

# A Case of Perampanel-Induced Psychosis in a Teenager with Intellectual Disability and Refractory Epilepsy

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## Abstract

*Perampanel is a non-competitive rationale AMPA receptor antagonist and used as add-on maintenance treatment in individuals with unresponsive epilepsy, as it was demonstrated to be effective in the management of seizures. It does however have numerous benefits but increasingly it has also been associated with serious psychiatric side effects which include acute psychosis. In the described case unsettling acute-onset psychotic symptoms manifested in form of hallucinations, paranoia, and disorganized behavior happened to a 22-year-old woman with longstanding pharmacoresistant epilepsy shortly after the start of perampanel treatment. They were psychiatric in nature with the symptoms arising within two weeks after initiating the medication and disappearing fully after withdrawing the medication thereby suggesting that there is probable causal association. An indepth clinical assessment and literature review indicates that perampanel-induced psychosis is a serious issue, nevertheless this is a rare one and is more dangerous in patients with predisposing psychiatric histories. This case demonstrates that targeting prescribing of perampanel requires close psychiatric observation and personalized risk evaluation and therefore, clinicians should be cautious of the initial symptoms of the neuropsychiatric decompensation.*

**Keywords:** Perampanel, drug-resistant epilepsy, psychosis, adverse events, AMPA receptor antagonists, treatment-emergent psychosis, antiepileptic drugs, psychiatric complications, case report, seizure management.

## 1.Introduction

Epilepsy is a complex condition of the nervous system that affects millions of people in the world, and its expressed forms differ significantly depending on the cause of the disease and its severity, as well as the specifics of the person. The population segment of the epilepsy patient with comorbid intellectual disability is one that poses a troubling clinical picture among the many other subgroups of this afflicted population. Such patients are prone to have a greater incidence of refractory or drug-resistant seizures and are more susceptible to negative adverse events associated with antiepileptic medicines (ASMs). The presence of neurobiological sensitivities coupled with lower ability to express the symptoms rendered treatment difficult and in need of an extremely customized approach in the drug choice and supervision. Alternative treatment schemes Over the past few years, the use of perampanel as an adjunctive drug in patients with focal-onset resistant seizures to conventional medicine has been found to be promising. Nevertheless, however, just like any new drug, its ever-spreading utilisation has brought out hitherto unreported side-effects- one of the worst ones being the drug-related psychoses.

ASM psychological and behavioral side effects are not novel. However, the workings of these drugs with the defective neurochemistry of intellectually disabled patients remain unclear. This is more true of newer generation ASMs such as perampanel that was planned to focus on the AMPA receptors in the brain to reduce excitation neurotransmission. On the one hand, its mechanism of action has therapeutic potential in the treatment of seizures, but on the other hand, it brings its own danger as it can interfere with other such important pathways as neuropsychiatric ones, which can lead either to aggression, instability of mood, or even to complete psychosis. This risk has been acknowledged by the U.S. Food and Drug Administration (FDA) through putting a black-box warning on perampanel, warning medical carers about the possible life-threatening psychiatric and behavioral responses to the drug(1). Nonetheless, even despite such a regulative concern, there are still very few reports on psychosis associated with the use of the particular medication perampanel specifically in medical literature. This gives rise to the issue of underreporting, overdiagnosis/misdiagnosis or failure to label psychiatric symptoms as being caused by drug and not being a primary mental illness.

The essence of the predicament of such clinical situations is that of attribution and balance: How can one know whether a psychotic experience is due to the antiepileptic regime, due to the underlying epilepsy diagnosis, and due to an incipient primary psychiatric condition? This diagnostic ambiguity is even further complex in those with

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intellectual disability where an abnormal degree of behavior may already have existed at a baseline which may then obscure the distinction of pathological and normal behavior. Further, in the case that seizure control was a difficult feat achieved with the help of a particular medication such as perampanel, the clinicians might be hesitant to withdraw it in presence of extreme psychiatric manifestations. This pre-determines an unenviable juggling act: continue to control seizures at the risk of causing psychological imbalances, or to regain psychiatric parity at a possible risk of heightened seizure rates. In this case exact thought must be given to risk and reward and in many cases will also demand the use of antipsychotic agents, which in themselves may reduce the seizure threshold and provide a host of other ill effects.

