

*Case Report***Clozapine withdrawal in catatonia: a case report**Yashasree Poudwal¹, Bindoo Jadhav², Bharat Shah³¹Senior Resident²Professor³Professor, Head of Department

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ABSTRACT

Catatonia following clozapine withdrawal is a phenomenon with rare documentation in medical literature. We present a case of a 50-year-old female with a history of paranoid schizophrenia who presented with catatonic features on discontinuation of clozapine and subsequently showed rapid improvement on reinitiating the drug. It is imperative that clinicians be aware of this occurrence so that clozapine maybe restarted without delay.

Key words: Clozapine, catatonia, discontinuation.

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INTRODUCTION

Clozapine is an atypical antipsychotic with actions on Dopaminergic D2 receptors as well as serotonin HT2A receptors. It also has actions on muscarinic, histaminic and noradrenergic receptors. It is effective in treating both positive and negative symptoms of schizophrenia, suicidal ideation and is the drug of choice for treatment resistant schizophrenia. Since it has a multi-receptor profile a multitude of withdrawal symptoms are seen [1]. Abrupt withdrawal of clozapine is often known to precipitate psychosis and rebound cholinergic symptoms like nausea, diaphoresis, diarrhoea, and agitation [2]. Catatonia following clozapine withdrawal is a rare phenomenon and is only available as case reports in literature.

CASE REPORT

A 50-year-old female was brought to the emergency room with complaints of slowing of activities, decreased movements, not speaking, withdrawn behaviour, maintaining odd postures, urinary incontinence, staring spells and sleep disturbances since 5 days.

The patient had the first episode of altered behaviour in 1987 when she presented with delusions of reference and persecution, auditory hallucinations. She was diagnosed with paranoid schizophrenia and treated for the same. She was compliant on treatment, however, had multiple similar exacerbations in later years, which were triggered by interpersonal conflicts within the family. Her last exacerbation was 8 years back and since then she had been well maintained on 50mg of clozapine. 20 days prior to her visiting the emergency room, following a conflict in the family, she again started having complaints of suspiciousness and hearing of voices. Her doses were increased to 125mg of clozapine and 20mg of olanzapine. She complained of excessive drowsiness and discontinued her medication 10 days back without medical supervision.

On examination in the emergency room, she had psychomotor retardation, mutism, negativism and posturing, which were suggestive of catatonia.

She was advised admission and investigated for medical causes of catatonia since this was the first time she was presenting with catatonic symptoms. However, her blood investigations (including CPK levels), Electroencephalogram (EEG) and computed tomography (CT) of the brain were all within normal limits. She was initially started on lorazepam 8mg and risperidone 3mg but there was minimal improvement.

In the absence of any improvement, a diagnosis of clozapine withdrawal induced catatonia was considered. On the 8th day of her admission, clozapine was restarted at the dose of 25mg. By the next day, there was slight improvement in her symptoms. The dose of clozapine was gradually increased to 200mg over the next week and there was corresponding improvement in her symptoms with her achieving near normal levels of functioning over the next 10 days.

DISCUSSION

It is widely known that stopping an antipsychotic can have a variety of withdrawal symptoms. However pre-clinical data regarding prevalence and presentation of withdrawal is scarce. Up to 50% of patients on clozapine become non-compliant due to the side effects or the need for regular monitoring [3,4].

Abrupt withdrawal can lead to clinical relapse or withdrawal syndromes within 1-11 days. The onset of withdrawal symptoms with clozapine is 5 times greater than that of other antipsychotics partly due to the rapid displacement of clozapine from its receptors by endogenous neurotransmitters or other compound [5]. While rebound psychosis is well documented, even rare presentations have been seen like catatonia [6-10], delirium [11], serotonin syndrome [12] and movement disorders [8,13]. Following the discontinuation of medication, the presentation maybe unrelated to the original episode [3,9].

These varied presentations of a common etiology are likely due to vast pharmacological action of clozapine. Studies have shown that clozapine increases GABA mediated inhibitory transmission [11]. One of the postulated theories for catatonia is alteration in the reactivity of GABA receptors especially in the right orbito-frontal, motor and parietal cortices [14]. Sudden withdrawal of clozapine leads to GABA super sensitivity causing sudden decrease in receptor activity subsequently leading to catatonia [1,6-8]. Most patients who develop catatonia subsequent to clozapine withdrawal have been seen to be on treatment with clozapine for duration of over 3 years. The response to other modalities of treatment including high dose lorazepam and ECTs, is poor. However, symptoms resolve rapidly on reinitiating clozapine therapy [10].

The study of withdrawal phenomenon has clinical implications in the tapering of doses of clozapine. It is suggested that clozapine be gradually tapered preferably at 50mg/week after another antipsychotic is started at therapeutic doses. When immediate withdrawal is mandated, e.g. in case of severe side effects like agranulocytosis, it is recommended that the patient be admitted and cholinergics may be started for preventing cholinergic rebound phenomenon [12, 15].

CONCLUSION

Sudden and abrupt withdrawal of antipsychotic medication can lead to a wide range of symptoms including psychosis. It is important to remember that the presentation of psychosis following abrupt cessation of antipsychotics could be completely different from the original presentation. The diagnosis of clozapine withdrawal induced catatonia is a diagnosis of exclusion but should be kept in mind in such a clinical scenario.

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