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## *Talking to God in the Walls: Prolonged Psychosis Associated with Left Insular Stroke.*

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### Abstract

We describe a 74-year old Caucasian man with a medical history of ESRD status post renal transplant, admitted for a 4-month history of worsening, abrupt-onset psychosis. Initial treatment with several different antipsychotics was unsuccessful. An extensive medical evaluation including multiple Neurology consultations was unrevealing. Cerebrospinal fluid and paraneoplastic panel were negative. No malignancy was identified. Head MRI revealed an area of T2 hyperintensity in the left insular region. An EEG demonstrated left temporal region changes, suggesting the potential for focal seizures. An empirical trial of valproic acid resulted in rapid resolution of psychotic symptoms. Focal seizure with psychosis secondary to insular stroke is an unusual manifestation that can be difficult to diagnose. This case reminds the busy clinician that sometimes common symptoms can and do present in an atypical fashion.

### Introduction

Anatomically, the insula is the part of the cerebral cortex lying within the lateral cerebral fissure, and includes the basal ganglia, external capsule, claustrum and the capsula extrema. Most of its blood supply comes from the middle cerebral artery (MCA) and its branches. Functionally, it plays a multitude of roles, including pain regulation and processing, motor and sensory perceptions, as well as speech, language and auditory processing.

### Case Presentation

A 74-year old Caucasian man with no prior formal psychiatric history presented to the Emergency Department complaining of psychotic symptoms that began abruptly four months previously. His presentation was notable for grandiose delusions and auditory and visual hallucinations. He believed that he could speak with his deceased wife, his parents and “someone all the way up the list in heaven, one of the most important guys”, whom he could also see. He believed his IQ was 420 and had been steadily increasing over the previous month, in preparation “for where (he) was going next,” and he expressed the somatic delusion that he was young and healthy, despite the obvious contrary medical evidence. He also exhibited paranoid delusions that someone was conspiring against his family and was coming to kill them.

### Family History

His son was diagnosed with schizophrenia.

#### Medical History

His pertinent medical history included end-stage renal disease (ESRD), and cadaveric renal transplant (November 2000), diabetes mellitus (DM), hypertension and dyslipidemia. He denied previous neurological disorders, and had been compliant with his medications, including amlodipine 5 mg BID, atenolol 25 mg daily, mycophenolate mofetil 500 mg BID, prednisone 5 mg daily and tacrolimus 1.5mg BID.

#### Mental Status Exam

He was a mildly obese Caucasian man who appeared his stated age and was alert and oriented to person, place and time. He was neatly dressed and his hygiene was good. Gait was unremarkable. He was agitated and angry, and was difficult to appease. Speech was of appropriate rate and rhythm but increased in volume and peppered with profanity. His psychomotor activity was normal. Recent memory was poor, but remote memory was completely intact (he was able to name the Nephrologist he saw a year earlier). Insight appeared to be limited.

#### Laboratory Data

CBC, electrolyte panel, urinalysis urine toxicology and TSH were unremarkable. Creatinine was stable at 1.7. Tacrolimus level of 5.4 was within normal range.

#### Hospital Course

He was initially treated with haloperidol 5 mg daily, however due to inefficacy was switched to olanzapine, which was titrated to 25 mg daily with no significant symptomatic improvement. Cross-titration with risperidone (maximum daily dose: 6mg), then of trifluoperazine (maximum daily dose: 30 mg) was also unsuccessful and he unfortunately developed parkinsonian-like motor symptoms. Throughout the hospital stay, he also required intermittent seclusion due to aggressive behavior and agitation. Lorazepam 1 mg was given on two separate occasions for anxiety and agitation. At other times he appeared to be exceedingly pleasant. His compliance with medications was also sporadic. He continued to exhibit auditory and visual hallucinations, repeatedly claiming that the hospital's CEO visited him through the walls, sometimes accompanied by the police, planning to return him home immediately. Early in the hospitalization, Neurology was consulted, but their initial examination and EEG were unrevealing. Over a month later, they were asked to re-evaluate him due to an ongoing psychosis despite aggressive neuroleptic treatment, and the updated EEG demonstrated generalized slowing and triphasic waves consistent with diffuse encephalopathy, as well as a single left temporal sharp slow and wave complex and intermitted rhythmic activity over the left temporal region suggesting potential focal seizures. Head MRI with and without contrast was negative for intracranial mass, but revealed mild generalized cerebral and cerebellar volume loss and moderate changes of chronic small vessel ischemia with a T2 hyper intensity in the left insular area. Brain PET imaging did not show neurodegenerative process. Serum paraneoplastic panel was unremarkable.