### Balancing seizure control and psychiatric well-being in epilepsy treatment.



**FIGURE 1** Balancing seizure control and psychiatric well-being in epilepsy treatment

Such interaction was displayed in an example of a 15-year-old girl with moderate intellectual disability with the presentation of drug-resistant epilepsy. It was only after multiple failures of using alternative ASMs that she controlled her seizures using perampanel. Nonetheless, within a few weeks of starting her therapy, she experienced an acute psychotic attack in the form of visual and auditory hallucinations, paranoia, and violent conduct. Her case provides miniaturization of a bigger clinical issue with perampanel its unquestionable usefulness in the treatment of seizures contrasted with the possible dislocation of sanity. The negativity of her personal and family history as it pertains to psychosis also lends more hypotheses to the theory that the origins can be traced to a medication etiology(2).

When dealing with this case, clinicians have selected a conservative form of pharmacological intervention; they have started with an insignificant amount of risperidone, which is the second-generation antipsychotic with its relative lack of propensity to induce seizures. This choice highlights one of the critical lessons in the care of neuropsychiatric patients: it is less important to withdraw the effective drug, ASM, but instead manages the new psychiatric symptoms with a selective but conservative drug. Patient started responding to risperidone and her psychotic symptoms improved gradually and she also continued being seizure-free. This treatment triumph did however, at a later stage become problematized with the advent of extrapyramidal side effects (EPSE) that are normally linked with prolonged use of antipsychotics. Again there was a critical treading of the balance, only this time between psychosis control and minimization of drug-induced movement disorder burden.

Overall, there are a few crucial lessons of clinical practice in this case. First, as it is, perampanel can still be a useful piece of equipment in the armory against drug-resistant epilepsy, clinicians are to be cognizant of its infrequent yet serious psychiatric adverse effects. Second, monitoring of such adverse events ought not to be instantaneous and of an oversimplified nature; rather, should be infused with a sophisticated sense of the personal health history, comorbidities and prioritization of therapeutic options in the case of such individual. This, lastly, in populations with intellectual disability, which are not only more vulnerable to epilepsy, but also more vulnerable

to drug side effects, the role of pre-treatment counseling, close monitoring and collaboration across disciplines, cannot be overestimated. Such patients should have a healthcare delivery model that does not get caught off-guard by complexity.

This introduction preludes the more clinical discussion, case exploration and synthesis of the literature that follows in the entire case report(3). It also leaves us with larger questions about how the modern practices of neurology and psychiatry are more and more having to go hand in hand and that these trends are particularly prominently felt in the treatment of vulnerable and diagnostically heterogeneous populations.

## **2. A Case of Perampanel-Induced Psychosis in a Teenager with Intellectual Disability and Refractory Epilepsy**

Each development that leads to a control of seizures is a milestone in the clinical environment of drug-resistant epilepsy. Nevertheless, in more complicated cases of comorbidity (including intellectual disability and intense medical interventions in the history of the patient) that breakthrough may have a not so obvious psychological price. The case report describes the experience of a 15-year-old girl, the clinical course of whom serves as a bright example of this dichotomy of a positive antiepileptic therapy that was also the probable cause of a horrific bout of acute psychosis. Her case sums the ethical, diagnostic and treatment ethical issues that evolve in treating patients who are neurologically vulnerable.

The patient is a young female of adolescent age and she had a complicated medical history, which was characterized by the presence of moderate intellectual disability and acute lymphocytic leukemia (ALL), to which she had been subjected to a bone marrow transplantation (BMT) at the age of ten due to the two relapses of the disease. Her neurological symptoms were not diagnosed until three years later, at the age of thirteen, and have mostly been noted in the form of her first appeared generalized tonic-clonic seizures. Her epilepsy was refractory at the very beginning(4). Levetiracetam constituted the first treatment plan and was titrated to 60 mg/kg/day. The seizure control could not be achieved even at this high dose.

As her epilepsy progressed, she was having more types of seizure semiology, and she was dropping attacks, which were very quick drop-offs of muscle tone, and she was more vulnerable to injury. To curb this topiramate was added and titrated slowly to 8 mg of kg/day. Unluckily, no substantive clinical benefit was achieved when topiramate was added. Within a year, a number of changes were done on medications. Topiramate was later taken off because it was not effective and replaced with clobazam. She was also added on valproic acid. However despite the changes her seizures were not adequately controlled and seizures were frequent and affected her everyday functioning greatly.

