Psychosis is an abnormal condition in which a person loses touch with reality and exhibits bizarre behavior in different grades of severity. However, psychosis is not necessarily a sign of a primary psychiatric disorder. Primary psychotic disorders, such as schizophrenia and the other disorders on its spectrum are therefore a diagnosis of exclusion [1]. Patients with new-onset psychosis require extensive medical workup to exclude other possible explanations for symptom onset [2]. A thorough history and physical examination is indispensable for finding a possible nonpsychiatric cause of the psychotic symptoms that may respond to interventions other than psychotropic medication. A common etiology for new-onset psychosis in patients with no prior psychiatric history is ingestion of a substance or medication that precipitates the symptoms [1,3,4]. In this report, we present the case of a 66-year-old female with history of temporal lobe epilepsy who presented with auditory, visual, and tactile hallucinations, as well as paranoia regarding harm to herself and a family member. Onset of the symptoms occurred shortly after initiating topiramate. She had previously experienced suicidal ideation and personality changes on levetiracetam. Her neurologist initiated a cross-taper from topiramate to carbamazepine that was continued in the hospital. As this proceeded, her symptoms improved until she was free of hallucinations and was discharged. The diagnosis of psychotic disorder due to medication (topiramate) was made due to sudden onset of symptoms after initiating the treatment and was confirmed by prompt resolution of symptoms after discontinuation. This case demonstrates the importance of recognizing topiramate-induced psychosis, a rarely documented clinical phenomenon in older adults, across neurology, psychiatry, and other disciplines that prescribe this medication.

**Abstract**

Psychosis is not necessarily a sign of a primary psychiatric disorder. New-onset psychosis requires extensive medical workup, including a thorough history and physical. A common etiology in patients with no prior psychiatric history is ingestion of a substance or medication that precipitates the symptoms. In this report, we present the case of a 66-year-old female with history of temporal lobe epilepsy who presented with auditory, visual, and tactile hallucinations, as well as paranoia regarding harm to herself and a family member. Onset of the symptoms occurred shortly after initiating topiramate. She had previously experienced suicidal ideation and personality changes on levetiracetam. Her neurologist initiated a cross-taper from topiramate to carbamazepine that was continued in the hospital. As this proceeded, her symptoms improved until she was free of hallucinations and was discharged. The diagnosis of psychotic disorder due to medication (topiramate) was made due to sudden onset of symptoms after initiating the treatment and was confirmed by prompt resolution of symptoms after discontinuation. This case demonstrates the importance of recognizing topiramate-induced psychosis, a rarely documented clinical phenomenon in older adults, across neurology, psychiatry, and other disciplines that prescribe this medication.

**Keywords:** Geriatric Psychiatry; Psychosis; Topiramate; Epilepsy

**Introduction**

Psychosis is an abnormal condition in which a person loses touch with reality and exhibits bizarre behavior in different grades of severity. However, psychosis is not necessarily a sign of a primary psychiatric disorder. Primary psychotic disorders, such as schizophrenia and the other disorders on its spectrum are therefore a diagnosis of exclusion [1]. Patients with new-onset psychosis require extensive medical workup to exclude other possible explanations for symptom onset [2]. A thorough history and physical examination is indispensable for finding a possible nonpsychiatric cause of the psychotic symptoms that may respond to interventions other than psychotropic medication. A common etiology for new-onset psychosis in patients with no prior psychiatric history is ingestion of a substance that precipitates the symptoms [1,3,4]. These substances range from recreational illicit drugs to various types of prescribed medications, including steroids, stimulants, and antiepileptics [5,6]. Topiramate, a positive allostatic modulator of GABAA receptors that causes an overall GABA mediated inhibition and higher GABA levels in brain, is one of such medication with unintended psychiatric manifestations [7]. Originally developed as an anti-diabetic drug, topiramate was later widely prescribed as an anti-convulsant medication due to its similarity to acetazolamide [8]. However, multiple reports have also identified induction of acute psychotic symptoms induced by topiramate in various treatment settings [9,10]. Although the use of topiramate for treatment of behavioral disturbances in geriatric patients are not uncommon, cases of psychotic symptoms associated with topiramate in older adults, is very rare [9-11]. Here we report a case of a female geriatric patient with depression and epilepsy who developed psychosis subsequent to topiramate treatment. This case adds to the literature as further evidence that this commonly prescribed medication should be considered in the differential diagnosis of late-onset and other atypically presenting psychotic illnesses, and evidence against the necessity of neuroleptics to treat the episode and achieve remission in older adults who may be more vulnerable to their adverse effects.

**Case Presentation**

Mrs. H. is a 66-year-old Caucasian female with a past medical history of temporal lobe epilepsy and unspecified depression who was presented to a psychiatric hospital, referred by her psychotherapist, for worsening auditory hallucinations of people talking to her, visual and tactile hallucinations of lasers going through her head, fears of hammers coming down from above to hurt her, and paranoia regarding her daughter. She had no history of primary psychiatric disorder and no prior episodes similar to her initial presentation. Mrs. H. started experiencing the symptoms subsequent to initiating topiramate treatment for her seizure disorder, about four months prior to admission. Her seizure disorder, initially diagnosed approximately 2 years prior to the psychotic
episodes, was complex partial, confirmed by EEG, localized to the temporal lobe, consisted of stereotypical movements such as lip smacking with loss of consciousness, staring spells and post ictal tiredness and confusion. Although her seizure disorder was under control with levetiracetam, it also appeared to have induced depressed mood, personality changes, and suicidal ideation at its therapeutic dose for her epilepsy. Initial intervention by her neurologist was to cross taper Keppra while slowly titrating topiramate to an effective dose. Topiramate dose was increased while Keppra was decreased over a three-month treatment and the taper of levetiracetam was completed approximately three months prior to admission. The patient initially reported memory problems and trouble with speaking after switching to topiramate, however, these symptoms resolved itself. Though the exact timing of psychotic symptom onset was unclear, Mrs. H. was certain that she began seeing “ant people” and “praying for intergalactic peace” at a dose of 150 mg of topiramate twice daily. She mentioned these symptoms to her neurologist who adjusted some other medications and continued the topiramate. She continued to experience hallucinations and then became paranoid, feeling unsafe in her own home due to dangerous objects approaching to harm her. Since she never had similar symptoms with levetiracetam, her neurologist began to decrease the topiramate, to 50 mg four times daily, and started carbamazepine, 400 mg nightly at bedtime. Her carbamazepine level at the time of admission was not detectable (less than 2.0 mcg/mL).

