Case Report

Oculogyric Crisis with Clozapine: A Case Report and Review of Similar Case Reports in the Literature

Naresh Nebhinani, Ajit Avasthi[1], Manish Modi[2]

ABSTRACT

Oculogyric crisis (OGC) is a dystonic reaction and commonly caused by typical antipsychotics and rarely occurs with clozapine. Here, we are presenting a case of OGC with clozapine therapy and reviewing the similar cases reported in the literature.

Key words: *Clozapine, dystonia, oculogyric crisis*

INTRODUCTION

Clozapine is an atypical antipsychotic and generally considered to have low risk of causing tardive syndromes and considered as an effective treatment in patients with tardive syndrome.[1] Oculogyric crisis (OGC) is one of the specific dystonic reactions, rarely reported with clozapine treatment[2-6] as well as on clozapine discontinuation.[7] We hereby present a case of OGC with clozapine therapy and review of literature.

CASE REPORT

A 25-year-old male student of masters in arts, presented to our psychiatric outpatient clinic on June 10, 2006, with 7 years history of continuous illness, characterized by academic decline, reduced social interaction and functioning, irritability, quarrelsome behavior, delusion of persecution, and reference. Above symptoms were evolved over a period of 1 year. Mental status examination confirmed these findings and diagnosis of paranoid schizophrenia was made as per International Classification of Diseases-10. At the age of 3 years, he had generalized tonic-clonic seizure, for which phenobarbitone was given for 3 years and thereafter, he remained seizure free without any antiepileptic medication. There was family history of depressive disorders in father and mother.

Earlier he had been given adequate trials of risperidone (6-12 mg/day), chlorpromazine (800 mg/day), and quetiapine (800 mg/day) for 3-6 months sequentially, but not responded. At our center he was labeled with treatment resistant schizophrenia in June, 2006 and thereafter clozapine option was discussed with patient and family. After hematological and biochemical tests, clozapine was started at 25 mg daily dose and gradually hiked to 300 mg as there was no response at 150-200 mg dose. He improved significantly on clozapine 300 mg dose, but had an episode of generalized tonic-clonic seizure in October, 2006. On investigations, biochemical parameters were normal, electroencephalogram had revealed mild bihemispherical dysrhythmia, and computerized tomography head was normal. Diagnostic possibility of clozapine induced seizure

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Department of Psychiatry, All India Institute of Medical Science, Jodhpur, Rajasthan, [1]Departments of Psychiatry and [2]Neurology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Address for correspondence: Dr. Naresh Nebhinani
Department of Psychiatry, All India Institute of Medical Science, Jodhpur - 342 005, Rajasthan, India. E-mail: drnaresh_pgi@yahoo.com

was made; option of dose reduction of clozapine was discussed with the patient and family but not considered due to remarkable improvement with 300 mg. He was started on sodium divalproate 750 mg/day, on which he remained seizure free and maintained reasonably well.

After a year, in mid of 2007, he started experiencing episodes of OGC on the same dosages. During the episode, he started reporting reduced mobility and fixation of eye balls at horizontal plane for short period of time, followed by up rolling of eye balls and upward fixation for 10-30 min. He was unable to see front objects properly and hence he started frequently bending his head downward. He also felt restlessness, reduced attention span, and inability to move eyeballs down during the episode. It was recurring 4-5 times/day in similar fashion irrespective of any situation, time, stress, diet, climate, or activities. He remained significantly distressed with these symptoms as he had experienced few of episodes while walking on the road. Possibility of clozapine-related OGC was kept, management options were discussed with family. Patient's family and treating team were concerned about his significant improvement with clozapine, so conservative management was considered. During 2009, sequentially trials of trihexyphenidyl 6 mg and promethazine 50 mg were given, but with no improvement. Thereafter, clozapine dose reduction was considered after discussing its pros and cons with family. On gradual reduction of clozapine dose from 300 mg to 150 mg, he perceived significant improvement in OGC frequency (from 4-5/day to 4-5/month) in late 2010. At this level, he started having mood swings, and irritability, but he was manageable. Option of further dose reduction of clozapine and combining with quetiapine was considered. In mid-2011, on gradual reduction to clozapine 100 mg and building up to quetiapine 400 mg/day, he started having further disturbances in form of mood swings, suicidal ideas, low, and irritable mood. His symptoms and disturbances continued despite addition of clonazepam 0.5 mg bid and hiking the dose of quetiapine to 300 mg bid. On which his parents got apprehensive and anticipated more disturbance like prior to clozapine therapy and asked to increase clozapine to manage this exacerbation. They were explained about the risk of worsening in OGC frequency and related disturbances. In August, 2011, clozapine was increased gradually to 150 mg/day and quetiapine was reduced to 400 mg, but in view of continuing symptoms clozapine was further increased to 200 mg and quetiapine was gradually tapered and stopped. Frequency of OGC increased to 4-5 times/week, but patient was manageable and gradually resumed his functioning. He remained compliant on clozapine 200 mg and following up regularly at our outpatient center.

