

**Case Report**

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# Hallucinations/Delusions in a Case of Cerebral Venous Sinus Thrombosis - Levetiracetam Induced: A Case Report



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## Abstract

Levetiracetam is a second-generation antiepileptic drug introduced in market in 2000, approved for complex partial seizures, generalized tonic clonic seizures and myoclonic seizures. Though it is well tolerated, it may cause some adverse reactions. This is a case of levetiracetam induced hallucination/delusion following the treatment for Cerebral Venous Sinus Thrombosis experienced by 24 yr old female in our hospital. Patient started experiencing some visual hallucinations (bones moving around her in the air) within 3 days of admission. She also complained of abnormal sensation of worms crawling over her body (tactile hallucinations). These symptoms were intermittent and there were no sleep disturbances or alteration in sleep-wake cycle. Clinical investigations and MRI revealed no parenchymal abnormality and significant results. Our patient recovered after withdrawal of the drug. Based on Naranjo causality assessment scale, causality of this hallucination being adverse drug reaction was calculated to be 7, hence probable. This case report indicates that though rare, hallucinations/delusions can occur as an adverse event with Levetiracetam treatment.

**Keywords:** Levetiracetam; Delusions; Hallucinations; Adverse drug reactions

## Introduction

Levetiracetam is a second-generation antiepileptic drug introduced in market in 2000, approved for complex partial seizures, generalized tonic clonic seizures and myoclonic seizures. It is widely used as adjuvant therapy in epileptic disorders. It is alpha-ethyl analogue of Piracetam and chemically unrelated to other antiepileptic drugs [1]. It is hypothesized to act by binding to synaptic vesicle protein 2A (SV2A) whereby curbing one or more of its actions, finally affecting neural excitability [2].

Though it is well tolerated, it may cause some adverse reactions. Commonly observed neurological problems include asthenia, ataxia, diplopia dizziness, dysarthria, fatigue, headache, light-headedness, nystagmus, paresthesia, somnolence and tremor. They usually are either dose related or transient. Behavioral effects include agitation, anxiety, depression, emotional lability, hostility, nervousness, and psychosis which are less clearly related to drug, dose or tolerance [3,4]. However rare, hallucinations have been reported since its introduction [5].

## Case Report

A 42 years old female patient presented with history of sudden onset of severe headache in the past 4 days. She is not a known case of DM, HTN. She had h/o right focal motor seizure which lasted 1-2 minutes. Her neurological exam was unremarkable for any deficits. MRI Brain revealed no parenchymal abnormality. Loss of flow void was noted in T2/FLAIR sequences in the right transverse sinus. Parasagittal cortical vein hyperintensity was noted. MR venography of brain was advised which revealed thrombosed superior sagittal sinus, right transverse and sigmoid sinuses with likely parasagittal cortical veins. Hematological investigations were normal. She was started on inj. Enoxaparin 40mg, Acitrom 2mg, Levetiracetam 500mg BD and other supportive medications. Extensive Thrombophilia work-up came back negative. ANA profile and Anticardiolipin -IgM/IgG were negative. Homocysteine levels were found to be high. And started on folic acid and other multivitamins. Patient started experiencing some visual hallucinations (bones moving around

her in the air) within 3 days of admission. She also complained of abnormal sensation of worms crawling over her body (tactile hallucinations). These symptoms were intermittent and there were no sleep disturbances or alteration in sleep-wake cycle. An MRI Brain with venogram was repeated to look for any new parenchymal abnormalities in view of the new symptoms. MRI Brain revealed the same earlier findings. Contrast venogram revealed filling defect (in the venous phase) in multiple sinuses as described earlier, suggestive of cerebral and cortical venous sinus thrombosis. Her headache resolved considerably and she had no recurrence of seizure. However, her hallucinations were intermittent and they persisted. Patient and relatives were counselled and educated about the condition, need for periodic follow up, risk of recurrence in case of non-compliance and need for long term anticoagulation. Patient was neurologically stable at discharge.