At this point, she had been admitted into an epilepsy monitoring unit to undergo a complete examination. The long-term video electroencephalography (EEG) showed slow background pattern of her age with swarmlike interictal discharges, generalized and frontal predominances in the proportions. Some of her usual seizures were recorded during the EEG and gave very vital diagnostic information. Magnetic Neuroimaging and spectroscopy imaging on the brain showed no abnormalities in the structure of the brain. Metabolic work up which included serum amino acids, urine organic acids and acylcarnitines were unrevealing. Considering her history of BMT and pattern of drug-resistant seizure, the medical team thought of possible presence of autoimmune as a cause. Based on this of course, intravenous immunoglobulin (IVIG) and corticosteroids were tried despite the serum and cerebrospinal fluid autoimmune panels being negative. Unluckily, these surgical treatments did not bear any clinical impression.

Against this background of ongoing problems, perampanel, a selective non-competitive AMPA receptor antagonist was started at a dose of 4 mg/day. The reaction was quite dramatic. The patient was seizure-free on a permanent basis, something that she could not have achieved since her diagnosis. This stability of neurological nature continued approximately three months and augmented the quality of her life strikingly. This improvement was however tampered with by the occurrence of the rise of alarming changes in terms of behavior.

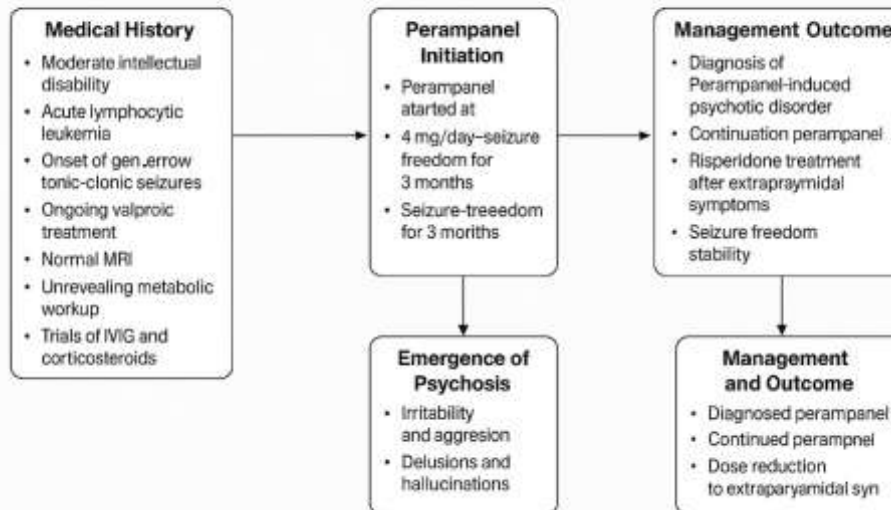
After around two months into usage of perampanel, the patient started exhibiting atypical irritability, as well as raising instances of verbal and physical aggression. All of these behaviors intensified during three weeks and led to a crisis when she threatened a family with a knife(5). She started to say delusional credences and thought that family members were plotting against her, claimed people were telling secrets that belonged to her to strangers and that people stole her personal items. She talked to what seemed to be no one and reported visual and auditory

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hallucinations including voices that she heard and people that she could see but no one could. She was very disturbed in her sleep and her behavior became seriously disorganized.

These physical signs were an extreme deviation of her normal. She had no history of psychiatric diseases. Her medical records did not contain the history of any aggression, disturbances of mood, or psychotic symptoms. No history of genetic disposition to psychiatric diseases was noted on her family. No changes in her physical health or new drugs were noted in the recent past other than perampanel. She was never subjected to drugs.

### A Delicate Balance: A Case of Perampanel-Induced Psychosis in a Teenager with Intellectual Disability and Refractory Epilepsy



**FIGURE 2** Case of Perampanel-Induced Psychosis

When admitted, she was examined thoroughly in hospital. Her various vital signs were stable and abnormal neurological examination remained unchanged. The restaging neuroimaging using MRI and a subsequent EEG did not show any new data. Her EEG was like her baseline studies. The level of plasma ammonia (32.43  $\mu\text{mol/L}$ ) and the level of valproic acid (88.2  $\mu\text{g/ml}$ ) before a dose were acceptable.

