencephalogram(EEG) and MRI brain with contrast were normal. His autoimmune encephalitis panel revealed positive voltage gated potassium channel(VGKC) antibodies, anti -leucine rich glioma inactivated 1 antibody (LG1) group and was give five doses of methylprednisolone and five sessions of plasmapheresis. Psychiatric symptoms took one month to respond. He had a complete recovery. Autoimmune limbic encephalitis should be diagnosed promptly in young patient with fit, psychosis and a high index of suspicion should be kept as initial work up including MRI brain with contrast, EEG and CSF examination can be normal in such patients.

Key words: Limbic encephalitis, anti-LG1 encephalitis, epilepsy

INTRODUCTION: Limbic encephalitis (LE) is an uncommon neurological disorder characterized by a subacute and progressive altered consciousness, memory disturbance, and recurrent seizures[1]. We present a case of anti LG1 associated limbic encephalitis in a young patient who had a very typical presentation and excellent outcome.

Case summary

A 21 years old boy with no premorbids, presented to us with one week's history of altered behaviour, fever and fits. One day prior to it he developed lethargy, headache, generalised body aches and decreased appetite. Fever was high grade intermittent associated with rigors recorded up to 104. Following it he developed altered behaviour, irritability, and fits which were generalised tonic clonic (GTC), with tongue bite and urinary incontinence. Along with GTC he also developed dystonic posturing of neck and arching of body. On examination, he was confused, there was no neck stiffness and there was no focal deficit. Initially he was investigated and treated on the lines of meningoencephalitis. Investigations revealed normal Computerised tomography (CT) brain, normal white blood cells, C reactive protein. CSF routine examination was normal (<5 cells, protein 19.8mg/dl, glucose 56mg/dl). Blood cultures, malarial parasite smears, urine routine examination were normal. He was started on injection Acyclovir along with injection Meropenem on day 1, his fever settled after 48hours but the fits persisted. EEG was done which came out normal. MRI brain with contrast was also normal as shown in figure 1. CSF Herpes Simplex Virus PCR also came back negative. His repeat EEG showed extreme delta brushes with some degree of background slowing as shown in figure[2].

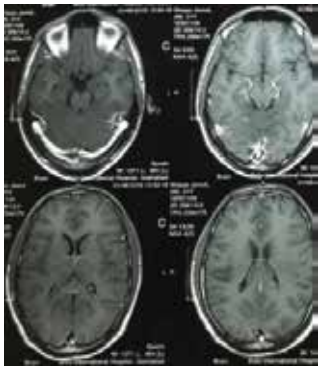

Figure 1. MRI brain with contrast showing no abnormality.

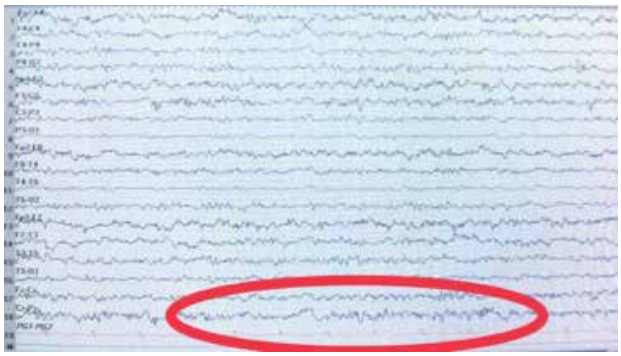

Figure 2. EEG showing extreme delta brushes over a slow background.

