

# **UCLA**

## **Proceedings of UCLA Health**

### **Title**

Olfactory Hallucination in a Young Woman

### **Permalink**

<https://escholarship.org/uc/item/4k55770k>

### **Journal**

Proceedings of UCLA Health, 23(1)

### **Authors**

Aung, Thanda

Sung, Kevin

### **Publication Date**

2020-02-11

## CLINICAL VIGNETTE

# Olfactory Hallucination in a Young Woman

Thanda Aung, MD, MS<sup>1</sup> and Kevin Sung, MS, MS4<sup>2</sup>

<sup>1</sup>Division of Rheumatology, UCLA

<sup>2</sup>David Geffen School of Medicine

### Introduction

Limbic encephalitis is a rare but serious neurological disorder. We present a case of limbic encephalitis that demonstrated symptomatic improvement with immunomodulatory drugs.

### Case

A 35-year-old female with history of idiopathic pulmonary arterial hypertension was admitted with 2-week history of olfactory hallucination "chemical smell", short-term memory deficits, emotional lability, and disorientation. She also reported intermittent numbness involving her left face and the left side of the body including arms and legs. She had no skin rash, oral ulceration, alopecia, arthritis, Raynaud's phenomenon, muscle weakness, previous thromboembolism, or miscarriage. Electroencephalograph (EEG) showed left temporal seizures. MRI brain showed with edema and abnormal enhancement in L temporal lobe, predominantly in hippocampal formation. Lumbar puncture revealed positive glutamic acid carboxylase (GAD)-65 antibodies with very high titers and elevated serum GAD antibodies. CSF tests for infections were negative. Computed tomography (CT) chest, abdomen and pelvis and full body PET scan did not reveal any underlying malignancies. N-methyl-D-aspartate (NMDA) receptor antibodies, and paraneoplastic panel was negative. Subsequent autoimmune studies were remarkable for positive ANA, nucleolar 1:320 titers. Other serologies including dsDNA, Sm, RNP, SSA, SSB, centromere, Scl-70, RF, CCP, ANCA and anti-phospholipid syndrome panel were negative.

The patient was diagnosed with GAD-65 positive autoimmune limbic encephalitis and received high dose pulse steroid (1 gram of Methylprednisone for 3 days followed by 60 mg of prednisone) and IVIG, with an excellent response evidenced by reduction in olfactory hallucination, significant improvement in disorientation and memory deficit within a week. She was subsequently treated with Rituximab every 6 months, IVIG once a month and oral Mycophenolate (1500 mg twice a day). Repeat MRI showed near resolution of associated enhancement in L hippocampus and amygdala. After 3 months of treatment, she was able to return to work with complete recovery of disorientation, memory deficits and the numbness. She continues to have infrequent episodes of transient olfactory hallucinations.

### Discussion

Limbic encephalitis was described initially in case reports from the 1950s where patients with acute and subacute onset encephalopathies were found to have inflammatory pathology in the temporal regions of the brain without inclusion bodies consistent with viral encephalopathies.<sup>1</sup>

Limbic encephalitis is an inflammatory process affecting structures of the limbic system (eg, hippocampus, amygdala, hypothalamus, cingulate gyrus, limbic cortex). Although the disorder is considered a classic paraneoplastic syndrome, it also can be autoimmune encephalitis. Main manifestations are acute or sub-acute mood and behavioral changes, short-term memory problems, focal seizures with impaired awareness (complex partial seizures), and cognitive dysfunction.<sup>2,3</sup> The most frequent neoplasms associated with paraneoplastic limbic encephalitis are lung cancer, testicular tumors, thymoma, breast cancer, and Hodgkin's lymphoma.<sup>2</sup>

GAD antibody is high in paraneoplastic stiff person syndrome, but typically GAD antibodies are non-paraneoplastic in nature.<sup>4</sup> In a systematic literature review in 2016, 48% of 58 cases of GAD-65 positive limbic encephalitis were associated with autoimmune diseases, with type 1 diabetes as the most common.<sup>4</sup> Other autoimmune conditions found in patients with GAD-65 include autoimmune thyroiditis, psoriasis, and common variable immune deficiency.<sup>5,6</sup> Voltage gated potassium channel antibodies encephalitis and N-methyl-D-aspartate (NMDA) receptor antibodies associated encephalitis are other autoimmune, non-paraneoplastic encephalitis that present with complex neuropsychiatric syndrome like GAD-65 positive limbic encephalitis.<sup>2</sup>