A mental status assessment showed severe psychomotor agitation, severe irritability, a persecutory delusion, disorganized thinking and both auditory as well as visual hallucinations. Although she had these psychiatric manifestations, she was still alerted and knew her orientation with no idea or actions of suicide or self-harm.

Since only the timing of presenting the patients with perampanel and no other possible causes could be identified, perampanel-Induced psychotic disorder was diagnosed. Another hard choice confronting the medical staff was eliminating perampanel that might lead to a relapse of crippling seizures, or continuing its treatment that would only deteriorate her mental condition. To make a compromise, it was decided to introduce risperidone with low dosage 0.5 mg daily. Amazingly her health started getting better. She was less annoyed, less violent and started sleeping better(6).

She was discharged on a controlled combination of risperidone 1.5 mg one time per day which effectively removed most of her psychiatric disorders. In the following six months, she did not have to struggle with her condition that shows stability both psychiatrically and neurologically. Nevertheless, she started to develop extrapyramidal symptoms i.e., notably bradykinesia and a pill-rolling tremor. There was suspicion of drug induced Parkinsonism and a workup to Wilson disease came out negative. Her dose of risperidone was tapered to 0.25 mg/day in a bid to reduce side effects. This dose reduction helped to reduce the extrapyramidal symptoms without causing much control over her psychotic symptoms.

At the last check-up, the patient has been seizure-free on perampanel as well as stable at a low dosage of risperidone. Her quality life has greatly improved and she is carefully followed up by neurology as well as by psychiatry. Her case demonstrates the problems of managing a dual-diagnosis client and the necessity of a well-informed pharmacovigilance when using perampanel with vulnerable groups.

## 3.Discussion

Treatment of epilepsy in persons with intellectual disability is one of the most complicated cross roads in neuropsychiatric treatment. This is a group of people that does not only have a significantly greater rate of epilepsy compared to the general population but also experiences the burden of the disease to a disproportionately high degree in regard to drug reactions and failure to control seizures. Many studies revealed that the percentage of people with intellectual disability, who can be diagnosed with epilepsy, can reach 30, which is 1530 times higher than the prevalence in neurotypical people. The intellectual retardation is positively correlated with resistance and frequency of seizures so it becomes a challenging clinical task to treat it. The improvements in antiseizure drugs (ASMs) have brought hope to use of medications in seizure control but also created a new set of risks with a possible most destructive effect of the drugs being psychiatric side effects especially in cognitively vulnerable patients.

Perampanel is one of the newer ASMs that are unique because it is a non-competitive antagonist of AMPA (alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) receptors. It was approved by the U.S. FDA in 2012 as an adjunctive therapy of focal-onset seizures, but it showed significant beneficial effects on controlling drug-resistant epilepsy(7). This pharmacological advantage however is not without any costs. The fact that perampanel successfully blocks the excitatory glutamatergic neurotransmission may seem like an excellent quality of this drug, helping inhibit neuronal hyperexcitability; it may also destroy emotional regulation in the brain circuit. This has culminated in the development of behavioral side effects whose common denominators are aggression, irritability, and anxiety especially in the initial titration stage or at an increased dose.

The FDA has made it clear to show these dangers. A black box warning on the use of perampanel also describes the presence of psychiatric and behavioral reactions with the potential of being severe and even life-threatening, such as hostility, homicidal ideation, and suicidal tendencies. Notwithstanding, cases of frank psychosis and perampanel are extremely uncommon in the literature, possibly because they were not acknowledged or they were attributed to underlying neurological disorders. The addition of our case and two earlier published cases to the body of evidence is growing but remains limited toward supporting a view that there is an important adverse outcome of perampanel-induced psychosis that needs more clinical awareness.

In the case in point, visual and auditory hallucinations, persecutory ideas, aggressive attitude, and cognitive attention started out of the blue right at about two months after the commencement of perampanel. The symptoms were also sharply contrasting to the normal behaviour of the patient and there were no known detectable psychosocial stress/medical changes prior to the symptoms. No family or personal history of psychiatric illness, absence of any other new therapeutic agent, and temporal relationship with the initiation of perampanel contributed strongly to an argument of causality. Notably, the psychotic symptoms of the patient were receptive to the practice of low-dose risperidone, which did the role of driving them away as far as the psychiatric symptoms were concerned without compromise to the antiseizure effect of perampanel, thus the viability of the dual-symptom treatment regimen in this tricky case.

