Case report

Ziprasidone-related oculogyric crisis in an adult

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ABSTRACT

Introduction: Drug-induced dyskinesias are common side-effects of first-generation antipsychotics (FGAs) but are not usually related to second-generation antipsychotics (SGAs). Oculogyric crisis (OGC) is a disabling acute dystonia that affects extra-ocular muscles usually resulting in an upward deviation of the eyes, which lasts from minutes to hours.

Case report: We describe an adult patient, previously exposed to an FGA, who developed OGC on 80 mg/day of ziprasidone. The movement disorder significantly improved after use of 1 mg/day of clonazepam without the need to switch to another SGA.

Discussion: The clinical features of the movement disorder of our patient meet the criteria for OGC. It is, sometimes, difficult to directly correlate a drug-induced dyskinesia to a SGA due to previous exposures to FGAs. The onset of OGC after exposure to ziprasidone without simultaneous use of other antipsychotic suggests a casual relationship between the former and the movement disorder. It is possible that previous use of an FGA was a risk factor for the development of OGC.

Conclusion: To the best of our knowledge, this is the first report of ziprasidone-related OGC in an adult patient. Physicians must be aware of its occurrence in order to improve care of patients treated with these agents.

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1. Introduction

Drug-induced dyskinesias are common motor disorders often related to exposure to first-generation antipsychotics (FGAs) occurring in any moment of their use. They can be classified as acute dystonias and tardive dyskinesias [1,2]. Ziprasidone is a benzisothiazolyl compound with a high 5HT_{2A}/D₂ receptor-affinity ratio of antagonism, 5HT_{2C} antagonism, 5HT_{1A} partial agonism and serotonin and noradrenaline reuptake inhibitor [1]. As a second-generation antipsychotic (SGA), it has a relatively low risk of motor side-effects [1,2]. Oculogyric crisis (OGC) is an acute dystonia, which affects the extra-ocular muscles and usually results in upward deviation of the eyes [2,3]. It is a common acute side-effect with reports of frequency of 10–60% among patients exposed to antipsychotic agents [4,5]. Younger age, male gender and first few days of treatment are considered risk factors of its occurrence [1,2]. While there are two reports of OGC related to ziprasidone in teenagers [6,7], to the best of our knowledge

this is the first published case of OGC related to ziprasidone in an adult.

2. Case report

A 28-year-old female was brought to our psychiatric out-patient unit to continue her treatment previously started elsewhere. She was diagnosed with schizophrenia at the age of 15 due to persistent mystic delusions, auditory hallucinations and psychomotor agitation. There was no family history of neurological or psychiatric disease. Since that time she was treated with haloperidol with poor compliance. However, at the age of 24 she developed upward deviation of the eyes and blefarospasm for 2 h. She denied loss of consciousness, visual hallucinations, torticollis or opisthotonus. The frequency of the episodes was 2 or 3 per week, which were considered as related to the neuroleptic. As she did not obtain clinical control with anti-cholinergic agents, haloperidol was changed to ziprasidone (80 mg/day). During the first 7 months of treatment, the patient did not develop OGC. Later, however, there was the recurrence of this movement disorder with the frequency of up to 3 episodes a month. Work up included an EEG which failed to show epileptic discharges. As she did not improve previously with

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biperiden, we started clonazepam 1 mg/day. She remained free of OGC for 8 months, but 3 days after withdrawal of clonazepam the movement disorder recurred.

3. Discussion

Acute drug-induced dyskinesias are generally related to introduction of an antipsychotic or after an increase of its dosage. The first signs occur within 48 h to 5 days [1–3]. The core clinical feature of OGC is involuntary, sustained, conjugated deviation of the eyes. Accessory features include malaise, pain, restlessness, agitation, other behavioral disturbances and autonomic dysfunction [4,8]. It can be accompanied by transient psychotic episodes with visual and auditory hallucinations, ironically induced by high-potency neuroleptics even in non-psychotic patients [8]. This phenomena may lead to an increase, rather than reduction, of medication dosage with subsequent worsening of the condition [8]. Because it often has a long duration (from minutes to hours), OGC may impair the activities of daily living, resulting in severe distress to patients. In addition, it is a meaningful risk factor for treatment discontinuation and, in rare occasions, it may be life-threatening when occurring while driving [1].