DISCUSSION

The term "oculogyric" refers to rotation of eyeballs. OGC is one of the dystonic reactions characterized by initial restlessness, agitation, malaise or a fixed stare followed by prolonged involuntary upward deviation of the eyes and sometime eyes may also deviate laterally or downward. Backward and lateral flexion of the neck, wide open mouth, tongue protrusion and ocular pain are other commonly reported symptoms.[8] Evidence of beneficial effects of clozapine is greater than its role in causation or worsening of tardive syndromes including dystonia.[1]

In our electronic search for "OGC" by using PubMed and Google Scholar, we could find 7 cases reported with clozapine treatment[2-6] and one on clozapine discontinuation[7] depicted in Table 1. Similar to Uzun

Table 1: Review of cases with clozapine related OGC reported in the literature

Author	Demographics	Diagnosis	Presentation	Treatment and outcome
OGC on clozapine therapy				
Uzun and Doruk, 2007	38 years female 19 years female 45 years female	Schizophrenia	Experienced multiple episodes of OGC on clozapine (dose unknown). Onset 6 months to 2 years after starting clozapine	Follow-up details were not mentioned
Chakraborty and Chatterjee, 2007	37 years male	Schizophrenia	Experienced episode of OGC on clozapine (150 mg/day) at 9th day of treatment	Treated successfully with stat IM promethazine (50 mg). Recurrence on discontinuing trihexyphenidyl (4 mg/day)
Hoseini Sheikh Moonesi, 2007	27 years female	Schizophrenia	Experienced multiple episodes of OGC on clozapine (dose unknown)	Treated successfully with anticholinergic medication (Artane)
Salehifar and Hosseini, 2007	42 years female	Schizophrenia	Experienced two episodes of OGC on clozapine (150 mg/day)	Treated successfully with biperiden
Dave, 1994	Male	Schizophrenia	Experienced multiple episodes of OGC on clozapine (dose unknown), and earlier also experienced with perphenazine	Treated successfully with anticholinergic agents
OGC on clozapine discontinuation				
Mendhekar and Duggal, 2006	18 years female	Mental retardation	OGC after 2 days of clozapine discontinuation (given 300 mg for 6 weeks)	Treated successfully with reinstatement of clozapine

OGC – Oculogyric crisis

and Doruk,[4] our patient had experienced tardive OGC 1 year after starting clozapine at 300 mg dose, while other cases have reported acute OGC at 1st month of clozapine therapy at 150 mg dose.[2,6]

At onset of OGC our patient was receiving daily dosages of tablet clozapine 300 mg, and sodium divalproate 750 mg for nearly 1 year. OGC continued with the same frequency despite addition of trihexyphenidyl 6 mg and promethazine 50 mg, while earlier reports[2,5,6] mentioned significant response with anticholinergic agents such as promithazine, biperiden, etc. Index patient had significant improvement in OGC frequency (from 4-5/day to 4-5/month) on reducing clozapine dose from 300 mg to 150 mg, but had exacerbation in primary illness.

As reported a risk factor for tardive dystonia,[4] index patient was a young male. Despite rarity of such presentation, after thorough evaluation clinicians should consider possibility of dystonic reaction with clozapine therapy and clozapine related OGC should be treated in stepwise approach-first addition of anticholinergic agents, if needed then clozapine dose reduction, or switching to other antipsychotics.

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