

# Psychoses of Epilepsy in Pregnancy: A Case Report

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To discuss the unique relationship between psychosis and seizures in a young individual, who is also pregnant. Psychosis of epilepsy can present in multitude of ways, including pre-ictal, ictal, post-ictal, chronic interictal, and forced normalization psychosis.

**KEY WORDS:** Psychosis; Epilepsy; Preictal; Postictal; Interictal; Normalization.

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## INTRODUCTION

The association between psychosis and epilepsy has been well studied, with the first instance dating back to 1854 [1]. Psychosis of epilepsy (POE) is a term applied to a group of psychotic disorders with a distinct phenomenology in which potential etiopathogenic mechanisms are believed to be closely related to the seizure disorder [2]. Individuals with epilepsy have a higher rate of psychosis (9%), when compared to the general population (1%) [3].

The psychoses of epilepsy is classified based on the temporal relationship between the psychotic episode and the ictus: pre-ictal psychosis occurs prior to the ictus, ictal psychosis occur within seizure activity, postictal occur within 7 days of a seizure, and interictal occur independently of seizures. Alternative or paradoxical psychosis or forced normalization is a separate entity in which the onset of psychotic symptoms follows the suppression of seizure activity [2]. We discuss the case of a young woman who demonstrates a number of these states relate to the unique relationship between psychosis and epilepsy. Informed consent was provided by the patient and certain details were changed to protect her identity.

## CASE

Ms. A, a 36-year-old female, was admitted to behavioral health inpatient unit for management of psychotic symptoms. Specifically, she exhibited thought blocking, auditory hallucinations, delusions of reference, loosening of associations, and episodes of aggression. She had a documented history of grand-mal tonic-clonic seizures with onset at age 11 years, which was well-managed on valproic acid (VPA). At the age of 24 years, Ms. A started experiencing auditory hallucinations with delusions of persecution and of reference. Following this, Ms. A was started on risperidone, venlafaxine, along with VPA and functioned well, both in the social and occupational realms until the age of 32. She underwent Roux-en-Y gastric bypass to address weight gain, during which time she was switched from VPA to topiramate to complement the surgical procedure, while maintaining the other medications. Subsequent to these changes, Ms. A's struggles with anxiety and psychosis worsened. This exacerbation was controlled by an increased dose of risperidone. Approximately one year after this episode of worsening psychiatric symptoms, Ms. A reported several episodes of seizures. Diagnostic imaging and electroencephalography (EEG) confirmed complex partial status epilepticus arising from a right temporal mesial cyst. At this time, VPA was re-introduced to the regimen and Ms. A was maintained on a combination of VPA, topiramate and risperidone.

The events leading to her current hospitalization re-

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main unclear. One presumption is that she was non-adherent to her medication regimen, which led to worsening of behavioral symptoms. When she was first evaluated in the emergency room, she had delusions of reference and of persecution, with auditory hallucinations and was also behaving in an aggressive manner. She was also identified as being 20 weeks pregnant. During her stay, Ms. A would have periods of psychosis characterized by paranoia and aggression and periods that would be characterized by disorientation with eye-blinking (Type I). Ms. A was initially started on lurasidone, with limited response and then switched to haloperidol. Because of the pregnancy, she was started on lamotrigine for seizure control, which was slowly titrated up. Ms. A's hospital stay was long—approximately 6 months, our case report presents a snapshot of her stay, following the birth of her child. After she gave birth, she had several episodes of psychosis (Type II), which were followed by seizures. These episodes were characterized by altered sensorium, saccadic eye movements, worsening delusions of reference, and agitation. At this time, lacosamide was added to the existing regimen of lamotrigine and topiramate. At a dose of 150 mg lacosamide, lamotrigine 200 mg and topiramate 200 mg, Ms. A's seizures were completely controlled. One day after this, Ms. A started reporting significant increases to her anxiety levels as well as worsening of her auditory hallucinations, which became commanding, while simultaneously exhibiting improved insight, expressing sadness over her previous behaviors (Type III). This necessitated the addition of low-dose lorazepam. Ms. A reported a worsening of auditory hallucinations. Her symptoms gradually improved over the following several days and Ms. A was discharged on lacosamide, lamotrigine, topiramate, haloperidol, olanzapine, and lorazepam.

