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Case Report

Levetiracetam Induced Acute Reversible Psychosis: A Case Report

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Abstract

Levetiracetam (Keppra) is a second-generation antiepileptic drug (AED) widely used for focal and generalized seizures due to its efficacy, favourable pharmacokinetics, and low risk of drug interactions. However, its neuropsychiatric side effects, including aggression, mood disturbances, and psychosis, are increasingly recognized. Keppra-induced psychosis (KIP) is a rare but serious adverse effect that can significantly impact patient safety and treatment adherence. While psychiatric symptoms associated with levetiracetam use have been described, reports of psychosis remain relatively uncommon. We present a case of Keppra-induced psychosis in a patient with no prior psychiatric history, emphasizing the importance of recognizing this rare but serious adverse effect.

Introduction

Levetiracetam (LEV) is a novel second generation anti-epileptic drug that is chemically unrelated to other antiepileptic drugs and is the α-ethyl analogue of the nootropic agent piracetam [1]. It is postulated to act by binding to synaptic vesicle protein 2A (SV2A) and thereby modulation of one or more of its actions, ultimately affecting neural excitability [2]. It has been found to be well-tolerated and has a favourable pharmacokinetic profile that includes minimal protein binding, lack of hepatic metabolism and twice a day dosing. LEV has a wide safety margin without any requirement for serum drug monitoring [3,4]. Somnolence, asthenia, coordination difficulties, and behavioural abnormalities are the reported central nervous system adverse drug reactions (ADR) of levetiracetam. Psychosis has been reported infrequently with LEV with a reported frequency of less than 1% [5].

Case Presentation

A 42-year-old male with a 5-year history of focal epilepsy was started on levetiracetam (500 mg twice daily) after experiencing recurrent focal seizures. Patient initially started on carbamazepine but due to increased episodes of seizures and was started on Levetiracetam. He had no previous psychiatric illness, substance abuse, or family history of psychiatric disorders.

Clinical Course

Two weeks after initiation of levetiracetam 500mg twice daily, the patient developed significant behavioural changes, including paranoid delusions, auditory hallucinations, and agitation. His family reported that he exhibited fearfulness, accusatory behaviour, and social withdrawal. Patient reports seeing a woman and child talking to him telling him he had ‘brain cancer’. Patient denied suicidal or homicidal ideation.

Medical Evaluation

On examination, the patient was alert but disoriented. He displayed persecutory delusions and active auditory hallucinations. No focal

neurological deficits were noted. Routine laboratory investigations, including complete blood count, renal and hepatic function tests, and serum electrolytes, thyroid function test and serum magnesium were within normal limits. Serum carbamazepine levels were 11 mg/L. An MRI of the brain showed no acute pathology. EEG findings were consistent with focal epilepsy but did not show ongoing seizure activity.

Management and Outcome

Patient was diagnosed with acute psychosis following his psychiatric assessment. His mental state examination was normal except for abnormal mood and thoughts. Psychiatric assessment revealed mild features of depression, abnormal mood and thoughts with visual hallucination suggestive of psychosis. Delirium was ruled out as there was no fluctuation in sensorium, focal deficits and meningeal signs. Metabolic abnormalities causing this clinical presentation were ruled out through the lab investigations.

Levetiracetam was discontinued, and the patient was switched to valproate (750 mg daily). Psychosis symptoms were controlled with haloperidol. Patient was given Lorazepam to manage an episode of focal seizure while admitted in hospital. Within 72 hours, his psychotic symptoms began to improve, and he returned to baseline mental status within a week. The adverse drug reaction causality assessment was done using the Naranjo scale [6]. A probable association (score 4) of the reaction with LEV was found on the causal analysis.

No recurrence of psychotic symptoms was noted on follow-up at three months.

Discussion

Keppra-induced psychosis is a rare but documented adverse effect, with incidence rates ranging from 1% to 5% in clinical studies [7]. The exact mechanism of psychosis related to Keppra (levetiracetam) remains unclear but may involve dopaminergic and serotonergic dysregulation [8,9]. Risk factors of levetiracetam induced psychosis include rapid dose escalation, underlying psychiatric history, and high-dose therapy [10,11].

Levetiracetam is known for its efficacy in clinical trials although the drug is reported to have significant safety margin with adverse drug reactions including malaise, headache, dizziness, upper respiratory tract infection, and somnolence. Although it has a favourable profile, behavioural adverse reactions are reported in up to 13.3% of the drug users [5]. However, severe symptoms such as hostility, depression, agitation, and psychotic behaviour are experienced by 0.7% of the patients [12]. LEV psychosis is reported to be common in patients with pre-existing psychotic disorder, also in patients on add-on therapy, and rapid titration when there is an underlying neurological disease [13,14]. LEV Psychosis is also reported to be common in children with prior cognitive defects who receive prescription of the drug [9]. Previous reports suggest that Keppra induced psychosis resolves with discontinuation of levetiracetam, though some patients require temporary antipsychotic therapy [6]. Alternative antiepileptic drugs such as valproate or lamotrigine are often better tolerated in such cases [14,15].

Our patient did not have any pre-existing psychiatric conditions or family history of psychiatric conditions. The psychosis noted in the patient was within a week of onset of new drug therapy and patient returned back to baseline with the withdrawal of the drug. Previous case reports demonstrated the psychosis with either increase in the drug dose [12,14] or after 10 days to one month of initiation of therapy [5,16], as noted in our patient who presented within 2 weeks of drug initiation.

Keppra-induced psychosis is an important differential diagnosis in patients developing new-onset psychotic symptoms after levetiracetam initiation. Psychiatric adverse reactions are common with antiepileptic drugs. The mechanism for this psychosis remains quite unclear. At present, there is no evidence to suggest that LEV produces psychosis at significantly higher rates than other antiepileptic drugs [17]. It is important to take a detailed clinical and psychiatric history of a patient presenting with psychosis on antiepileptic medications with close monitoring with regard to psychiatric adverse effects when starting treatment with levetiracetam especially in patients with risk factors for psychiatric conditions. Early recognition and drug withdrawal typically result in symptom resolution. Clinicians should remain vigilant for neuropsychiatric adverse effects in patients on levetiracetam therapy.

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