

Anti-Voltage-gated Potassium Channel Limbic Encephalitis with Psychiatric Features: a Case Report

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Abstract

We report a case of anti-voltage-gated potassium channel (VGKC) limbic encephalitis in a 47-year-old man presenting with a 2-year history of psychiatric features. The patient had cognitive impairment, slurred speech, and a mildly unsteady gait but no other neurological deficits or seizures. Results of blood, urine, and cerebrospinal fluid tests and magnetic resonance imaging of the brain were normal. However, electroencephalography showed an epileptogenic focus in the bilateral temporal regions with mild to moderate diffuse encephalopathy. Autoimmune panel results confirmed the diagnosis of anti-VGKC limbic encephalitis, with a serum VGKC concentration of 6730 pmol/L. The patient was treated with Keppra and pulsed intravenous methylprednisolone for 3 days, and his behaviour improved.

Key words: *Electroencephalography; Limbic encephalitis; Methylprednisolone; Potassium channels, voltage-gated*

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Case presentation

In December 2014, a 47-year-old Chinese man presented with a 2-year history of psychiatric features such as change in personality, child-like behaviour, increasing irritability, mood lability, suicide threats, and auditory hallucinations. On examination, the patient had cognitive impairment including short-term memory loss and inability to perform simple calculations, as well as slurred speech and a mildly unsteady gait, but no other neurological deficits or seizures. Results of blood tests and magnetic resonance imaging of the brain (without contrast) were normal. The condition was deemed to be psychiatric, and the patient was transferred to a psychiatry outpatient clinic and started on olanzapine.

However, the patient responded poorly to olanzapine and deteriorated considerably within 3 weeks. His family reported worsening cognitive impairment with new-onset agnosia, poorer ability to perform executive functions, disorganised thought processes, and increased daytime somnolence. He was increasingly agitated, euthymic, and had persistent auditory hallucinations and paranoia. Repeat physical examination revealed worsening slurred speech and unsteady gait but no new neurological signs. The patient

was not oriented to place or person.

One week later, the patient was referred to the neurology department and underwent extensive re-evaluation involving serum ceruloplasmin/urine copper, N-methyl-D-aspartate antibody, anti-thyroid peroxidase antibody, anti-thyroglobulin, blood and urine toxicology, tumour markers (prostate-specific antigen, α -fetoprotein, carbohydrate antigen 19-9, carcinoembryonic antigen), and paraneoplastic antibodies; cerebrospinal fluid examination for 14-3-3, oligoclonal bands, cytology, and infective markers; and repeat magnetic resonance imaging of the brain (with contrast). All results were negative.

However, electroencephalography showed an epileptogenic focus in the bilateral temporal regions with mild to moderate diffuse encephalopathy. A provisional diagnosis of autoimmune encephalitis was made while awaiting the autoimmune panel results involving anti-voltage-gated potassium channel (VGKC) Ab, anti-paraneoplastic Ab, and anti- γ -aminobutyric acid Ab. Keppra and pulsed intravenous methylprednisolone (for 3 days) was initiated, and the patient had improvement in behaviour. Results showed a serum VGKC concentration of 6730 pmol/L, and the diagnosis of anti-VGKC limbic encephalitis was confirmed.

Malignancy workup was negative and the patient was discharged with no further episodes of agitation. Six months later, the patient had a relapse and did not respond well to intravenous methylprednisolone and needed plasma exchange. He has since recovered and remained symptom-free for 1.5 years on low-dose prednisolone.

Discussion

Anti-VGKC limbic encephalitis is a non-paraneoplastic

variant of limbic encephalitis.¹ This case highlights some important implications for the diagnosis, evaluation, and management of limbic encephalitis. The criteria for the diagnosis of limbic encephalitis include²: (1) subacute onset (rapid progression within <3 months) of working memory deficits, seizures, or psychiatric symptoms suggesting involvement of the limbic system; (2) bilateral brain abnormalities on T2-weighted fluid-attenuated inversion recovery magnetic resonance imaging highly restricted to the medial temporal lobes; (3) at least one of the following: cerebrospinal fluid pleocytosis (white blood cell count of >5 cells per mm³), electroencephalography showing epileptic or slow-wave activity involving the temporal lobes; and (4) reasonable exclusion of alternative causes.

In our patient, initial presentation with mood and behavioural changes and cognitive impairment such as short-term memory loss were typical features of limbic encephalitis.³ Hallucination and agitation were less common features.³ Slurring of speech could suggest cranial nerve or brain stem involvement. However, no diplopia or facial numbness was noted. He did not manifest any seizures such as facial-brachial dystonia seizure, which is common in patients with anti-VGKC limbic encephalitis.^{1,3} Hypothalamic and extrapyramidal dysfunction were absent. Although the onset of limbic encephalitis is usually acute or subacute, cases with a more chronic course (2 years) have been documented.^{1,3}

The presentation of psychiatric features and the absence of some typical features of limbic encephalitis led to the initial diagnosis of a psychiatric disorder. Although the initial cognitive dysfunction, unsteady gait, and slurring of speech suggested a neurological aetiology, prompt neurological investigation was not performed. Thus, clinicians should be vigilant for any neurological signs, including evolving signs that may not be initially evident. Minimal neurological signs should not preclude a neurological diagnosis.

The turning point was the patient's sub-optimal response to conventional psychiatric treatment, which warranted re-evaluation that yielded positive electroencephalographic findings. Thus, clinicians should consider alternative aetiologies in cases with progressive cognitive deterioration that responds poorly to conventional psychotropic treatment.

The absence of radiological findings alone should not rule out limbic encephalitis, as such findings may not be sensitive or specific.³ When limbic encephalitis is clinically suspected, neuroimaging is useful to exclude other causes and needs to be supplemented with electroencephalography, cerebrospinal fluid examination, and serologic testing for biomarkers.

Cognitive, mood, and behaviour disturbances

involve a broad range of differential diagnoses. Diagnostic criteria can assist clinicians in judging the likelihood of limbic encephalitis. This case demonstrates that greater flexibility is required in interpreting the existing criteria to include the broad spectrum and evolving nature of limbic encephalitis presentation and findings.³ This can help to avoid presumptive exclusion and enable earlier diagnosis of limbic encephalitis.²

Autoimmune encephalitis is often treatment-responsive, and a delay in diagnosis and treatment may precipitate persistent cognitive impairment. Our patient had a good prognosis despite delayed diagnosis and treatment. Empiric immunosuppression treatment was initiated before confirmatory antibody results were available. A thorough consideration of differentials, especially infective aetiologies, is thus essential.

This case showed that the line separating neurology and psychiatry is thinner than once thought. There has been debate on whether the distinction between psychiatric and neurological disorders should be abandoned.⁴ Emerging imaging findings indicate that these differences are subtler than expected.⁵ The diagnostic process is a testament to clinical vigilance and close collaboration between neurologists and psychiatrists. A more patient-centred, collaborative approach between different specialties is warranted.

Conclusion

Anti-VGKC limbic encephalitis remains a diagnostic challenge. Our case highlights the need for clinical vigilance for neurological signs in psychiatric presentations, re-evaluation of diagnostic criteria for limbic encephalitis, and close collaboration between neurologists and psychiatrists.

Declaration

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