Such a case is not unique. Comparative analysis of two previously described cases by Rodriguez et al (2021) and Leite et al (2021) showed incredible similarities. The two patients were females, and none of them had any prior history of psychiatric problems before developing acute psychotic symptoms upon the increase in perampanel dose or restarting it. Such bouts needed institutionalization and treatment using antipsychotics. Interestingly, in the Rodriguez case, self-escalation of perampanel dose led to compensating missed doses of the drug by increasing the dose to 12 mg within the same day, which lead to an occurrence of an immediate psychotic episode, defined by confusion and agitation. According to the report by Leite, psychosis occurred after two weeks of the dosage increase to 12mg/day with the symptoms of olfactory hallucinations and paranoia.

Collectively, in the context of our case, these results seem to indicate that there is a dose dependent pattern to psychiatric adverse outcomes with perampanel, though at a low dose of 4 mg/day our patient was experiencing the symptoms. It is possible that mentally disabled patients would be even more susceptible to the neuropsychiatric definite effects of perampanel than the rest of the population, even at lower doses of therapeutic consideration. In support of this hypothesis, one should mention a retrospective study by Andres et al., in which 27 patients with intellectual disability and drug-resistant epilepsy completed perampanel treatment. The most common behavioral disturbance was aggressive behavior, and even though psychosis was not mentioned specifically, the results showed a high risk of neuropsychiatric complications. In the same line of thinking, Snoeijs-Schouwenaars et al. reported that 40 percent of intellectually disabled patients being treated with perampanel showed behavioral disturbance, which is a very high percentage in contrast to the epilepsy in general.

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Yet another insightful study performed by Yamamoto et al. with the sample size of 895 patients revealed a number of predictive risk factors of psychiatric adverse events in the conditions of perampanel treatment. These were case of intellectual disability, psychiatric comorbidity and increased doses of the drug. Remarkably, the incidence of adverse psychiatric effects was lower in patients under 16 years of age and in patients which took lamotrigine or enzyme-inducing ASMs. Such a subtle interpretation puts a strong focus on individualized pharmacotherapy, particularly in children and in intellectually challenged individuals(8).

When trying to explain the potentially devastating psychiatric effects of perampanel, its diffuse action on the AMPA receptor has been the topic of interest by researchers trying to rationalize this process. The exact neurochemical processes are still somewhat conjectural but it would likely be that the ability of perampanel to block excitatory neurotransmission in limbic and prefrontal regions disrupts the normal system of thought and perception regulation. Its tendency to act quickly, often after the first six weeks of treatment, during titration, is evidence in favor of a model whereby the rate and extent of AMPA antagonism could be too fast for the brain to adapt quickly, especially when an individual brain is already compromised by prior cognitive impairment or polypharmacy.

As we have seen, stoppage of perampanel and antipsychotics induction in the treatment of emergent psychosis was not a careless decision. The risk of relapse of seizures upon discontinuation of perampanel was highest among the dangers of this drug use option, but it was too high to be acceptable, considering the fact that the seizure burden of the patient before the treatment was very advanced. However, this was not an easy decision without complications. New clinical challenge was made with the appearance of extrapyramidal symptoms (EPSE) presumably because of risperidone. Eventually, it was solved through a decrease of the antipsychotic dose into minimal but efficient level.

This subtle clinical follow up emphasizes the role of measurement observation and dynamic dose requirements in the treatment of complicated neuropsychiatric. Care providers are encouraged to warn families and other caregivers about possible psychiatric adverse effects before they start using perampanel. Assessments must be carried out regularly particular in the initial two months of treatment and after any dose change. In high-risk populations (people with intellectual disability, mood disorders, or a history of psychiatric condition), slow titration and proactive contact with psychiatrists may be appropriate(9).