On hospital day 52, given the EEG findings possibly correlating with the left insular hyperintensity, and limited response to antipsychotics, empiric treatment with divalproex sodium was started. Incremental daily improvements in psychosis, agitation, sleep and medication compliance began almost immediately. Repeat EEG demonstrated moderately severe diffuse non-specific

slow wave abnormalities, but no epileptogenic activity. On hospital day 58, risperidone was re-started due to persistent delusions, and was gradually titrated to 3 mg daily. He was discharged home on hospital day 76, on divalproex sodium 500 twice daily and risperidone 3 mg at bedtime. Posthospital course was unremarkable. He remained stable, with no subsequent psychiatric re-admissions for the following 13 months.

#### Discussion:

To our knowledge, this is the first case report of psychosis in the context of insular stroke. It presented a real diagnostic and treatment challenge for clinicians, especially that the patient developed seizures and partially responded to AED treatment. Ictal, postictal and interictal psychosis were entertained in the differential diagnosis. Ictal psychotic symptoms are part of the seizures, with sudden onset and a brief course, inconsistent with our case, in which the psychotic symptoms lasted for weeks to months. Additionally, our patient's prominent delusions and hallucinations are less commonly associated with ictal psychosis, and he did not demonstrate the motor or oral automatisms typical in ictal psychosis. Interictal psychosis appears in both brief and chronic forms, manifested mostly with delusions and hallucinations that can last several months. Patients experience psychotic symptoms when they are seizure free (between seizures), but our patient continued to be psychotic regardless of seizure status. Postictal psychosis manifests with delusions, hallucinations and aggressive behavior, usually occurring in patients who have suffered from temporal seizures for years, which our patient did not. As in the case for interictal psychosis he continued having symptoms while having seizures. Again, our patient demonstrated psychotic features before, during and well after any evidence of seizure activity.

In the initial stages of differential diagnosis, we also considered limbic encephalitis (normal paraneoplastic panel, normal brain PET scan), delirium (oriented to person, place and time on mental status exam), neurodegenerative dementia syndromes (no gross abnormalities with his memory), thiamine deficiency in Wernicke-Korsakoff syndrome (normal), and late onset schizophrenia (no negative symptoms). Also drug induced psychotic symptoms and seizures, including phencyclidine, cocaine and psychostimulants was entertained (normal urinary drug abuse screen). While prednisone is known to decrease the seizure threshold, it has also been used for the treatment of infantile spasms. The use of steroids in the treatment of epilepsy beyond infantile spasms has been limited. Tacrolimus-related seizure in the early postoperative period after liver transplantation has been reported (6). It is also known that neuroleptics may be associated with seizures. Our patient did very well on a combination of prednisone and tacrolimus for at least five years prior to developing the above-described symptomatology.

We arrived at the diagnosis of psychosis due to left insular stroke complicated by temporal seizures. A literature review reveals that insular cortex is actively involved in a wide variety of functions and is closely connected to the frontal, temporal and parietal lobes (20), but to our knowledge this is the first case of left insular infarct manifesting as psychosis, serving as a reminder for the busy physician to remain diligent in seeking the underlying etiology of even common symptoms that can sometimes present in an uncommon manner. The insular cortex plays a major role in motor control, dysautonomia, speech, language, homeostatic regulation, gustatory, somatosensory and vestibular-like syndromes, and neuropsychology. (4, 10, 13, 5, 3, 11)

Insular volumes have been associated with psychotic symptom severity in schizophrenia and affective psychoses; posterior volumes were significantly reduced in patients with PMD compared to healthy controls, and left anterior insular volume correlated with both overall psychotic symptom severity and positive symptoms severity in PMD. (5)

Due to the confluence of functions in a restricted region, an insular stroke may result in multimodal deficits (12). Five main presentations of posterior insular infarct have been described, including transient pseudothalamic syndrome with somatosensory deficits in posterior insular stroke (19, 7), gustatory disturbances with taste perversion in left posterior insular infarct (4, 17), vestibular-like syndrome with dizziness, gait instability, and tendency to fall, without nystagmus in posterior insular strokes (14), cardiovascular manifestations such as hypertension in right posterior insular infarct (4, 15) and neuropsychological disorders such as aphasia (2) with left posterior insular infarct, dysarthria (16) & transient somatoparaphrenia with right posterior insula infarct (8, 19, 7, 18).

Additionally, there are multiple case reports of insular lesions manifesting as affective aberration (e.g. in amusia), alterations in pain, temperature or tactile perception, anosognosia, and hemiplegia (4, 1, 17, 3). Focal seizure with psychosis secondary to insular stroke is an unusual insular stroke manifestation.

