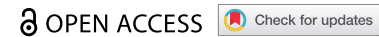


CASE REPORT



## A case of anti-VGKC antibody encephalitis and prolonged encephalopathy despite spontaneous resolution of imaging abnormalities

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### ABSTRACT

Anti-voltage-gated potassium channel (anti-VGKC) antibody encephalitis is a common form of autoimmune encephalitis (AE). AE is usually associated with autoimmune diseases or paraneoplastic phenomena such as seen in small cell lung cancer. Clinical presentation can include memory impairment, seizures, and psychiatric symptoms. We report a case of a 72-year-old male with non-small lung cancer in remission who presented with erosive gastritis and acute severe encephalopathy. Anti-VGKC antibody limbic encephalitis was diagnosed. Spontaneous resolution of encephalitis-associated changes on brain Magnetic Resonance (MR) with concomitant decreased circulating antibody levels were observed despite lack of overall cognitive improvement.

**Abbreviations:** AE: autoimmune encephalitis; AMPAR: antibody limbic encephalitis - anti- $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor encephalitis; Anti-VGKC encephalitis: anti-voltage-gated potassium channel antibody encephalitis; CRP: c-reactive protein; CT: computed tomography; EEG: electroencephalography; ESR: erythrocyte sedimentation rate; GCS: Glasgow Coma Scale; MRImaging: Magnetic resonance imaging; NMDA-R encephalitis: Anti-N-methyl D-aspartate receptor encephalitis; PCR: polymerase chain reaction.

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## 1. Introduction

Autoimmune encephalitis is a group of inflammatory brain conditions with diverse clinical, laboratory, and imaging presentation. Anti-VGKC antibody encephalitis is a relatively common autoimmune encephalitis. Although previously was described in other AE such as anti- $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPA) encephalitis [1] and NMDA-R encephalitis, a clinical presentation consistent with severe encephalopathy seem unusual with anti-VGKC antibody encephalitis [2]. Hyperammonemia is a well-known cause of severe encephalopathy and can be seen in patients with cirrhosis, infections with urea-producing bacteria, small intestinal bacterial overgrowth syndrome, recent surgery such as lung transplant, bariatric surgery, ureterosigmoidosis, and as a side effect of drugs [3,4,5].

## 2. Case

A 72-year-old nursing facility male resident with non-small lung cancer in remission, previous cerebrovascular accident with residual right-sided hemiparesis, deep venous thrombosis with vena cava filter in situ, and hypothyroidism, presented with acute encephalopathy, abdominal distension, and melena. At baseline, the

patient required assistance with most daily activities except feeding and used a motorized scooter for ambulation. On presentation, physical examination revealed Glasgow Coma Score (GCS) of 6 without meningeal signs and chronic right-side hemiparesis. Laboratory findings revealed mild hyperlactatemia of 3.7 mmol/L (normal range 0.5–2 mmol/L), sodium of 140 mmol/L (normal range 136–145 mmol/L), significantly elevated ammonia of 407  $\mu$ mol/L (normal < 34  $\mu$ mol/L, unknown baseline) with normal hemoglobin of 12.1 g/dL as well as normal hepatic and biliary parameters. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were elevated at 120 mm/hr and 4.56 mg/dl, respectively (ESR normal range 0–20 mm/hr; CRP normal < 0.3 mg/dl). Non-contrast Computed Tomography (CT) of the brain showed old cerebral infarcts involving portions of the temporal lobe, periventricular region, and basal ganglia. CT chest was unremarkable. CT abdomen and pelvis demonstrated fecal impaction without findings of liver cirrhosis or gastrointestinal (GI) process. During the next 24 hours, a significant decrease in hemoglobin to 8.7 g/dL was observed (normal 12.0–15.6 g/dL) without evidence of overt GI bleeding. An upper endoscopy revealed erosive gastritis. Blood transfusion was not required. Despite correction of ammonia level down to 40  $\mu$ mol/L, the patient remained encephalopathic.