To sum up, the case can be added to the growing awareness that even though uncommon, psychosis is a severe and valid side effect of perampanel treatment. This risk should be further quantified in prospective (preferably) kinds of pharmacovigilance studies carried out just in the future. In the meantime, clinicians are recommended to focus on achieving a compromise between seizure control and mental health preservation understanding that they might not always be compatible and can, however, be safely non-conflicting when approached in a collaborative, patient-centered practice.

## **4. Conclusion and Future work**

With new developments in pharmacology, the store of antiseizure medications (ASMs) is only now as large as it was previously thought it was, thus, providing the clinicians with more convenient opportunities to treat a complex form of epilepsy, particularly the ones classified as drug-resistant. But each of the new treatments has its own set of risks, and novel mechanisms of action come with hitherto underreported or ill-explained side effects. Providing an important lesson regarding the dual care demanded by epilepsy care, which is that one must not only manage the seizures, but must also protect the mind, the case of a young girl with moderate intellectual disability with refractory epilepsy who was affected by perampanel-induced psychosis illustrates how important it is to attend to mental as well as physical wellbeing.

The key issue highlighted in this case is that the same drug that promises to bring respite through freedom of seizures can spell doom on the psychological stability of a patient. In the case of our 15-year-old patient, the drug perampanel provided what no other ASM had ever provided, an assured end to all seizures. However, shortly after reaching such a milestone, she started experiencing a sudden occurrence of very severe psychiatric problems, such as delusions, hallucinations, aggression, and disorganized behavior. No history of psychiatric illness, no other pharmacologic issue, and no underlying medical reasons made it the most likely that the patient should be diagnosed with the perampanel-induced psychosis.

The dilemma of clients in this case of whether to discontinue the offending medication or continue to manage the psychiatric side effects and assume seizures control is a synopsis of a more general dilemma in neuropsychiatric

practice. On the one hand, discontinuing perampanel would have caused the recurrence of seizures, which would have posed a direct threat to the material welfare of the patient as well as a certain risk to functional stability. Conversely, it was possible to continue the drug without controlling the psychosis, which may result in self-damage or other people. This was a tough choice and it was settled by adding a low dosage typical of antipsychotic medications that would provide resolution to the psychotic symptoms but will not compromise seizure control, that is by introducing low dosage atypical antipsychotics by the name of risperidone. These side effects were extrapyramidal side effects that the patient started experiencing later, but it was possible to overcome them by dosage reduction without compromising the therapeutic balance that was finally achieved.

Such a trend of treatment can serve as the model of the approach that future clinicians should use. Rather than posing the issue as an either-or dichotomy of managing seizures versus treating psychiatric symptoms, a multidisciplinary, integrative concept of care ought to be stressed wherein neurologic stability and psychiatric safety are co-equal matters of concern. A working unit should be made among psychiatrists, neurologists, caregivers, and the patients themselves in which treatment decisions are made on a personalized, individual, and flexible basis.

The fact that there are only two other documented cases of psychosis induced by perampanel use before this report should not give the rest of the clinical community false confidence. In fact, the total few cases indicated could be the result not of a true rate, but of equivocal diagnosis, underreporting, or be due to another condition, notably pre-existing intellectual disability, psychosis related to epilepsy, or primary psychiatric pathology. The psychological weakness of patients with intellectual disability (particularly) makes the diagnostic process confusing. Outbursts in behavior, hallucinations or violence could be confused as being normal, or a developmental scale, causing the disregard of drug-induced drug phenomena. The clinicians should hence have a very high index of suspicion towards any notable behavior change after starting perampanel.

More to this, it is vital that clinicians are knowledgeable of the fact that behavioral side effects are dose related. Large pooled trials and retrospective studies have shown that, irritability, aggression, and psychotic symptoms increase in significance with high doses of perampanel. Our case is also somehow special because psychosis in our case was achieved at a rather low dose (4 mg/day), which is why we should support the idea that some people, and especially some people with intellectual disability, can have quite high sensitivity to the psychiatric effects of perampanel despite ordinary high doses of this medication. This observation argues against the assumption that dose thresholds are predictive and also implies that factors related to individual patients, age, baseline neurodevelopmental status and medications used may be strong determinants of risk.

The clinical conclusion to be understood is the necessity of pre-treatment screening. Not only should the common adverse effects such as dizziness or fatigue be discussed with families and caregivers of patients who have begun therapy with perampanel, but also the more serious (though not very common) risks of psychosis, suicidal, and extreme aggression. Another important step that should be taken prior to the treatment is to create behavioral baselines so that when the change of the usual conduct would occur it would be detected and acted upon immediately.