In the absence of prospective and randomized data, treatment decisions should be individualized and with consideration age, symptom severity, presence of co-existing medical conditions, and presence of underlying malignancies. Based on observational studies, patient cohorts with autoimmune limbic encephalitis have shown high response rates to immunotherapy with most common regimens involving corticosteroids, IVIG, and plasma exchange.<sup>7,8</sup> Patients with poor response to those treatments have shown clinical improvement with second line therapies such as cyclophosphamide, rituximab, or basiliximab.<sup>7</sup> Given the rapidly progressive symptoms in patients with

autoimmune limbic encephalitis, the literature supports empiric treatment with steroids and immunotherapy after infectious etiologies have been ruled out.<sup>7,8</sup>

The overall prognosis in patients with autoimmune encephalitis is highly variable ranging from a complete recovery to death or having permanent neurologic sequelae of varying severity including gait disability, incontinence, and cognitive deficits.<sup>9</sup> Delay in diagnosis and treatment can be associated with a worse prognosis and increased recurrence.<sup>9</sup>

Our case illustrates symptomatic improvement of GAD-65 limbic encephalitis treated with rituximab, IVIG, and mycophenolate. Since autoimmune encephalitis is potentially treatable encephalitis, the disorder should be considered on the differential diagnosis of patients presenting with encephalopathy.

## REFERENCES

1. **Greenfield JG.** Encephalitis and encephalomyelitis in England and Wales during the last decade. *Brain.* 1950 Jun;73(2):141-66. PubMed PMID: 14791785.
2. **Gultekin SH, Rosenfeld MR, Voltz R, Eichen J, Posner JB, Dalmau J.** Paraneoplastic limbic encephalitis: neurological symptoms, immunological findings and tumour association in 50 patients. *Brain.* 2000 Jul;123 ( Pt 7):1481-94. PubMed PMID: 10869059.
3. **Lawn ND, Westmoreland BF, Kiely MJ, Lennon VA, Vernino S.** Clinical, magnetic resonance imaging, and electroencephalographic findings in paraneoplastic limbic encephalitis. *Mayo Clin Proc.* 2003 Nov;78(11):1363-8. PubMed PMID: 14601695.
4. **Murinson BB, Guarnaccia JB.** Stiff-person syndrome with amphiphysin antibodies: distinctive features of a rare disease. *Neurology.* 2008 Dec 9;71(24):1955-8. doi: 10.1212/01.wnl.0000327342.58936.e0. Epub 2008 Oct 29. PubMed PMID: 18971449; PubMed Central PMCID: PMC2676978.
5. **Gagnon MM, Savard M.** Limbic Encephalitis Associated With GAD65 Antibodies: Brief Review of the Relevant literature. *Can J Neurol Sci.* 2016 Jul;43(4):486-93. doi: 10.1017/cjn.2016.13. Epub 2016 Mar 31. Review. PubMed PMID: 27030381.
6. **Akman CI, Patterson MC, Rubinstein A, Herzog R.** Limbic encephalitis associated with anti-GAD antibody and common variable immune deficiency. *Dev Med Child Neurol.* 2009 Jul;51(7):563-7. doi: 10.1111/j.1469-8749.2008.03217.x. Epub 2009 Feb 3. PubMed PMID: 19191828.
7. **Dalmau J, Gleichman AJ, Hughes EG, Rossi JE, Peng X, Lai M, Dessain SK, Rosenfeld MR, Balice-Gordon R, Lynch DR.** Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. *Lancet Neurol.* 2008 Dec;7(12):1091-8. doi: 10.1016/S1474-4422(08)70224-2. Epub 2008 Oct 11. PubMed PMID: 18851928; PubMed Central PMCID: PMC2607118.
8. **Bataller L, Kleopa KA, Wu GF, Rossi JE, Rosenfeld MR, Dalmau J.** Autoimmune limbic encephalitis in 39 patients: immunophenotypes and outcomes. *J Neurol Neurosurg Psychiatry.* 2007 Apr;78(4):381-5. Epub 2006 Sep 15. PubMed PMID: 16980333; PubMed Central PMCID: PMC2077770.
9. **Titulaer MJ, McCracken L, Gabilondo I, Armangué T, Glaser C, Iizuka T, Honig LS, Benseler SM, Kawachi I, Martinez-Hernandez E, Aguilar E, Gresa-Arribas N, Ryan-Flanagan N, Torrents A, Saiz A, Rosenfeld MR, Balice-Gordon R, Graus F, Dalmau J.** Treatment and prognostic factors for long-term outcome in patients with anti-NMDA receptor encephalitis: an observational cohort study. *Lancet Neurol.* 2013 Feb;12(2):157-65. doi: 10.1016/S1474-4422(12)70310-1. Epub 2013 Jan 3. PubMed PMID: 23290630; PubMed Central PMCID: PMC3563251.