Case Report

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Olanzapine-induced oculogyric crisis in a patient with mania without psychotic symptoms: a case report

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Introduction and importance: Oculogyric crisis (OGC), marked by upward eye deviation, is rare and linked to diverse causes, including drugs and neurological conditions. This study details a 16-year-old male's OGC onset after olanzapine treatment for an initial mania episode, highlighting the need to recognize this potential side effect.

Case presentation: A 16-year-old male with nonpsychotic mania was treated with olanzapine and sodium valproate. On day 30, he developed OCG due to olanzapine, managed with medication. After discharge, similar ocular symptoms emerged. Gradual olanzapine tapering alongside anticholinergic administration led to symptom relief. The Young Mania Rating Scale score decreased; psychoeducation was provided to the patient and family.

Discussion: This study presents an exceptional case of olanzapine-induced OGC, a rare dystonic eye movement reaction. The patient's presentation matched OGC criteria, confirmed by a high Adverse Drug Reaction Probability Scale score. Unusually, symptoms appeared 30 days postolanzapine initiation. A thorough assessment ruled out alternative causes. Mechanisms, possibly related to dopamine-choline balance and receptor sensitivity, remain uncertain. Despite atypical antipsychotics' lower risk, olanzapine's moderate D2 receptor binding led to this unusual response. Management involved dose reduction and anticholinergic therapy.

Conclusion: This case report highlights the rare occurrence of olanzapine-induced OCG in a patient with nonpsychotic mania. Effective management requires proper history taking, examination, regular follow-up, monitoring, and appropriate medication use. The case demonstrates the need for caution when increasing olanzapine dose in manic patients with untreated mental illness and a history of neurological symptoms.

Keywords: case report, dopamine antagonist, mania, oculogyric crisis, olanzapine

Introduction

Oculogyric crisis (OGC) is a rare neurological condition characterized by dystonic upward eye deviation that can last from a few seconds to hours. It can be caused by various factors, including drug-induced, neurometabolic, neurodegenerative movement disorders, and focal brain lesions[1]. Atypical antipsychotics such as ziprasidone and risperidone have been reported to cause OGC in patients with schizophrenia and advanced

HIGHLIGHTS

- Oculogyric crisis (OGC) is a rare neurological condition characterized by involuntary upward deviation of the eyes due to dystonic movements in the extraocular muscles and can occur as an adverse effect of antipsychotic medications such as olanzapine.
- The occurrence of acute dystonia, including OGC, is rare and can occur within a week of starting or increasing antipsychotic medication, or reducing anticholinergic medication used to treat them.
- Olanzapine is an atypical antipsychotic that is commonly used to treat acute manic episodes and reducing the risk of relapse in patients with bipolar disorder, but it can cause acute dystonia, including OGC.
- A comprehensive evaluation is necessary to rule out other potential pathologies that may cause similar symptoms to OGC, such as functional neurological movement disorder, ocular tics, ocular dyskinesia, ocular bobbing, epilepsy, and various genetic and neurometabolic disorders.
- The exact mechanism behind the development of OGC is unknown; however, a hypodopaminergic state contributed by a number of factors, altered ratio of cholinergic to dopaminergic stimulation, and increased sensitivity of postsynaptic dopamine receptors due to blockade of postsynaptic dopamine receptors have been suggested as potential causes.

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Parkinson's disease, respectively[2,3]. However, cases of OGC associated with olanzapine, an atypical antipsychotic, are less commonly reported. Olanzapine is also less likely to cause extrapyramidal side effects and acute dystonia, with OGC being an even rarer form of dystonic movements[4]. Although OGC is not a life-threatening condition, it can cause extreme distress to patients and may even be mistaken for worsening psychosis in psychiatric patients. Therefore, immediate diagnosis and medical intervention are necessary[5]. Herein, we present a case of a 16-year-old male patient with no prior physical co-morbidities, treated for a first episode of mania without psychotic symptoms, who later developed an OGC after being treated with olanzapine. The work has been reported in line with the Surgical CAse REport (SCARE) 2020 criteria[6] (Supplemental Digital Content 1, http://links.lww.com/MS9/A233).