His fits persisted and were refractory to treatment. As he was a young patient with refractory seizures and psychiatric manifestations so autoimmune encephalitis profile was also sent, which came out positive for Voltage gated potassium channel (VGKC) antibodies (LG1 group) in serum. The patient was started on intravenous high dose steroids in form of intravenous methylprednisolone in dose of one gram daily, but the fits persisted, his antiepileptics were escalated to four antiepileptics including valproate sodium, levitiracetam ,lacosamide and phenytoin at about near maximal doses but the fits did not respond. Along with GTC fits he had facial twitching, faciobrachial dystonic seizures. As seizures were refractory and patient was not improving, he was started plasma exchange (PLEX), he had five sessions of plasma exchange each session being 50ml/kg. After PLEX fits were controlled but neuropsychiatric symptoms persisted. He was started on antipsychotics and was given good nursing care. He was also worked up for other causes, like autoimmune profile, CT chest abdomen and pelvis came back negative. Anti N-methyl-d aspartate (NMDA) antibodies and other autoimmune encephalitis panel antibodies also came back negative. Paraneoplastic antibodies panel also came back negative. After two weeks of completion of PLEX patient started improving, fits settled, antiepileptics were tapered off gradually, antipsychotic were also gradually withdrawn. At one month followup patient had no cognitive deficits.

Discussion

Limbic encephalitis with LG 1 antibodies is a rare neuroimmunological disorder characterized by cognitive decline, psychiatric disturbances and seizures (distinctively faciobrachial dystonic seizures) in association with detection of LG1 antibodies in serum or CSF. Additional features are hallucinations, sleep cycle disturbances, agitation, and delusions[2].

Faciobrachial dystonic seizures(FDSP) are highly distinctive seizures associated with VGKC complex antibodies, almost always in the LGI 1 subtype. Every FBDS is characterized by a dystonic posturing of the arm, both proximally and distally, and may involve also the ipsilateral face and less commonly, the trunk and the ipsilateral leg. They carry a high chance of developing VGKC LE, and their recognition should prompt consideration of immunotherapies[2]. Hyponatremia is present in about 60% of patients[2]. Serum sodium are often reduced in FBDS patients presenting also with cognitive impairment but they were repeatedly normal in our patient.

Although there are currently no agreed-upon diagnostic criteria for limbic encephalitis; a useful set of criteria for both paraneoplastic limbic encephalitis (PLE) and non-paraneoplastic limbic encephalitis(nPLE) was proposed by Bien and Elger in 2007 as shown in table 1[3].

Domains	Criteria
Recent onset (<5 years) clinical "limbic" syndrome in adulthood	At least one of the following three: Disturbance of episodic memory Temporal lobe seizures Affective disturbance, typically loss of inhibition and lability of mood
Autoantibodies	Voltage-Gated Potassium Channel (VGKC)
Brain MRI	Otherwise unexplained temporo-medial T2/FLAIR signal increase
Histopathology	Lymphocytic micronodular encephalitis mainly affecting the temporo-medial structures. No histopathological indication of other primary pathology, including stroke, tumor, posttraumatic scar, neurodegenerative disorder

TABLE 1. Bien and Elger's Diagnostic Criteria for Limbic Encephalitis3.

Anti LG1 encephalitis is most often non-paraneoplastic. Neoplasms are detected only in a minority of seropositive patients for VGKC complex and do not significantly associate with Caspr 2 or LG1[2]. A normal brain MRI does not exclude these cases. MRI brain was also normal in our patient and one should not rely on MRI to diagnosis these conditions. Similarly, MRI does not differentiate between infective and these autoimmune etiologies[4]. Because of the nature and complexity of non- paraneoplastic limbic encephalitis (nPLE), a greater awareness of this condition is warranted, particularly among psychiatrists in order to establish the correct diagnosis and commence early treatment as VGKC complex antibody-associated non paraneoplastic limbic encephalitis is potentially treatable and has good response to early initiated immunotherapy[2].

Conclusion

Autoimmune encephalitis should always be suspected in a young patient with neuropsychiatric problems, fits and movement disorders. CSF routine examination, EEG, even MRI brain with contrast could all be normal in a patient with autoimmune encephalitis and a high index of suspicion should be kept to diagnose and promptly treat such conditions.

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Farheen Niazi; concept, data collection, data analysis, manuscript writing, manuscript review
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Rizwan Ali; concept, data collection, data analysis, manuscript writing, manuscript review
Dr Tahir Aziz; data collection, data analysis, manuscript writing, manuscript review