Throughout Mrs H.'s hospitalization, this lasted fifteen days, the team planned to continue cross-tapering her antiepileptics with goal to discontinue topiramate. Her lab reports on liver and kidney functions were within the normal ranges and she was not started on any neuroleptics. Topiramate (50 mg) four times daily was immediately decreased to three times daily. She did start low-dose sertraline on day 2 for mood and anxiety symptoms in light of her previous suicidality, which was titrated to 50 mg daily on day 14. Carbamazepine was gradually increased to 700 mg per day by day 8, split 400 mg daily and 300 mg nightly. Her initial level at this dosage was 7.2 mcg/ml, however, she continued to experience visual hallucinations of knives that were causing cuts on her arms and gashes on her legs. At that time, taper of topiramate continued, with reduction to 50 mg twice daily, and then to 50 mg once daily on day 10. After complete discontinuation on day 13, her symptoms became “less terrifying” and gradually subsided. She was discharged from the hospital on the above 700 mg daily dose of carbamazepine with follow-up one week later at an outside facility, having maintained a carbamazepine level of 6.4 mcg/ml measured on day 14. Due to the sudden onset of the symptoms shortly after initiation of treatment with topiramate, she was given a diagnosis of substance-induced psychosis secondary to topiramate. This diagnosis was further supported by the resolution of symptoms once the medication was discontinued. Carbamazepine was ruled out as a causative factor in this case, since the symptoms were present when the agent was undetectable and resolved on an increased dose in therapeutic range.

Discussion

Psychotic symptoms are often associated with other medical conditions, including epilepsy; or precipitated by ingestion of substances, including several antiepileptic medications [1,4,6]. Both categories of external causes must be ruled out prior to making a primary psychiatric diagnosis. This case, and at least three others in the literature, represents evidence that topiramate is a precipitant of acute psychotic symptoms at dosages exceeding 50 mg daily [12-15]. Patients described in these reports, including for indications as seemingly benign as migraine prophylaxis, experienced paranoid delusions, hallucinations, depersonalization, suicidal ideation, severe mood swings, and impaired cognition [13]. Despite the known effects on precipitating psychotic symptoms, topiramate is being widely prescribed as a regimen for obesity control and weight loss, in addition to its canonical use in the treatment of epilepsy [16-18]. Similarly, in addition to its much-noticed psychogenic effects, reports on other undesirable side effects of topiramate also are on the rise [19,20]. Although implicated as one of the “potentially inappropriate medication (PIM)” for geriatric patients with Alzheimer dementia, topiramate has been increasingly prescribed as one of the new generation antiepileptic drugs in treating older adults with epileptic disorders [21-22]. Here we report a case of a 66-year-old female presented to an inpatient geriatric psychiatry unit with severe psychotic symptoms subsequent to topiramate intake. The patient in this study experienced onset of symptoms at a total daily topiramate dose of 300 mg, which was initially continued and later decreased modestly to a total dose of 200 mg, still four times the minimum dose implicated by the previous reports. While the psychosis, like primary schizophrenia spectrum disorders, responds to neuroleptics, it can resolve completely with reduction of dose or discontinuation of topiramate, obviating the need for additional medication exposure. Although depression-related psychosis and potential roles of polypharmacy cannot be ruled out in this case, the observation that Mrs. H.'s symptoms did not completely subside until total discontinuation of the offending medication strongly suggest a stronger association of topiramate to her psychotic episode. Further, normal liver and kidney functions in this patient, as suggested by the laboratory reports also eliminated the possibility of adverse drug metabolism as apotential precipitating factor. However, the possibility that topiramate acts as a poor monotherapy antiepileptic agent in elderly, resulting in breakthrough partial seizure activity leading to ictal, inter ictal, and postictal psychosis, cannot be ruled out. Whenever the underlying mechanism and precipitating factors for the development of psychotic symptoms is unclear in a patient treated with topiramate, or other antiepileptic medications including carbamazepine, the treating physician should evaluate carefully for this potential adverse effect [12]. Since topiramate is being prescribed for increasing numbers of indications across various specialties, incidence and prevalence of topiramate-induced psychosis requires further clinical attention to avoid exacerbations that result in otherwise avoidable psychiatric hospital admissions and possible unnecessary exposure to neuroleptics [23]. Especially important is to apply these considerations for geriatric patients who may have multiple cooccurring physical and mental health issues.

Disclosures

Consent for publication: Institutional consent form obtained from the patient is available upon request.
Authors’ contributions

TR acquired clinical information and contributed interpretations of general medical events described in the manuscript.

TK conceived the study, provided major background and discussion points, interpretations of psychiatric events described in the manuscript, and prepared the manuscript.

Both TR and TK read, revised and approved the final manuscript.

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