Case Report

When Antipsychotics Imitate Epilepsy: Diagnostic Dilemma in a Case of Treatment-Resistant Schizophrenia

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ABSTRACT

Oculogyric crisis (OGC), a form of acute dystonia, is a recognized adverse effect of antipsychotics. However, certain seizure disorders can mimic OGC, complicating diagnosis and treatment. This report describes a rare case of seizure disorder presenting as OGC in a patient with treatment-resistant schizophrenia, highlighting a critical diagnostic challenge in clinical psychiatry. This is a case of a 21-year-old female with a 3-year history of schizophrenia developed recurrent upward eye deviation episodes after switching antipsychotics from Olanzapine to Aripiprazole. These were initially diagnosed as antipsychotic-induced OGC but failed to respond to standard anticholinergic therapy. The introduction of Clozapine improved her psychosis but exacerbated the eye movements and led to new symptoms including jerky limb movements, stammering, and two episodes of loss of consciousness with postictal confusion and tongue biting. Electroencephalogram (EEG) revealed generalized rhythmic slowing, suggestive of an underlying seizure disorder. Her symptoms resolved following cross-tapering of Clozapine to Haloperidol and initiation of Lamotrigine. This case underscores the importance of considering epilepsy in patients presenting with movement abnormalities unresponsive to anticholinergics, especially in the presence of a seizure history. Clozapine is known to lower the seizure threshold, potentially unmasking latent epilepsy. EEG findings, although non-specific, supported cortical dysfunction. The favorable response to antiepileptic therapy reinforced the revised diagnosis. Clinicians should maintain a high index of suspicion for seizure disorders in schizophrenia patients presenting with atypical or treatment-resistant movement symptoms. Comprehensive neurological assessment and individualized pharmacologic strategies, including EEG and antiepileptic therapy, are essential for accurate diagnosis and effective management.

Keywords: Anticholinergics, Antipsychotics, Clozapine, Electroencephalogram, Haloperidol, Lamotrigine, Oculogyric Crisis, Schizophrenia, Seizure Disorder

INTRODUCTION

The diagnostic boundaries between movement disorders and seizure-related phenomena in psychiatry are often blurred, especially in patients with treatment-resistant schizophrenia undergoing pharmacologic modulation. Among these, oculogyric crisis (OGC), a subtype of acute dystonia characterized by sustained upward deviation of the eyes, stands out as a well-recognized, though occasionally underdiagnosed, extrapyramidal side effect of antipsychotic medications, including both first- and second-generation agents[1,3,6]. The clinical presentation of OGC may closely mimic seizure activity, especially when accompanied by additional motor symptoms, leading to a diagnostic conundrum

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with significant implications for treatment.

Antipsychotic-induced OGC has traditionally been associated with high-potency typical antipsychotics but has also been reported with atypical agents like Aripiprazole and Clozapine[3,6]. While these adverse effects typically respond to anticholinergic agents, atypical or refractory cases should prompt clinicians to consider alternative diagnoses, such as seizure disorders, particularly when other features, such as loss of consciousness, postictal confusion, or a personal history of convulsions are present[3,5,6].

Clozapine remains the gold standard for treatment-resistant schizophrenia but is notorious for its dose-dependent epileptogenic potential[5,7]. Even at therapeutic doses, Clozapine may precipitate seizures, especially in predisposed individuals with underlying or latent neurological vulnerability such as a history of febrile convulsions[5,8]. Electroencephalographic (EEG) abnormalities, although often non-specific in this patient population, may support cortical dysfunction or unmask latent epilepsy[7,9]. Moreover, emerging neurophysiological concepts such as "forced normalization," where improvement in psychosis is paradoxically accompanied by worsening seizure activity, add further complexity to such presentations[9,10].

This case report illustrates a rare but clinically significant scenario in which antipsychotic-induced OGC was initially suspected but later determined to be a manifestation of seizure disorder, unmasked by antipsychotic treatment in a young female with schizophrenia. Through this case, we underscore the necessity for heightened diagnostic vigilance and multidisciplinary collaboration when managing neuropsychiatric symptoms that do not follow typical therapeutic trajectories.