Two midbrain pathways seem to play a role in OGC generation. The first one arises from the substantia nigra pars reticulata and ends at the superior colliculi [9]. The second one is the projection from the substantia nigra pars compacta, pars reticulata and the ventral tegmental area to the reticular formation neighboring of the oculomotor nuclei [9]. Lesion of the first pathway is related to paralysis of upward gaze and of the other one to abnormal eye movements [9].

Basal ganglia also seems to be involved since OGC has been reported in Wilson's disease and in patients with focal lesions in basal ganglia and thalamus [10]. Moreover, Sydenham's Chorea with OGC and motor or vocal tics has also been reported [11] as well as in Tourette's disorder and postencephalitic parkinsonism syndrome [12]. Inherited errors of metabolism, such as hyperphenylalaninemia and aromatic amino acid decarboxylase deficiency, can present with OGC although patients usually exhibits other symptoms during neonatal period and childhood [12]. It is important to rule out abnormal eye movement due to seizures, especially in absence epilepsy that may present with associated upward tonic followed by clonic rhythmic upward jerks of the eyes [13].

Tardive dyskinesias related to discontinuation of antipsychotics are generally classified as withdrawal dyskinesia that disappears within 3 months of drug withdrawal or covert dyskinesia, which becomes apparent upon its reduction and persists for longer periods [2]. So far, the sole unquestionable risk factor for tardive dyskinesia is older age [14]. Poor compliance to treatment must be assessed since each time the patient stops and then recommence treatment may lead to acute drug-induced dystonia. There are two reports of tardive OGC related to FGAs [15,16]. In these cases, however, the phenomenology is different from the usual acute form of OGC: it lacks pain, the movement disorder often occurs with other phenomena typical of tardive dyskinesia and it worsens with withdrawal of the neuroleptic. There is also the possibility of acute OGC becoming chronically recurrent [16].

The previous reports of ziprasidone-related OGC describe adolescent patients with onset of movement disorders shortly after introduction of neuroleptic [6,7]. Our patient developed OGC during a previous exposure to haloperidol, but after its discontinuation had a symptom free period of more than 6 months. Obviously the recurrence was unrelated to haloperidol. The remission of OGC with simultaneous use of benzodiazepine and ziprasidone rules out TD. A clear response to benzodiazepine is not expected in TD [17], while

there are reports of improvement with these agents in acute drug-induced OGC [8,18,19]. Once TD develops, it is usually persistent with a remission rate of not more than 7.5–14% in 8.5-year-follow up studies [20,21]. Tardive dystonia is known to be responsive to anti-cholinergic agents and to be more persistent after neuroleptic suspension than TD [2,22], which where neither the case of our patient.

There is an increasing number of reports of drug-induced dyskinesias related to SGAs [23–31]. However, it is difficult to estimate the real prevalence and the direct correlation to an SGA induction, due to previous exposures to FGAs [10], as well as the limited evidence based on case reports.

4. Conclusion

To the best of our knowledge, this is the first report of ziprasidone-related OGC in an adult patient. Even though SGAs are good therapeutic options considering the lower incidence of acute side-effects and malignant neuroleptic syndrome, further studies of patients in long-term exposure only to specific SGAs are still necessary. Physicians should be aware of possible occurrence of drug-induced dyskinesias in association with these agents. Recognizing the characteristics of these side-effects such as onset and duration is important to select the best therapeutic strategy. Acute persistent movement disorders have obvious implications to adherence and response to treatment.

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