Monitor-wise, it would also be recommended that patients, particularly the ones with known psychiatric vulnerability, should be closely tracked within the first six to eight weeks of the treatment a critical period during which most unpleasant behavioral events are likely to occur. The follow-up should be conducted through regular checks on mental health, observation of the caregivers, and evaluation of behavior. Child and adolescent psychiatry, or neuropsychology can also be collaborated on in some situations prior to medication start.

In cases that psychiatric symptoms do develop, treatment strategies must take into account minimizing the antiseizure advantages of perampanel in any strategy where feasible, especially when it pertains to patients in whom seizure control has been achieved at the cost of great effort. The problem of psychotic features may be successfully treated at low doses by antipsychotic drugs risperidone, quetiapine, or olanzapine, although those drugs are not without side effects. Nevertheless, the clinicians should stay cautious of secondary complications, extrapyramidal symptoms, metabolic side effects, or interaction with other ASMs. Medication should be titrated and trounced over and over again.

At a more macro systems level, this case indicates the need in terms of a more systematic pharmacovigilance in association with newer ASMs, such as perampanel. Clinician reporting systems, and post-marketing surveillance systems should be promoted and optimized. Observation of trends, risk factors, and clinical predictors of psychiatric adverse events may also be possible through patient registries, particularly those that include

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vulnerable subpopulations including pediatric populations and populations with intellectual disabilities. Also, potential studies aimed at investigating genetic or neurobiological markers in terms of ASM sensitivity may provide some useful answers in terms of the people who would potentially be the most susceptible to develop such side effects.

To conclude, regardless of the breakthrough offered by perampanel in epilepsy treatment, particularly drug-resistant ones, its psychiatric safety concern cannot be underestimated. The example of the teenage girl depicted in the present case shows that a miracle epilepsy cure may open the gates to the possibly life-threatening psychiatric disorders. Fortunately, when diagnosed early, managed multidisciplinary, and medication considerably, a balance can often be reached between two goals of neurological stability and psychological well being.

It is recommended that clinicians should consider any epilepsy treatment plan, not as a personal prescription, but an ever-evolving activity, which continues to be modified through partnership, monitoring, and individual attention. By means of this approach, we have a chance to make sure that the patients get all the benefits of modern pharmacotherapy, not being surprised by its dark side.

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### **Conflicts of interest**

The authors have no conflicts of interest to declare

### **References**

1. Villanueva V, López-González FJ, Mauri JA. Psychiatric adverse events in patients with epilepsy treated with perampanel. *Epilepsy Behav.* 2015;44:70–74.
2. Steinhoff BJ, Bacher M, Bucurenciu I. Adverse psychiatric effects of perampanel: a real-world study. *Acta Neurol Scand.* 2019;140(1):57–64.
3. Tsai JD, Lin CY, Huang YC. Perampanel-induced psychosis in adolescents with epilepsy: a case series. *Brain Dev.* 2018;40(9):784–787.
4. Cilio MR, Biton V, Nordli DR. Safety and tolerability of perampanel in pediatric patients with refractory epilepsy. *Epilepsia.* 2014;55(8):1295–1302.
5. Baykan B, Altindag E, Bebek N. Psychiatric side effects of perampanel in intellectual disability: clinical perspectives. *Seizure.* 2020;81:247–251.
6. Chaitanya G, Satishchandra P, Sinha S. Perampanel and psychosis in developmental disorders: a rare but severe adverse effect. *Epilepsy Res.* 2021;176:106713.
7. Perucca E, Gilliam FG, Sander JW. Adverse effects of antiepileptic drugs: focus on psychiatric and behavioral issues. *Lancet Neurol.* 2022;21(2):117–129.
8. Paredes J, Pineau F, Kaoutar B. Acute psychosis triggered by perampanel: case report and pharmacovigilance insights. *J Neurol Sci.* 2017;381:224–226.
9. Ulate-Campos A, Loddenkemper T, Duffy FH. Behavioral complications of epilepsy therapies in adolescents with intellectual disability. *Dev Med Child Neurol.* 2020;62(5):539–545.