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Twenty-four-hour electroencephalography (EEG) monitoring did not show seizure activity but diffuse slowing was observed. MR imaging of the brain revealed cortical diffusion restriction without gadolinium enhancement involving the left frontal, right parietal, and bilateral temporal lobes. Cerebrospinal fluid (CSF) examination was acellular and showed elevated protein of 77 mg/dL (normal 12–60 mg/dL) as well as elevated immunoglobulin G of 13.5 mg/dL (normal 0.0–8.6 mg/dL). CSF herpes simplex virus type-1 and 2 PCR was negative. Repeat EEG showed improvement of diffuse slowing and remained without signs of seizure activity. Given electroencephalographic improvement and clinical stability, the patient was discharged on hospital day 8. At discharge, the patient was unable to participate in cognitive assessment. Shortly thereafter, anti-VGKC antibody was found to be elevated at 134 pm/L (normal 0–31 pm/L). The patient was readmitted to the hospital for repeat clinical evaluation. GCS had improved to 15. Montreal Cognitive Assessment score of 12 was obtained (normal >26, unknown baseline). Decreased ESR to 63 mm/hr and stable CRP of 4.67 mg/dl were observed. Repeat MR Imaging of the brain showed resolution of previously seen abnormalities as described. Repeat anti-VGKC antibody titer was also decreased to 93 pm/l. Pulse dose corticosteroid therapy was initiated given continued yet improved cognitive impairment. The patient was again discharged but unfortunately lost to follow-up. Months later, repeat hospitalization for recurrent gastrointestinal bleeding and persistent severe cognitive impairment led to hospice care and demise.

### 3. Discussion

Anti-VGKC antibody encephalitis is more common in non-paraneoplastic syndromes. In fact, only 30% of cases were associated with malignancy such as small cell lung cancer and thymoma [6]. Classic symptoms include behavioral and mood changes, memory impairment, and temporal lobe seizures [7]. Although our patient presented with acute severe encephalopathy and hyperammonemia resulting from an upper GI bleeding source, the lack of improvement in mental status coupled with the multi-lobar abnormalities seen on MR imaging, the presence of CSF immunoglobulins, and the presence of serum anti-VGKC antibody point towards the diagnosis of anti-VGKC antibody encephalitis. Kotsenas *et al.* have previously reported a lack of correlation between MR Imaging changes and antibody titer or clinical presentation in anti-VGKC encephalitis although spontaneous or post-immunotherapy resolution of findings was uncommon [8]. Moreover, according to Scott *et al.*, imaging abnormalities may be non-specific [9]. Improvement of anti-VGKC antibody encephalitis with anti-seizure treatment has been previously described as transient postictal changes cannot

be excluded despite absence of EEG abnormalities [10]. Anticonvulsant treatment can lead to resolution of anti-VGKC antibody-related seizures due to an indirect immunomodulatory effect [10,11]. In our patient, we cannot exclude an anti-convulsive effect of propofol and/or midazolam. In our patient, immunomodulation using pulse dose corticosteroid showed limited clinical improvement. Hyperammonemia may be secondary to nitrogen bypassing the liver through portosystemic shunts in the setting of gastrointestinal bleeding or severe fecal impaction or small intestinal bacterial overgrowth syndrome [12,13], and in turn, may explain the slight improvement in mental status reported early on in our patient's course of illness. Interestingly, acute encephalopathy and diffuse edema on MR imaging have been previously reported in patients with non-hepatic hyperammonemia, although unrelated to anti-VGKC antibodies [12,14,15]

Anti-VGKC antibody encephalitis and its pathophysiology remain undefined. We postulate that a prolonged period of elevated circulating anti-VGKC antibodies could lead to prolonged neuroinhibition by modulation of pre or postsynaptic receptors, thus resulting in permanent neurobehavioral changes.

