



## Case Report

# Altered Behavior: An Infrequent Presentation with Levetiracetam

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### ABSTRACT

Levetiracetam has been associated with aggressive behavior and mania. We are reporting a case of agitation and aggressive behavior following levetiracetam monotherapy for focal seizure prophylaxis. A 48 years old man, who presented to the neurology department with history of four episodes of sudden onset abnormal body movements. Patient was diagnosed with focal seizures with secondary generalization and was prescribed tablet levetiracetam 500 mg twice a day for seizure prophylaxis. Three weeks later patient presented with complaints of excessive sleepiness during daytime, agitation and aggressive behavior, though seizure free. According to World Health Organization Uppsala monitoring Centre (WHO-UMC) causality assessment system the case was classified as probable/likely for levetiracetam-induced altered behavior. Levetiracetam was discontinued, and tablet carbamazepine controlled-release 300 mg twice daily was substituted. Within 2 days of switching therapy the agitation and aggression reduced substantially. Although levetiracetam has fewer side effects than traditional antiepileptic medications, but it is imperative to continuously monitor the patient for infrequent adverse effects also, so that required modifications to drug label may be done.

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## 1. Introduction

'Seizure' refers to transient alteration of behavior due to the disordered, synchronous and rhythmic firing of brain neurons. Antiseizure drugs are administered orally for prevention of seizure recurrence.<sup>1</sup>

Levetiracetam is a novel antiseizure drug with better pharmacokinetic profile and with the advantage of less drug interactions with broader therapeutic range.<sup>2,3</sup> It acts by binding to synaptic vesicle protein 2A, and modifies the release of glutamate and GABA.<sup>4</sup> It also inhibits N-type calcium Channels and calcium release from intracellular stores. Plasma half-life of levetiracetam is 6-8 hours and adult dose is initiated at 500-1000 mg per day and increased every 2-4 weeks by 1000 mg to a maximum dose of 3000 mg per day. Somnolence, asthenia, ataxia, dizziness is often

noted with levetiracetam but behavioral and mood changes are infrequent.<sup>5</sup> Some unusual cases of cutaneous reactions like levetiracetam induced urticaria with rash and hives have also been reported.<sup>6</sup> Aggression is a social behavior that is aimed at eliciting uneasiness, pain or physical damage to oneself, to another person or to things or at shielding oneself against a threat.<sup>7</sup> Aggressive behavior can occur as a symptom of various medical conditions such as brain damage, encephalitis, drug use, dementia, intoxication, psychosis, affective disorders, and personality disorders as well as in relational, behavioral, developmental and adaptational disorders.<sup>8</sup>

Antiepileptic drugs are potent agents that can tempt several adverse reactions and drug interactions. Psychiatric and behavioral adverse reactions include depression, anxiety, psychosis, and aggressive behavior.<sup>7</sup> Levetiracetam, perampanel and topiramate has higher association with aggressive behavior as compared

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to adverse effects with typical antiepileptic agents.<sup>8</sup> Although levetiracetam has fewer side effects than traditional antiepileptic medications, but it is imperative to continuously monitor the medication for infrequent adverse effects also, so that required modifications to drug label may be done timely.

## 2. Case

It is a case of 48 years old male who was a study participant for post-graduate academic thesis in the Department of Pharmacology and Department of Neurology. The patient visited the neurology outpatient department at Dr. R.P.G.M.C., Kangra at Tanda with complaints of history of four episodes of abnormal body movements starting from right side of body then spreading to whole of the body with teeth clenching and loss of consciousness. Each episode lasted for 3 to 5 minutes. The patient sustained post-ictal confusion for 20-25 minutes. The seizure was sudden in onset and did not precede by aura. Out of total 4 seizure episodes 2 were nocturnal and 2 happened in evening. No family history of seizures was recorded. EEG, CT scan of brain, MRI of brain and blood investigations were within normal limits. The patient was diagnosed clinically as a case of focal seizures with secondary generalization. Patient had no history of known drug or food allergy. The patient was enrolled for post-graduate academic thesis after written informed consent and was randomly allocated into levetiracetam study arm. The patient was prescribed tablet levetiracetam 500 mg twice daily orally. Next morning patient complained of somnolence and dizziness. Patient was advised to continue the treatment. Three weeks later patient was seizure free but was anxious, agitated and had aggressive behavior in form of anger outbursts as described by the care taker. General physical examination was normal. Blood biochemistry parameters, revealed normal results. Levetiracetam was discontinued, and tablet carbamazepine controlled-release 300 mg twice daily was substituted. Within 2 days of switching therapy the agitation and aggression reduced substantially. Patient was advised to continue altered treatment regimen and follow-up regularly.

According to World Health Organization Uppsala monitoring Centre (WHO-UMC) causality assessment system the case was classified as probable/likely for levetiracetam-induced altered behavior.

## 3. Discussion

A 48 years old man having new onset focal seizure with secondary generalization have developed agitation and aggressive behavior. Our case was classified as drug induced altered behavior. Dannaram S. et al.<sup>9</sup> described a case of acute psychosis after levetiracetam therapy in a 50 years old male. Levetiracetam was stopped and olanzapine 5mg was started orally. Patient's psychotic symptoms resolved over next 48 hours.

Nair CV. et al.<sup>10</sup> reported a case of 76 years old male with traumatic brain injury induced seizures. The patient sustained sleep-wake cycle disorder and agitation. After cessation of levetiracetam, there was a marked reduction in his altered behavior and his sleep wake cycle gradually normalized.

Kumar N. et al.<sup>11</sup> reported a case of 52 years male with epilepsy who developed acute psychosis shortly after initiation of treatment. Within 2 days of levetiracetam discontinuation, the patient recovered from psychosis, without any treatment.

Hwang ES. et al.<sup>12</sup> reported a case of 77-year-old Caucasian male who developed disorientation, agitation, and lethargy on I.V. levetiracetam to prevent post-traumatic seizures. This problem continued for 12 days despite treatment with sedatives and neuroleptics. Levetiracetam was discontinued. The patient's mental status improved dramatically within 24 hours.

## 4. Conclusion

Levetiracetam is prescribed if adverse drug reactions occur with classical antiepileptics. Although levetiracetam have fewer side effects than traditional antiepileptic medications, but it is imperative to continuously monitor the medication for infrequent adverse effects also, so that the required modifications to drug label may be done aptly.

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## 6. Conflict of Interest

The authors declare they have no conflict of interest.

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