After 1 week of discharge, patient experienced worsening of the hallucinations both tactile and visual. She started having abnormal delusions that the male servant at home wanted to harm her and tried to kill her. These symptoms worsened over 3-4 days and she presented to the Neurology OPD with these fresh symptoms. She had no past/family history of psychiatric illness. She appeared to be in morbid fear. She was conscious and oriented, no other abnormal behavior. Her neurological exam was unremarkable. Psychiatry consultation was taken. Repeat MRI Brain showed same old findings. She was loaded with Inj Valproate f/b Tab Valproate 500mg BD. Levetiracetam was stopped. She was started on Tab Risperidone 2mg by the psychiatrist. She became symptom free in 2 days and at 1-month follow-up she is doing well with no symptoms of delusions/hallucinations/psychosis. She has no recurrence of seizure. Risperidone was tapered off and she had no recurrence of these psychiatric symptoms. A final diagnosis of levetiracetam induced psychosis/hallucinations/delusions of persecution was made.

### Discussion

The syndrome of psychosis is common, affecting 3 to 5 % of the population. Psychosis is a disturbance in the perception of reality, evidenced by hallucinations and delusions [6,7]. Hallucinations are false sensory perceptions occurring in any of the five sensory modalities. Auditory hallucinations are the most common, followed by visual, tactile, olfactory, and gustatory. Delusions are false beliefs that are firmly held despite obvious evidence to the contrary, and not typical of the patient's culture, faith, or family, is classified as delusions. Persecutory, grandiose, religious, somatic, and other delusions are all common.

Psychosis can occur in Schizophrenia, Schizophreniform disorder, Schizoaffective disorder, Delusional disorder, Dementia, Bipolar disorder (manic depression), Major Depressive Disorder, Postpartum psychosis, Brief psychotic episode, Psychosis due to a general medical condition and Substance/Drug induced state.

Some of the important drugs which can precipitate psychosis include adrenergic agents, Anticholinergics, Antihistamines,

Benzodiazepines, Cimetidine, Corticosteroids, Anti-infective Agents like (Ant malarial, Antibiotics, Ant tubercular agents), Dextromethorphan, Digoxin, Dopamine Agonist Ketamine, Phenytoin, Opioids, Organophosphates and Thyroid hormone [8].

Levetiracetam is a newer antiepileptic drug that has shown promise in number of long term, open label, follow up clinical studies. Neurobehavioral adverse effects are very common with recently introduced antiepileptic drugs [9,10]. This drug has been reported to have significant safety margin with ADRs like dizziness, fatigue, headache, upper respiratory tract infection and somnolence; reported ADRs are up to 13.3% of drug users [11]. Severe symptoms such as depression, agitation, hostility and psychotic behavior are experienced by 0.7% of the patients [12].

Psychosis is commonly reported in patients with preexisting psychotic disorder, also in patients on add-on therapy and rapid titration in underlying neurological disease [13,10]. Levetiracetam induced psychosis is also reported to be common in children with prior cognitive defects who receive prescription of the drug [9]. Our patient did not provide any history of preexisting or family history of psychotic disorder. The episode was also evident at clinically permissible dose range (1000 mg) and at the onset of therapy.

Previous case reports demonstrate the problem with either increase in the drug dose [14,11] or after 10 days to 30 days of initiation of therapy. However, like the previous reports, our patient recovered after withdrawal of the drug [15,16]. Based on Naranjo causality assessment scale, causality of this hallucination being adverse drug reaction was calculated to be 7, hence probable. This case report indicates that though rare, hallucinations/delusions can occur as an adverse event with Levetiracetam treatment. One of the limitations of this report is that we could not do assessment of blood levels of levetiracetam due to limited resources.

### Conclusion

Psychiatric ADRs are common in antiepileptic drugs use. The mechanism for this psychosis remains unclear. However, detailed clinical history and close monitoring with regard to psychiatric adverse effects is advised when commencing treatment with levetiracetam, especially in patients with risk factors for psychiatric adverse effects. Further studies are required to assess the effect of levetiracetam on behavioral changes in larger population.

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