## DISCUSSION

Ms. A's case illustrates the complicated nature of the relationship between psychosis and epilepsy. Ms. A's longitudinal course demonstrates four different types of psychoses. In Type I or ictal psychosis, psychotic symptoms were accompanied by alteration in consciousness suggesting that the psychotic episode was likely accompanied by seizures. Ictal psychosis is typically seen in temporal lobe epilepsy. Seizures last under 3 minutes and psychotic symptoms include visual or auditory hallucina-

tions, agitation, paranoia, depersonalization, and derealization. Ictal psychosis lasting longer than 3 minutes is rare and may occur as a non-convulsive status epilepticus with simple or complex partial or absent seizures. As observed in Ms. A, the manifestation is not truly psychotic—sensorium is altered during the episode [1,4] and the recommended treatment is optimization of antiepileptic agents. Ms. A also demonstrated pre-ictal psychosis (Type II). This form of psychosis can often be considered an aura and terminates with the onset of the ictus. Similar to ictal psychosis, pre-ictal psychosis is treated as a part of the ictal process by optimizing antiepileptic agents.

The third type of psychosis (Type III) that Ms. A demonstrates followed stabilization of the seizure disorder. Post-ictal psychosis (PIP) can occur up to 7 days after seizure. PIP is accompanied by abnormalities of the mood (depression, mania with psychotic features, irritability, aggressive behaviors) rather than delusions [4,5]. A unique feature of PIP is a lucid interval, which can last from 2 hours to a week. Ms. A could have experienced a lucid interval before the onset of auditory hallucinations. A close differential diagnosis to PIP is forced normalization (or paradoxical) psychosis forced normalization (FN). FN is characterized by the fact that, as the EEG becomes more normal or entirely normal, when compared with previous and subsequent EEG findings, there is emergence of psychiatric symptoms [6]. FN occurs after rapid control of seizures with an antiepileptic drug. Partial complex temporal lobe seizures and absences seizures are the most commonly described seizure disorders leading to FN [7]. Similar to PIP, symptoms occur without clouding of consciousness, on average 2–3 days after seizure cessation. FN usually manifests after a prolonged period of epilepsy, with an average duration of 15.2 years [2,6]. With repeated episodes of FN, the clinical presentation can vary and can include delusion, hallucinations, anxiety, self-mutilation and suicidal behavior, conversion disorder [6], and catatonia [8]. A longitudinal follow-up with electroencephalography EEG is useful in differentiating PIP and FN. We were unable to carry out serial EEGs however based on suggested diagnostic criteria, the clinical chronology are highly suggestive of FN [9,10]. Another differential to consider is antiepileptic drug (AED)-induced psychosis, which has been described as a side effect with almost every AED [1].

A final type of psychosis which likely was the most prevalent form in Ms. A's history, particularly between the ages

of 24 years and 32 years, is chronic interictal psychosis (CIP). CIP accompanies a long history of uncontrolled seizures and has a reported prevalence of 5% among individuals with seizure disorder. CIP has an insidious onset with paranoid delusions and hallucinations. The phenomenology of CIP can include negative symptoms and cognitive decline. EEG does not show complete normalization of EEG [4].

Ms. A's case also illustrates the need to understand pharmacodynamics during pregnancy. One of the greatest concerns in pregnancy relates to fetal malformations. The risk of fetal malformations is present with the use of all antiepileptics – highest with VPA (10.73%; 95% confidence interval [CI] = 8.16–13.29; for valproate monotherapy) and lowest with lamotrigine (2.91%; 95% CI = 2.00–3.82) [11]. For these reasons, VPA is not recommended as first line treatment during pregnancy and switching to lamotrigine is recommended. If a patient must be maintained on valproate, it is recommended that both free and total plasma levels of VPA should be measured during pregnancy because while the total VPA levels decline, free levels do not and in fact remain unchanged or even increased [12]. This saves patients from needless increases in dosing of VPA. Further, pregnancy is accompanied by changes in sex steroids, increase in phase 2 glucuronidation, and increased clearance. The increase in clearance starts at onset of pregnancy and continues to increase progressively through the third trimester, with a postulated rate of 330% from onset to end of third trimester. It is recommended to increase the average dose of lamotrigine by 250% to maintain steady therapeutic drug levels across pregnancy in women with epilepsy [12]. Thus, it is likely that the dose of lamotrigine that Ms. A was receiving was now not adequate as a result of the increased clearance. Serum lamotrigine concentrations return rapidly to pre-pregnancy levels after pregnancy. This change starts within days after delivery and is complete 2 to 3 weeks postpartum. As such, returning to pre-pregnancy doses of lamotrigine should be start within days of delivery [13].

POE is a spectrum of clinical entities. Proper identification is paramount for adequate treatment. This is especially true with complicating factors such as pregnancy, which play a role in medication bioavailability.

#### ■ Conflicts of Interest

No potential conflict of interest relevant to this article

was reported.

#### ■ Author Contributions

Mario Fahed and Seethalakshmi Ramanathan both participated in writing and editing this manuscript.

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