CASE PRESENTATION

Ms JM is a 21-year-old female undergraduate who was diagnosed with schizophrenia at age 18 years. She received oral Olanzapine 10 mg daily (Nocte) with good control of her symptoms. About six months following the commencement of treatment, she was switched to oral Aripiprazole 15 mg/day due to weight gain and complaints of excessive sedation. However, Ms JM returned to the hospital within 72 hours following the switch to Aripiprazole with bilateral involuntary episodic upward eye deviations. Initially, Aripiprazole-induced oculogyric crisis (OGC) was suspected. However, these episodes were unresponsive to Diphenhydramine, and Benztropine. Switching back to Olanzapine significantly worsened her psychotic symptoms, necessitating her admission into the ward. When Aripiprazole was restarted and titrated to 15 mg/day, the upward eye deviations recurred. These episodes occurred up to three times daily, lasting for several seconds and sometimes up to a minute, and her psychotic symptoms unabated.

To address treatment-resistant schizophrenia, and the presumed OGC, Aripiprazole was cross-tapered to clozapine 200 mg/day (10 mg bd). The psychotic symptoms improved; however, the upward eye deviations became more frequent, with emergence of new-onset symptoms, including stammering, jerky body movements, head twisting and turning, oro-facial twitches, and tongue movements. Within a period of two weeks, she had two episodes of loss of consciousness leading to falls, and tongue biting, with associated postictal confusion lasting up to 30 minutes. These events raised concerns for a possible seizure-like activity. Probing further, Ms JM had history of childhood febrile convulsions.

Electroencephalogram (EEG) findings were abnormal with frontal-predominant generalized rhythmic delta activity and nearly continuous bilateral theta > delta slowing. No definitive epileptiform abnormalities were detected. Differential diagnoses included juvenile myoclonic epilepsy or idiopathic generalized epilepsy, likely unmasked by clozapine. Brain magnetic resonance imaging findings were unremarkable, ruling out the possibility of a space occupying lesion.

Cross-tapering the clozapine to Haloperidol 10 mg/day and initiating Lamotrigine 150 mg twice daily led to the resolution of the OGC, episodes of loss of consciousness, and other involuntary movement, as well as effectively controlling the psychosis.

DISCUSSION

This case underscores the neurotoxic potential of atypical antipsychotics in susceptible individuals.

OGC, a type of acute dystonia, is often associated with first generation antipsychotics but may also occur with second generation antipsychotics like Aripiprazole[3-5]. However, the unresponsiveness to anticholinergics in this case raises doubts about a classic OGC. Furthermore, the recurrence of symptoms with re-initiation of Aripiprazole and clozapine suggested a broader spectrum of movement and seizure disorders, possibly drug-induced or unmasked by therapy.

Clozapine, although effective for treatment-resistant schizophrenia, has been linked to dose-dependent seizure risk[7,12]. Even at lower doses, seizures may occur in genetically predisposed patients or those with prior seizure history[8]. Our patient had a history of childhood febrile convulsions, a known risk factor for later epilepsy. Additionally, generalized slowing seen in EEG, though non-specific, may indicate underlying cortical dysfunction or evolving epilepsy[9]. In addition, forced normalization can paradoxically improve psychosis as seizures worsen, adding complexity to the clinical picture.[9,10]

Lamotrigine, a broad-spectrum anticonvulsant effective in juvenile myoclonic epilepsy and psychosis augmentation, proved beneficial both for seizure control and mood stabilization[11]. Haloperidol was cautiously introduced as it carries a lower risk for seizure induction and OGC at modest doses compared to Second Generation Antipsychotics (SGAs).

A multidisciplinary approach, involving psychiatry, neurology, and pharmacology, was critical in achieving a satisfactory outcome.

CONCLUSION

This case illustrates the importance of maintaining a high index of suspicion for atypical movement and seizure-like disorders when treating schizophrenia, especially in young females with prior seizure history. EEG, careful drug cross-tapering, and individualized pharmacologic strategies are key to resolving complex neuropsychiatric side effects.

Recommendations

This case highlights the importance of distinguishing between antipsychotic-induced extrapyramidal side effects and seizure-related phenomena in patients with treatment-resistant schizophrenia, particularly when clinical symptoms do not follow the expected response to standard therapies. Based on the insights derived from this case, we recommend that clinicians should consider seizure disorders in patients presenting with atypical or refractory movement abnormalities, especially when associated with features such as loss of consciousness, postictal confusion, or a history of febrile seizures. The use of electroencephalography (EEG) and other neuroimaging to improve diagnostic accuracy should be the rule rather than the exception.

Author Contributions

All authors substantially contributed to the clinical care of this patient. All authors performed critical revision of the manuscript for intellectual content and approved of the version to be published.

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Patient Consent

Consent was received from the patient to publish the case report, and information has been de-identified to protect patient anonymity.

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