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Clozapine-Induced Stuttering after a Seizure: About a Case Report

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Abstract **Case Report**

Clozapine is an atypical antipsychotic with proven efficacy in the management of treatment-resistant schizophrenia. It has well-documented side effects. Stuttering is defined as a disturbance in the normal functioning of fluency and temporal structuring of speech. In adulthood, it can occur because of various causes including the side effect of medications. Previous case reports have found that clozapine-induced stuttering can coexist. In this article, we describe a case in which stuttering following a generalized seizure was observed when increasing doses of clozapine.

Keywords: Clozapine, schizophrenia, Stuttering, adulthood.

INTRODUCTION

Clozapine is an atypical antipsychotic drug with proven efficacy in the management of treatment-resistant schizophrenia [1]. It has well-documented side effects that include agranulocytosis, myocarditis, seizures, side effects and hyper salivation [1]. Stuttering is defined as a disturbance in the normal functioning fluidity and temporal structuring of speech. Appearance in adulthood stuttering can occur as a result of trauma or stroke or as a side effect of medications. It is also a rare side effect of clozapine that has been reported in a number of case studies [2, 3].

The underlying pathophysiological mechanisms of stuttering remain unresolved but have been postulated to include dopamine dysregulation, genetic mechanisms, and structural and functional brain changes [4].

Previous case reports have found that clozapine-induced stuttering can coexist with extrapyramidal symptoms [5, 6], epileptic activity [6-9], brain pathology [5, 6, 10], and a family history of stuttering [5].

In this case report we describe a case of clozapine-induced stuttering after a convulsive seizure observed during an increase in clozapine doses.

CLINICAL VIGNETTE

K.B aged 27 years, single, without profession, native and inhabitant of Rabat. She was admitted to the psychiatric department for a behavioral disorder consisting of agitation and hetero aggression towards her family, with threats of homicide and suicide.

The onset of the symptomatology appears to date back to the age of 18 years. During this time, the patient began to report auditory hallucinations repeating that the Jnoun were trying to control her thinking. Her behavior changed and she became aggressive, hence her first psychiatric consultation. She was put on an unspecified treatment with good clinical improvement, regular outpatient follow-up and the diagnosis of schizophrenia was established. The patient was stabilized for approximately 9 years. In February 2022, her condition changed without any notable triggering factor. She became unstable, aggressive and uttering delusions of persecution and mystico-religious statements hence her hospitalization in psychiatry.

From her history:

1. Follow-up in psychiatry for 9 years
2. A paternal aunt followed in psychiatry for a chronic psychiatric disorder.

The psychiatric interview had objectified a calm patient on the psychomotor plan, of weak corpulence, her corporal care was done, her mimic was mobile, the contact with her was easy and fruitful and her basic psychic activities were preserved.

Her speech was normal in its course and its continuity, her thought was seat of a badly systematized fuzzy delirium of persecution and bewitchment with

intuitive and hallucinatory mechanism reported with weak affective load. She reported auditory hallucinations, her mood was neither sad nor euphoric, her affect was blunted, her judgment and insight were disturbed, her sleep was disturbed and her appetite diminished.

In total, she was a 27-year-old patient, with a history of psychiatric care for 9 years and a maternal aunt with psychiatric care, admitted for psychomotor agitation and aggression, and in whom the psychiatric interview revealed a delusional syndrome, a hallucinatory syndrome, impaired judgment and insight with disturbed sleep and decreased appetite.

The patient was put on olanzapine 20mg/day for 4 weeks without any clinical improvement. The patient was always aggressive, keeping auditory hallucinations and delusions of persecution and possession. She was then put on Haloperidol 9mg after which she developed neuroleptic malignant syndrome. After stabilization of her vitals, she was put on a progressive dose of Amisulpride, but at a dose of 600mg/day she had a second neuroleptic malignant syndrome.

A decision to initiate clozapine was made after her clinical stabilization. Oral clozapine was started at a dose of 25 mg/day. This was increased by 25 mg/day to a dosage of 400 mg/day.

At this dose of 400mg/day of clozapine, the patient experienced a generalized tonic-clonic seizure with loss of consciousness, urine output and post critical amnesia. An EEG was performed and the clozapine doses were decreased to 275mg/day. The patient did not have another seizure but a few days after her seizure she began to exhibit dysfluency characterized by random hesitations during speech and repetition of sounds. The patient had no personal or family history of stuttering.

Psychotic elements persisted, and the stuttering did not stop.

A slow increase in clozapine to 25mg/week was resumed with strict monitoring of the patient. Delirium and hallucinations persisted; a combination with Aripiprazole was initiated. Then at 300mg/d of clozapine with 15mg/d of Aripiprazole for 3 weeks, the patient reported a disappearance of the hallucinations and a remission of her delirium with a total disappearance of her stuttering.

DISCUSSION

The mechanism of clozapine-induced stuttering is not completely elucidated. It has been linked to extrapiramidal side effects including dopaminergic hypersensitivity states such as tardive dyskinesia and dystonia [11]. It is indicated that other neurotransmitter systems such as muscarinic and a-adrenergic receptors, which are affected by clozapine, can cause stuttering [12]. Lyall *et al.*, [14] reported that the risk of clozapine-induced stuttering was increased in patients who had stuttering in childhood and a family history of stuttering. A few other studies on clozapine-induced stuttering suggest an association between stuttering and seizure-like activity in the EEG and improvement with antiepileptic drugs [13]. In addition, some cases have reported that anticonvulsant drugs can reduce stuttering complaints [14].

Several case reports suggest an association between clozapine-induced stuttering and seizure activity. Rachamallu *et al.*, [6] report epileptiform discharges on the EEG recording of a 16-year-old man with clozapine-induced stuttering. Similarly, Duggal *et al.*, [8] reported abnormal EEG findings and generalized tonic-clonic seizures in a 28- year-old man on clozapine who developed stuttering. Begum [9] and Suprian *et al.*, [15] reported myoclonic jerks in patients with clozapine-induced stuttering. In all the above cases, the stuttering and seizures resolved with valproate administration.

Our patient had normal EEG findings and a single seizure that did not recur after clozapine dose reduction. Therefore, we did not propose an anticonvulsant.

Dose reduction for the treatment of clozapine-induced stuttering has been reported to have successfully controlled side effect without decompensation of psychotic symptoms [2, 3, 7].

Florence Jaguga [16] reported normal EEG findings in a 28-year-old man on clozapine who developed stuttering. Clozapine dose reduction was limited in improving psychotic symptoms as well as stuttering but the patient improved after administration of Aripiprazole [16].

Our case is important because it highlights that stuttering can develop after seizures on clozapine and that both stuttering and psychotic symptoms can improve by reducing clozapine doses and combining it with another antipsychotic "aripiprazole".

CONCLUSION

This case highlights the need for clinicians to be aware of clozapine-induced stuttering. Furthermore, it highlights the need for future research to investigate the pathophysiology of clozapine-induced stuttering and the exact course of action for effective management.

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