Case presentation

A 16-year-old male patient presented to a psychiatric outpatient with features of increased talk and irritability for 4–5 days. There was a decreased need for sleep as the patient would appear fresh and energetic with increased activities during the daytime. He had become more demanding and would get irritable if his demands were not fulfilled, which was not observed before. His mental status examination revealed increased tone and volume of speech, irritable affect, increased production of thoughts, increased confidence and energy, and a flight of ideas. The patient was diagnosed with mania without psychotic symptoms and had a Young Mania Rating Scale (YMRS) score of 38/60. As he was difficult to control at home, he was admitted. During admission, his vitals were stable. His body weight was 48 kg.

His systemic and neurological examination did not show any abnormalities.

Further history-taking revealed a presumable stressor to be the pressure of studies. The patient's mother had a history of mental illness suggestive of bipolar illness and was receiving Tablet Lithium 600 mg and Tablet olanzapine 10 mg. The patient had no history of substance/medication use. The patient had a history suggestive of features of apprehension, vacant staring, and startle response after witnessing a road traffic accident one year ago, but he did not receive treatment for these symptoms, and he got better on his own. After admission, he was started on Tablet olanzapine 10 mg, which was optimized to 30 mg on the 8th day of admission and continued. Tablet sodium valproate was started from 600 mg (6th day of admission) and was optimized to 1000 mg (16th day of admission). Tablet lorazepam 5 mg was started and gradually tapered off. Injection haloperidol 10 mg and promethazine 50 mg were administered on a twice daily basis as he was difficult to control initially. Parenteral medication was stopped after improvement was noted after the 10th day of admission.

On the 30th day of admission, the patient developed an OGC, as shown in the video illustration provided (Supplemental Digital Content 2, http://links.lww.com/MS9/A234). The patient had a bilateral conjugate upward deviation of the eyes with an inability to look straight, lasting for a few seconds with periorbital twitches, and protracted staring episodes with preserved consciousness (provided in the video illustration, Supplemental Digital Content 2, http://links.lww.com/MS9/A234). Episodes typically lasted for minutes and occurred in conjunction with other dystonic symptoms (shaking of the hands as demonstrated at the end of the video, Supplemental Digital Content 2, http://links.lww.com/MS9/A234). The symptoms were preceded by anxiety and discomfort. The patient denied any other symptoms, including fever, nausea, or vomiting. No other neurological deficits were noted. Vital signs were within normal limits. Laboratory tests, including a complete blood count and electrolytes, were unremarkable. The MRI and electroencephalogram of the patient showed normal findings and after consulting with the neurologist the diagnosis of acute dystonia in the form of OGC was made ruling out other possible pathologies in the disease process.

Considering the high dose of olanzapine, it was tapered to 20 mg and trihexyphenidyl was added. There was rapid improvement in his dystonic symptoms and he was asymptomatic at the time of discharge. He was discharged on the 48th day of admission on a medication regimen including olanzapine, sodium valproate, propranolol, trihexyphenidyl, and lorazepam for a short period. At the time of discharge, the patient experienced a weight gain of 4 kg but showed significant improvement in manic symptoms. His YMRSS was 9/60. The patient's mental status examination showed normal to increased psychomotor activity, euthymic affect, and normal production of thoughts. The patient was advised to maintain good hydration and follow-up visits, including blood tests for liver function and blood count, every 6 months.

After 2 weeks of discharge, the patient again presented with similar abnormal ocular movements, which was distressful to him. The dose of olanzapine was decreased to 10 mg in the morning, and the patient was also continued with trihexyphenidyl 2 mg twice daily in the morning followed by 1 mg in the afternoon, along with Tablet sodium valproate 500 mg twice daily. His OGC was resolved. However, in subsequent follow-up, he reported of significant weight gain, so olanzapine was gradually tapered down along with trihexyphenidyl, which was later discontinued. There was no recurrence of dystonic symptoms. Adequate psychoeducation was provided to the patient and their family members, and he is maintaining well on Valproate 1000 mg.

