



## Role of pattern identification, electroencephalography and antiepileptic medication in a patient with schizophrenia on Clozapine - a case report

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**Abstract :** Schizophrenia and epilepsy co-occur at rates more than that by chance occurrence. Psychotic symptom by itself can be an ictal phenomenon. Seizure-potential of most antipsychotics further complicates the scenario. The clinical presentation, use of diagnostic tools and choice of antiepileptic medication pose challenge to the psychiatrist. We report a case where an individual presents with a typical pattern of auditory hallucination while taking Clozapine. We highlight the following - the importance of pattern identification in clinical diagnosis, judicious use of diagnostic test like electroencephalography and the choice of Sodium valproate as antiepileptic in Clozapine-treated individual.

**Keyword :** Clozapine, Seizure, Sodium valproate, EEG

### Introduction

Schizophrenia is associated with brain electrophysiological abnormalities at different stages of the illness (1). Antipsychotics, the mainstay therapeutic option in schizophrenia, too are associated with changes in electroencephalography (EEG) (2). Second generation antipsychotic, Clozapine, induces seizure in a dose dependent manner (3). Moreover, seizure by itself can manifest as episodic psychosis (4). These bring in close relation between schizophrenia, seizure disorder and medications namely antipsychotic and antiepileptic. We highlight this interrelation in a clinical setting and the challenges in such case management including the role, the choice and the safety of antiepileptic medication.

### Case report

Mr A, a 21-year old gentleman, got admitted in the Department of Psychiatry during the year 2011. He had no history of traumatic brain injury. His brother had history of schizophrenia. There was no past history or family history of seizure disorder. He was admitted for psychiatric management of his continuous psychotic illness. The illness started while he was fifteen years of age. The illness was characterised by positive psychotic symptoms – delusion of persecution (expressing false belief with conviction that his relatives are trying to harm him), 2nd person auditory hallucination (hearing non-existent voices in clear consciousness, of upto ten unknown people from close-by, communicating to him in second person) and, thought broadcasting (expressing that others were thinking in unison with him). He had negative symptoms like amotivation (lack of initiative in pursuing his academics) and asociality (progressive loss of skills in socialisation). These were confirmed in mental status examination (MSE) too. A review of his earlier management details was made. He had undergone

Magnetic Resonance Imaging (MRI) of brain in the year 2008. The MRI was normal. There was no previous EEG done. Treatment history revealed that he had failed a trial of Risperidone in the past. He has been on Clozapine for the last one year. He was taking Clozapine 400mg per day at the time of admission. A diagnosis of Paranoid schizophrenia of continuous course was made. The severity of his illness as assessed on Positive And Negative Syndrome Scale (PANSS) was – Positive score: 20, Negative score: 25, General psychopathology score: 34. His general physical examination and systemic examinations were normal. Parents reported that there was overall reduction in the positive psychotic symptoms after starting Clozapine. However a nique clinical situation was reported in relation to starting Clozapine. Prior to starting Clozapine, he was experiencing the auditory hallucinations daily and irrespective of time of the day. However, after starting Clozapine, he was experiencing auditory hallucinations in a stereotyped pattern. That is he still experiences auditory hallucinations daily; however the hallucinations starts only by evening hours and lasts for three hours. The other characteristics of the auditory hallucination remained the same as mentioned in the earlier paragraph. During this stereotyped hallucinatory experience, consciousness is preserved and his higher mental functions remain intact. There was no aura or involuntary movements including automatism. There were no hallucinations in any other sensory modality. The episodic periodicity in hallucinatory experience while on Clozapine raised the following differential diagnosis for the symptom. Does it represent residual psychosis (indicating partial clinical response to Clozapine) or Does it represent a seizure phenomenon. In the latter case it could be Clozapine-induced seizure.

In order to clarify, 2-4 hour telemetry during the time period of occurrence of such an episode was done. The electroencephalography (EEG) revealed paroxysmal bilateral and synchronous slow wave dysrhythmia. The electrophysiological abnormality being confirmed, it was decided to start him on antiepileptic medication. Sodium valproate was chosen. No further change in the dose of Clozapine was made. The dose of Sodium valproate was titrated upto 1500mg per day on which serum level of Valproate was 111mmol/L. He received in-patient care for two weeks after starting Sodium valproate. Serial MSEs during this period showed minimal improvement in his symptoms – he reported auditory hallucination less frequently (once in two days) and lasting for less duration of time (less than three hours). On discharge, the PANSS score was - Positive

score: 19 Negative score: 21 General psychopathology score: 25. A repeat EEG done after reaching adequate level of Sodium valproate revealed normal electrical activity. He was followed up over phone three months later. He then reported further improvement - auditory hallucination occurring once in three days and lasting for less than thirty minutes.

#### **Discussion**

The case report brings about three clinical discussions. First, the importance of looking for patterns in clinical presentation in making diagnosis. Second, the role and the choice of EEG in the management of schizophrenia. Third, the role and safety of Sodium valproate as antiepileptic medication in Clozapine-treated individuals. Epidemiological studies reveal co-occurrence of schizophrenia and epilepsy at rates higher than expected (5,6). There is high prevalence of epilepsy among those with schizophrenia (7). Population based studies conclude high prevalence and high risk of schizophrenia among those with epilepsy (8). For this, common genetic susceptibility and/or common aetiology (like Leucine-rich glioma inactivated gene [LGI] mutation) have been proposed (5). Moreover, psychotic symptoms can be manifestation of complex partial seizure of temporal lobe origin (9). However, the clinical distinction between schizophrenia-like psychosis in epilepsy and schizophrenic syndrome is difficult on the ground of phenomenology alone (5). The picture is made further complex by the fact that neuroleptics can induce seizure. These imply the need for high index of suspicion for seizure among people diagnosed with schizophrenia; the need to focus on clinical pattern than on phenomenology alone in diagnosing seizure phenomenon. In this case report, an adolescent age of onset of illness denotes greater chance of genetic loading/brain pathology, the change in clinical pattern of auditory hallucination to an episodic stereotyped pattern after starting Clozapine, temporal correlation of this new pattern to initiating Clozapine, all favoured high index of suspicion for underlying electrophysiologic abnormality. Focus on phenomenology alone could have resulted in further increase in dose of Clozapine with worsening of clinical condition.

(10) EEG telemetry involves prolonged monitoring over periods of time varying from hours to weeks while the patient is generally confined to a particular room. (11) This is particularly useful in situations where no seizure manifestations might be picked up for prolonged periods of time because seizures are occurring only occur paroxysmally. In suspected temporal lobe epilepsies, prolonged recordings offers greater yield (12). In this clinical case, evaluation using 2-4 hour telemetry during the time of the day when the hallucinations are mostly reported reflect the need to link clinical judgment with judicious use of appropriate diagnostic tool in case evaluation (13).

Clozapine can induce a spectrum of EEG changes and seizure (3). In people treated with Clozapine, the indications for starting antiepileptic might include Clozapine plasma level exceeding 500µg/L, EEG showing clear epileptiform discharges, if seizures, myoclonic jerks or speech difficulties occur and when there is concurrent use of epileptogenic medication (14). In this case report, Sodium valproate was well tolerated without any specific adverse drug reaction. Normalisation of EEG after achieving adequate serum level of Sodium valproate indicates its effectiveness in individual case. Thus the case report adds to the existing literature that Sodium valproate is a safer and effective option in Clozapine-treated individuals (14,15).

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