A Case of Clozapine-associated Myoclonus & Seizure in Schizoaffective Disorder.

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Introduction:

First line treatment for schizophrenia and schizoaffective disorder is antipsychotic medication. Despite this, approximately 10-30% of patients have little or no response to these medications. Treatment-resistant patients continue to struggle with disabling symptoms related to psychosis. Clozapine, an atypical antipsychotic, is indicated for partially or fully treatment-resistant schizophrenia (TRS) or schizoaffective disorder. It is limited specifically to treatment-resistant cases, as deemed by poor tolerance criteria--namely failure to respond to at least two antipsychotic trials (including one atypical agent).[9]

Even though clozapine is a promising treatment option for TRS, it presents with a wide variety of potentially serious side effects. These include agranulocytosis[2], myocarditis[3], decreased GI motility[4], hypersalivation[5], and seizures. Seizures induced by clozapine can be missed or misinterpreted. It is important to recognize signs of seizure activity, despite potentially normal EEG findings, to ensure optimal treatment. This poster will discuss a case involving clozapine-associated myoclonus and seizure, despite treatment of a previously-diagnosed seizure disorder in this patient.

Case:

Presented is a 34-year-old female with a past history of schizoaffective disorder, bipolar type and a seizure disorder of unknown type. She was admitted to an involuntary unit of a standalone psychiatric hospital for further evaluation and treatment of current diagnosis. During the course of her hospitalization, antipsychotics and mood stabilizers were trialed, tapered, and titrated. After titration of olanzapine and chlorpromazine, as well as fluphenazine decanoate, the patient showed mild improvement. However, she continued to have persistent auditory hallucinations, delusions, and negative symptoms. In addition to psychiatric medication, the patient arrived on a regimen of lacosamide and oxcarbazepine from neurology in order to treat her seizure disorder.

Due to persistent symptoms in the face of concurrent antipsychotics, clozapine was considered despite the increase in seizure risk.[7] Over the course of approximately 10 weeks, clozapine was slowly titrated while tapering other daily antipsychotics with improvement in psychotic symptoms. As the clozapine dose reached 150mg daily, the patient began to demonstrate occasional myoclonus. By this time, olanzapine had been discontinued and chlorpromazine taper was progressing. Clozapine was continued at 150mg daily until chlorpromazine was discontinued before resuming titration, which improved myoclonic symptoms. Once a total daily dose of 400mg was reached, the patient once again demonstrated myoclonic jerking movements, this time with increasing severity. These movements were observed on the unit, often multiple times a day, and were distressing to the patient. Shortly after myoclonus returned, there was a reported ground-level fall. Clozapine dose was reduced to an eventual total of 300mg daily with significant improvement in symptoms and no additional falls. Symptoms of psychosis remained well-controlled with occasional breakthrough hallucinations and paranoia during the 1-2 days surrounding biweekly fluphenazine decanoate injection. Approximately 11 weeks after clozapine initiation, the patient tested positive for COVID-19. She experienced minor symptoms (low grade fever, body aches, cough), but no sustained abnormalities in oxygenation per bedside pulse oximetry.

Approximately 12 weeks after clozapine initiation, the patient was found sitting up in bed, but unresponsive to verbal stimuli. She had increased symmetric jerking movements of the bilateral upper extremities, showed evidence of enuresis, and appeared to be acutely post-ictal or interictal. She was sent emergently to a nearby medical hospital for neurologic evaluation where she was admitted for observation overnight and demonstrated no further seizure activity. While admitted, she underwent electroencephalography, head CT and lab work--all with no major findings. Repeat COVID-19 testing was negative.

Keppra 500 mg bid was added to her antiepileptic regimen by neurology staff. Since that discharge, and return to psychiatric facility, the patient continued to tolerate clozapine well, displaying improvement in her psychotic symptoms. She exhibited no further myoclonus or seizure activity.

Seizure type	*n*	%	Mean dosage of clozapine, mg daily (*n* = available sample)	References[a]
Generalized				
Tonic-clonic	55	54	461 (*n* = 49)	13,14,17,23,24,29,31,32, 34,37–53
Myoclonic	23	23	535 (*n* = 15)	1,10,27,30,38, 40,44,45,50,54–57
Atonic	1	1	600 (*n* = 1)	53
Myoclonic and atonic	4	4	488 (*n* = 4)	1,30
Tonic-clonic with other seizure types	12	12	419 (*n* = 12)	2,7–9,15,44,50,58,59
Partial				
Simple	3	3	400 (*n* = 2)	27,53,60
Complex	3	3	275 (*n* = 1)	27,53
Total	101	100		

[a]A table with the number of cases and the mean and range of the doses of clozapine administered in each report is available from the authors.

Figure 1: Frequency of clozapine-induced seizure types

Discussion:

Although all antipsychotics lower the seizure threshold to some degree, clozapine is known to increase seizure risk more than others.[7] While tonic-clonic seizures are among the most common form of seizure activity associated with clozapine, myoclonus is also possible (reference Figure 1).[7] It is important to recognize that myoclonus can lead to tonic-clonic seizure activity and also to falls.[6,7,8]

In patients being treated for primary psychotic disorders with comorbid seizure disorder, it is often necessary to utilize antipsychotic medications that lower the seizure threshold. At times, two or even three antipsychotics may be required to control symptoms. While clozapine is renowned for its seizure risk, it is important to remember that it is possible to use the drug in patients with seizure disorder, provided careful monitoring and titration. In the case described, the addition of clozapine ultimately allowed for the reduction of total antipsychotic use from three to two, which alone might result in a positive change in seizure risk for this patient.

Although clozapine has a known higher side effect profile compared to other antipsychotics, it is important to keep in mind that its role is particularly for TRS. Many patients, such as one mentioned in this case, show noticeable improvement of psychosis with clozapine. With that, being oftentimes last-line therapy, manageable side effects should not dissuade further use of this medication. One may be concerned with new or worsening presentation of myoclonus/seizure activity and may decide to discontinue clozapine treatment. However, early partnership with neurology may be helpful in allowing further continuation of clozapine treatment while also managing seizure-like symptoms and presentations. Even in the context of normal encephalographic studies, neurology was able to recognize the need for additional antiepileptic coverage which allowed for further clozapine titration.

Reference

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