### 4. Summary

AE may be more common in patients presenting with acute severe encephalopathy without seizure activity or meningeal signs that may be otherwise attributed to a toxic metabolic etiology. Discrepancy between neuroimaging findings, anti-VGKC antibodies titer decline and clinical resolution of disease have been reported, making its management very challenging. The pathophysiologic changes associated with this disease remain unclear.

### Disclosure statement

No potential conflict of interest was reported by the authors.

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### References

- [1] Urriola N, Soosapilla K, Drummond J, et al. Fulminant thymomatous AMPAR-antibody limbic encephalitis with hypertonic coma, bruxism, an isoelectric electroencephalogram and temporal cortical atrophy, with recovery. *BMJ Case Rep.* 2019 Feb 21;12(2):e227893. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/30796080>

- [2] Hermetter C, Fazekas F, Hochmeister S. Systematic review: syndromes, early diagnosis, and treatment in auto-immune encephalitis. *Front Neurol.* 2018 September 5;9. Available from: <https://www.frontiersin.org/articles/10.3389/fneur.2018.00706/full>
- [3] LaBuzetta JJN, Yao JZ, Bourque DL, et al. Adult non-hepatic hyperammonemia: a case report and differential diagnosis. *Am J Med.* 2010 Nov 1;123(10):885–891.
- [4] Cordano C, Traverso E, Calabrò V, et al. Recurring hyperammonemic encephalopathy induced by bacteria usually not producing urease. *BMC Res Notes.* 2014;7:324.
- [5] Kiyokawa H, Igawa Y, Ish Izawa ON. Hyperammonaemic encephalopathy associated with retention of urine in multiple large diverticula. *BJU Int.* 2001;88:122±123.
- [6] Dalmau J, Rosenfeld MR. Paraneoplastic syndromes of the CNS. *Lancet Neurol.* 2008 Apr;7(4):327–340.
- [7] Kelley BP, Patel SC, Marin HL, et al. Autoimmune encephalitis: pathophysiology and imaging review of an overlooked diagnosis. *AJNR Am J Neuroradiol.* 2017 Jun;38(6):1070–1078.
- [8] Kotsenas AL, Watson RE, Pittock SJ, et al. MRI findings in autoimmune voltage-gated potassium channel complex encephalitis with seizures: one potential etiology for mesial temporal sclerosis. *Am J Neuroradiology.* 2014 Jan;35(1):84–89.
- [9] Scott JT, Scally C, Peden N, et al. Voltage-gated potassium channel antibody-related encephalopathy: a case which may extend the documented phenotype of this condition. *BMJ Case Rep.* 2012;2012(jun11 1):bcr0720114476-bcr0720114476.
- [10] Gast H, Schindler K, Z'graggen WJ, et al. Improvement of non-paraneoplastic voltage-gated potassium channel antibody-associated limbic encephalitis without immunosuppressive therapy. *Epi Lepsy Behav.* 2010 Apr;17(4):555–557.
- [11] Radja GK, Cavanna AE. Treatment of VGKC complex antibody-associated limbic encephalitis: a systematic review. *J Neuropsychiatry Clin Neurosci.* 2013 Fall;25(4):264–271.
- [12] Hawkes ND, Thomas GA, Jurewicz A, et al. Non-hepatic hyperammonaemia: an important, potentially reversible cause of encephalopathy. *Postgrad Med J.* 2001 Nov;77(913):717–722.
- [13] Bures J, Cyrany J, Kohoutova D, et al. Small intestinal bacterial overgrowth syndrome. *World J Gastroenterol.* 2010 Jun 28;16(24):2978–2990.
- [14] Odigwe CC, Khatiwada B, Holbrook C, et al. Noncirrhotic hyperammonemia causing relapsing altered mental status. *Proc (Bayl Univ Med Cent).* 2015 Oct;28(4):472–474.
- [15] Edwards RH. Hyperammonemic encephalopathy related to ureterosigmoidostomy. *Arch Neurol.* 1984;41(11):1211–1212.