

CASE REPORT

Clozapine-Induced Drop-Attack and Myoclonus

Romika Dhar¹, Tushar Singh² and B. S. Chavan³

^{1,2,3}Department of Psychiatry, Government Medical College & Hospital, Chandigarh 160047, India

Corresponding author: Dr. Tushar Singh, Senior Resident, Dept. of Psychiatry, Government Medical College & Hospital, Sector 32, Chandigarh; E-mail: psychiatrist999@yahoo.co.in

Abstract

Clozapine is the second-generation antipsychotic most frequently associated with seizures with risk varying from 1-5%. The seizure types are diverse, varying from generalized tonic-clonic subtype, partial, atonic or myoclonic jerks. Myoclonic and atonic subtypes are more likely to go unrecognized and have been shown to be a harbinger for further seizures of tonic-clonic variety. We report a case of clozapine-induced drop attack and myoclonus and its resolution by decreasing the dose and addition of sodium valproate (German J Psychiatry 2008;11: 29-31).

Keywords: clozapine, myoclonic, jerks

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Introduction

Since the re-approval of clozapine by the U.S.F.D.A in 1989, several review papers have addressed the prediction and treatment of clozapine-induced seizures. Recognition of clozapine-induced seizures remains a difficult task due to varied presentations like generalized tonic-clonic seizures and subtle types like atonic, myoclonic and partial seizures. Clinicians often misinterpret myoclonic jerks as nervousness or weakness (Gouzoulis et al, 1991; Haberfeller, 2002). The clinical picture can be further complicated due to associated tremors and other extra-pyramidal side effects of conventional anti-psychotics.

We report a case presenting with a typical drop-attack followed by myoclonic jerks of head, neck, upper and lower limbs in a patient of paranoid schizophrenia on clozapine therapy, 400mg per day.

Case report

A 26 year old male, high school pass, unmarried, unemployed, belonging to a Hindu nuclear family of middle socio-

economic status, presented to emergency unit of the Department of Psychiatry in Government Medical College and Hospital, Sector 32, Chandigarh, India with a one day history of sudden fall while standing with intact consciousness, followed by jerky movements of head, neck, upper and lower limbs. He was a diagnosed case of paranoid schizophrenia since 8 years having almost continuous and deteriorating type of course, without any significant improvement with conventional anti-psychotics. He was put on clozapine therapy which was started in March 2007 with the dose being gradually increased to 300 mg/ day on outpatient basis with regular, monthly follow-up. He again presented in November 2007, with an episode of relapse on this dosage, requiring admission in ward where his symptoms were controlled with clozapine increased to 400 mg and benzodiazepines. Patient was then discharged in satisfactory condition, at clozapine 400mg/ day. After 6 days of discharge, he again presented in emergency unit with the history of sudden fall few hours earlier, while standing with intact consciousness; patient remembered the fall and reported weakness in lower limbs prior to fall. The fall was followed by jerky movements of head, neck, upper and lower limbs. On examination, the patient was conscious, well oriented to time, place and person, having myoclonic jerks of neck, upper limbs and lower limbs occurring periodically after 1-2 minutes' gap. There was no history of head injury, prolonged

fever, urinary incontinence, uprolling of eye balls, tonic-clonic movements or altered sensorium.

A diagnosis of clozapine induced drop-attack and myoclonus was made. Patient was given injection lorazepam 4 mg intravenously and after an hour, the jerks disappeared. No psychotic symptoms were observed. All investigations including complete hemogram, renal and liver function tests, fasting blood sugar and serum electrolytes were conducted and found to be within normal limits. Contrast-enhanced Computed Tomography of Head (CECT head) was also normal. Clozapine was reduced to 200mg/day and Sodium valproate 500 mg was added. During ward stay of 4 days, no further drop attacks or myoclonic jerks were observed and the patient was discharged on the fifth day. An EEG could not be done immediately at the time of presentation of patient, due to financial restrictions. It was conducted 2 days after the discharge of patient. The findings were non-specific, exact wording of the report being “*Abnormal graph of post-ictal activity*” and did not provide any further insight into diagnostic clarification or management issues.

Discussion

Generalized tonic-clonic seizures are the most common type of clozapine-induced seizures (Pacia & Devinsky, 1994). The risk of seizures increases with higher dosages of clozapine; there is a 1% risk at dosages of less than 300 mg daily, 2.7% at 300 to 600 mg daily, and 4.4% at dosages of more than 600 mg daily (Devinsky et al, 1991). Seizures can, however, occur at dosages as low as 37.5 mg daily (Landry, 2001).

EEG abnormalities are frequent and “normal” during clozapine therapy. There is controversy as to whether the EEG is a good predictor of seizure activity. Some authors have suggested that EEG changes induced by clozapine should not be used as a harbinger of seizures (Fink, 2002; Risby et al, 1995).

Myoclonus occurs in approximately 2% of patients treated with clozapine (Lieberman & Safferman, 1992). In a series of 5 cases, these were primarily oro-facial and sometimes associated with weakness of extremities (Bak et al, 1995). These symptoms improved when clozapine was discontinued or dose reduced or anti-convulsant added. In our case, dose reduction prevented further episodes; stopping clozapine was not a feasible option as patient was treatment-resistant. Myoclonic and atonic seizures constitute about one-quarter of the reported cases, but these types of seizures may be underreported (Devinsky & Pacia, 1994). The development of myoclonic jerks is often a forerunner of tonic-clonic seizures (Meltzer & Ranjan, 1994; Gouzoulis et al, 1993). Atonic seizures represent another important potential precursor of a tonic-clonic seizure (Berman et al, 1992). Drop attacks can result from atonic seizures but may be difficult to recognize and these may be interpreted as myoclonic flexion of the knees instead of a loss of muscle tone (Antelo et al, 1994). Once a first seizure has occurred, the dosage of clozapine should be decreased and any other seizure-provoking factors (such as sleep deprivation) must be elimi-

nated (Haller & Binder, 1990). The dosage is usually reduced by about 40% to 50% to maintain the therapeutic effect of clozapine (Bak et al, 1995; Funderberg et al, 1994; Baker & Conley, 1991). If a second seizure occurs, then treatment with an anticonvulsant agent should be considered. The types of seizures that can be precipitated by the administration of clozapine are varied, including tonic-clonic, myoclonic, and atonic seizures; and, myoclonic seizures may presage tonic-clonic seizures. Because of the eclectic pathogenesis of these diverse seizures, a broad-spectrum anticonvulsant agent is preferable (Wong & Delva, 2007). Valproic acid and lamotrigine are thus first-line drugs for the treatment of clozapine-induced seizures. Plasma clozapine levels and EEG findings may be of limited practical value in predicting or diagnosing seizures. Therefore, careful observation and a high index of suspicion are crucial for the recognition of seizure activity. Special attention should be paid to those patients with a pre-existing history of seizures; such people are at a higher risk.

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