Discussion

This case highlights the rare occurrence of olanzapine-induced dystonic movement, OGC in an adolescent male patient with mania who was treated with olanzapine where the dose was increased within a short time frame.

Acute dystonia as observed in our patient, are rare involuntary muscle contractions that include torticollis, OGC, and opisthotonus. OGC is a relatively rare symptom of acute dystonia[7]. It was first observed in patients with postencephalitic parkinsonism during the encephalitis lethargica epidemic in the early 20th century. It is characterized by an involuntary upward deviation of the eyes due to dystonic movements in the extraocular muscles. OGC can have an acute or chronic onset and last for a few seconds to hours, triggered by various factors[1,5]. OGC can also cause lateral and downward eye deviations, pain, twitches, and staring. Other symptoms include increased blinking, neck dystonia, autonomic symptoms, and anxiety or hallucinations. A video illustration has been provided for a clear understanding of the symptoms[8] (Supplemental Digital Content 2, http://links.

lww.com/MS9/A234). The clinical features of the above-mentioned case were under the diagnostic criteria for OGC, as suggested by the previous literature, induced by olanzapine[9]. The adverse drug reaction (ADR) probability scale was scored at 9 indicating a definite relationship between the acute dystonic reactions in the form of OGC and olanzapine. The ADR probability scale, comprising 10 specific questions, was employed to assess the likelihood that the adverse event was indeed linked to the medication. In this case, the score of 9 out of 10 on the ADR probability scale suggested a strong association between olanzapine and the OGC. The high score indicated that: there were no conclusive reports of this reaction previously, the adverse event occurred after drug administration, the reaction improved upon discontinuation of the drug, the reaction reappeared upon drug readministration, no other plausible causes for the reaction were identified, the reaction did not reappear with placebo, the drug was detected in potentially toxic concentrations (not assessed in our case), the reaction was dose-dependent, there was no prior history of similar reactions, and the adverse event was confirmed by other objective evidence[10].

Acute dystonia, including OGC, can occur within a week of starting or increasing antipsychotic medication, or reducing anticholinergic medication used to treat them. Typical antipsychotics, particularly Haloperidol, have a faster onset of antimanic action commonly used in the treatment of behavioral disturbances despite having a greater potential to cause acute dystonia as compared to atypical antipsychotics[4]. Unlike in literature, where dystonia is reported to occur within a week after starting antipsychotic; however, in our patient, it developed after 30 days of receiving olanzapine, even though Haloperidol was discontinued on day 10. Symptoms subsided after tapering olanzapine. Recurrence of OGC in subsequent follow-up, which improved after decreasing the dose of olanzapine, indicates olanzapine's potential to cause acute dystonia in the form of OGC, not haloperidol.

A comprehensive evaluation is necessary to rule out other potential pathologies that may cause similar symptoms to OGC. These may include functional neurological movement disorders, ocular tics, ocular dyskinesia, ocular bobbing, epilepsy, and various genetic and neurometabolic disorders[11]. A detailed patient history and thorough examination are critical for accurate diagnosis for which relevant laboratory investigations, an MRI, and an electroencephalogram were performed in the above case, which were unremarkable.

The exact mechanism is unknown; however, the hypodopaminergic state is contributed by several factors like drug-induced, neurodegenerative disorders, and focal brain lesions are some of the suggested pathophysiology behind the development of OGC[8]. Moreover, the altered ratio of cholinergic to dopaminergic stimulation (excess of acetylcholine) supported by the successful outcome after treating OGC with anticholinergics like trihexyphenidyl is another hypothesis behind the development of OGC[12]. Literature suggests that blockade of postsynaptic dopamine receptors causes increased sensitivity of postsynaptic receptors (seen in a patient with a mania, which is a spectrum of bipolar disorder) or compensatory release of dopamine, which alters the acetylcholine to dopamine ratio leading to motor disorders which partially explains the reason for OGC with atypical antipsychotics which are loosely bound to D2 receptors, particularly olanzapine as in our case[13].