## Conclusion

Our patient offers a unique example of an insular infarct manifesting as a prolonged psychosis. This case reminds clinicians that it is important to maintain vigilance for the underlying etiology of common symptoms and keep the possibility of an uncommon presentations in their diagnostic armamentarium

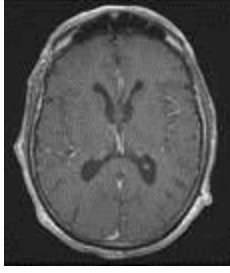
## References:

1. Birklein F, Rolke R, Müller-Forell W. Isolated insular infarction eliminates contralateral cold, cold pain, and pinprick perception. *Neurology*. 2005;65:1381.
2. Carota A, Annoni JM, Marangolo P. Repeating through the insula: evidence from two consecutive strokes. *Neuroreport*. 2007 Aug 27;18(13):1367-70.
3. Cattaneo L, Chierici E, Cucurachi L, Cobelli R, Pavesi G. Posterior insular stroke causing selective loss of contralateral nonpainful thermal sensation. *Neurology*. 2007;68:237.
4. Cereda C, Ghika J, Maeder P, Bogousslavsky J. Strokes restricted to the insular cortex. *Neurology*. 2002;59:1950–1955.
5. Cohen JD, Nichols T, Keller J, Gomez RG, Schatzberg AF, Reiss AL. Insular cortex abnormalities in psychotic major depression: relationship to gender and psychotic symptoms. *Neurosci Res*. 2013 Apr;75(4):331-9
6. Sevmis S1, Karakayali H, Emiroglu R, Akkoc H, Haberal M. Tacrolimus-related seizure in the early postoperative period after liver transplantation. *Transplant Proc*. 2007 May;39(4):1211-3.
7. Guenot M, Isnard J, Sindou M. Surgical anatomy of the insula. *Adv Tech Stand Neurosurg*. 2004;29:265–288.

8. Hyman BT, Tranel D. Hemianesthesia and aphasia. An anatomical and behavioral study. *Arch Neurol*. 1989 Jul;46(7):816-9.
9. Jones CL, Ward J, Critchley HD. The neuropsychological impact of insular cortex lesions. *J Neurol Neurosurg Psychiatry*. 2010 Jun;81(6):611-8. doi: 10.1136/jnnp.2009.193672.
10. Karnath HO, Baier B, Nägele T. Awareness of the functioning of one's own limbs mediated by the insular cortex? *J Neurosci*. 2005 Aug 3;25(31):7134-8.
11. Kodumuri N, Sebastian R, Davis C, Posner J, Kim EH, Tippett DC, Wright A, Hillis AE. The association of insular stroke with lesion volume. *Neuroimage Clin*. 2016 Jan 12;11:41-5.
12. Lemieux F, Lanthier S, Chevrier MC, Gioia L, Rouleau I, Cereda C, Nguyen DK. Insular ischemic stroke: clinical presentation and outcome. *Cerebrovasc Dis Extra*. 2012 Jan;2(1):80-7.
13. Lemieux F, Lanthier S, Chevrier MC, Gioia L, Rouleau I, Cereda C, Nguyen DK. Insular Ischemic Stroke: Clinical Presentation and Outcome. *Cerebrovasc Dis Extra*. 2012 Jan-Dec; 2(1): 80–87.
14. Liou LM, Guo YC, Lai CL, Tsai CL, Khor GT. Isolated ataxia after pure left insular cortex infarction. *Neurol Sci*. 2010;31:89–91
15. Mandrioli J, Zini A, Cavazzuti M, Panzetti P. Neurogenic T wave inversion in pure left insular stroke associated with hyperhomocysteinaemia. *J Neurol Neurosurg Psychiatry*. 2004;75:1788–1789.
16. Manes F, Springer J, Jorge R, Robinson RG. Verbal memory impairment after left insular cortex infarction. *J Neurol Neurosurg Psychiatry*. 1999 Oct;67(4):532-4.
17. Metin B, Melda B, Birsen I. Unusual clinical manifestation of a cerebral infarction restricted to the insulate cortex. *Neurocase*. 2007;13:94–96.
18. Nguyen DK, Nguyen DB, Malak R, Leroux JM, Carmant L, Saint-Hilaire JM, Giard M, Cossette P, Bouthillier A. Revisiting the role of the insula in refractory partial epilepsy. *Epilepsia*. 2009;50:510–520.
19. Ostrowsky K, Magnin M, Ryvlin P, Isnard J, Guenot M, Mauguière F. Representation of pain and somatic sensation in the human insula: a study of responses to direct electrical cortical stimulation. *Cereb Cortex*. 2002;12:376–385.
20. Shelley BP, Trimble MR. The insular lobe of Reil--its anatomico-functional, behavioural and neuropsychiatric attributes in humans--a review. *World J Biol Psychiatry*. 2004 Oct;5(4):176-200.

#### Disclosure:

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.



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