A major fraction of the cases reported with OGC has been contributed by the use of neuroleptic drugs, which involves the disruption of dopamine pathways and comprise the major portion of the drug-induced OGC[1,3,13]. Atypical antipsychotics like olanzapine are less commonly reported to cause OGC as compared to typical antipsychotics like haloperidol, perphenazine which is in contradiction to our case[14]. Erden Ferahkaya[15] suggests that while atypical antipsychotics are indeed safer than typical antipsychotics in relation to extrapyramidal adverse effects, they are potential to cause dystonic features like OGC.

The high binding affinity of atypical antipsychotics to Serotonin 5HT2 receptors and lower affinity to Dopamine (D2) receptors suggests a lower incidence of EPS and dystonic reactions with these drugs. Typical antipsychotics bind tightly to D2 receptors, leading to a hypodopaminergic state and parkinsonism. Atypical antipsychotics are more loosely bound to D2 receptors, resulting in rapid elimination and a lower incidence of parkinsonism. Despite the lower propensity for dystonia and EPS, olanzapine is moderately and loosely bound to D2 receptors, and dose-dependent parkinsonism may occur, which could explain the development of the OGC in our case[16]. Young age (<45 years), male sex, liver failure, recent substance abuse (particularly cocaine), higher doses and potency of neuroleptics, and personal or family history of dystonic reactions are some of the risk factors for developing dystonia like OGC[5]. Our patient has a few of the risk factors mentioned above, such as young age and being male.

Management of drug-induced OGC typically involves tapering down the causative drug. If symptoms persist, discontinuation of the drug is recommended, and switching to other agents with a lower risk of causing dystonic reactions is advised. Centrally acting anticholinergic or antihistaminergic agents are used for treatment, duration depends on symptom severity[5]. In our case, a gradual dose reduction of olanzapine and anticholinergic treatment with close monitoring improved OGC symptoms and the patient's illness.

There have been fewer case reports on olanzapine-induced OGC in patients with bipolar disorders/mania. Rosenhagen *et al*.[17] described a rapid onset of OGC in a 22-year-old woman with a low dose of olanzapine who had been treated for general anxiety disorder with lithium and paroxetine for several years. Her symptoms subsided after being treated with IV administration of biperiden 5 mg. Similarly, Editor[18] described an incidence of OGC in a young female patient with schizophrenia treated with olanzapine. Administration of trihexyphenidyl 2 mg per day failed to stop recurrences of the OGC, which ultimately required the replacement of olanzapine with risperidone.

This case highlights the importance of monitoring patients prescribed antipsychotic medications, even olanzapine, which has a low propensity to cause extrapyramidal side effects. It emphasizes the need for a detailed medical history to identify any potential risk factors followed by a proper physical and neurological examination along with relevant investigations to rule out differential diagnoses. The patient was concerned about the reoccurrence of the condition. Future research could investigate the prevalence and risk factors of OGC, explore underlying mechanisms, and identify preventive strategies.

Conclusion

This case report highlights the rare occurrence of olanzapine-induced OGC in a patient with mania without psychotic

symptoms. The report emphasizes the importance of monitoring patients on olanzapine, especially young, male patients with mania, for the development of OGC and the need for decrement or discontinuation of causative drugs along with the addition of anticholinergics during acute attacks. Subsequent dose adjustments (olanzapine tapering, trihexyphenidyl discontinuation), psychoeducation, and regular follow-up led to sustained dystonic symptom relief and clinical improvement. Effective management of OGC requires proper history taking and examination, regular follow-up, monitoring, and the use of appropriate medications.

Ethical approval

The study is exempt/waived from ethical approval in our institution as it poses minimal risk to the patient and the study is for educational purpose/activities.

Consent

Written informed consent was obtained from the patient's parents/legal guardian for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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T.N.Y., A.B., S.L., P.B.C., S.L., and R.K.: literature review, follow-up the patient, writing the manuscript, and final approval of the manuscript.

Conflicts of interest disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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