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LETTER TO THE EDITOR

# A case of aripiprazole-associated oculogyric crisis

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Dear Editor,

Aripiprazole, a third-generation atypical antipsychotic, functions as a partial agonist at D2 and 5-HT1A receptors, and as an antagonist at 5-HT2A receptors. It is generally associated with a lower risk of extrapyramidal symptoms (EPS). However, several case reports have documented that aripiprazole can, albeit rarely, cause dystonic reactions such as oculogyric crisis (OGC), characterized by a sustained, involuntary upward deviation of the eyes (1–3). Oculogyric crisis can occur shortly after the initiation or dose escalation of aripiprazole (4). For instance, Bhachech (1) and Hadler et al. (2) reported cases of OGC following dose increases of aripiprazole, successfully managed with anticholinergic treatment. Canol et al. (5) also described a case of tardive OGC with long-term aripiprazole, highlighting the need for caution even with prolonged treatment. These cases underscore the importance of considering the risk of OGC, particularly in young patients, those with a history of dystonia, or those undergoing rapid dose escalation (6, 7). This report details an OGC case in a young adult following aripiprazole initiation, emphasizing the need for vigilance for this rare but significant side effect.

A 22-year-old woman with moderate intellectual developmental disorder (IDD) presented to our clinic with complaints of sudden, involuntary upward rolling of her eyes, occurring two to three times daily and lasting 15–20 minutes, primarily in the evening. She reported that during these episodes, it was difficult to return her eyes to their original position, but the episodes would eventually resolve spontaneously. These symptoms began after one month of treatment with aripiprazole at a dosage of 15 mg/day, which was prescribed following a brief psychotic episode characterized by persistent visual and auditory hallucinations that had not improved with an initial dose of 5 mg/day. The patient was not on any other medications, and her psychiatric evaluation revealed that she was conscious, oriented, and free of delusions or hallucinations at the time of presentation. However, mild involuntary tremors were noted, without signs of rigidity, bradykinesia, or other extrapyramidal symptoms. Laboratory tests, including complete blood count, liver and kidney function tests, and urine drug screens, were all within normal limits, as were neurological examinations, brain magnetic resonance imaging (MRI), and electroencephalography (EEG). There was no history of substance abuse or familial psychiatric disorders. Given the significant improvement in psychiatric symptoms and the development of oculogyric symptoms, which greatly concerned the patient and her family, a decision was made to discontinue aripiprazole in accordance with their strong preference to avoid further medication. Following the discontinuation of aripiprazole, the ocular symptoms resolved within a week, with no recurrence of psychiatric symptoms or extrapyramidal side effects during follow-up. The patient's Positive and Negative Syndrome Scale (PANSS) score improved significantly, decreasing from 68 to 42 throughout the treatment. A Naranjo Adverse Drug Reaction Probability Scale score of 6 was calculated, indicating that the oculogyric crisis was likely associated with aripiprazole use.

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Oculogyric crisis (OGC) is known as a rare but serious extrapyramidal side effect of antipsychotic medications, typically characterized by an abrupt, involuntary upward deviation of the eyes. This condition can last from a few seconds to several hours and is less commonly observed compared to other extrapyramidal symptoms like parkinsonism or akathisia (8). The development of OGC is linked to an imbalance between dopaminergic and cholinergic systems. Dopamine D2 receptor blockade can increase cholinergic transmission, leading to extrapyramidal symptoms such as dystonia (9, 10).

Aripiprazole, an antipsychotic with partial agonist activity at D2 receptors, is generally associated with a lower risk of extrapyramidal symptoms (11). However, some cases have shown that aripiprazole can still induce dystonic reactions (1, 2, 12). This might be attributed to aripiprazole's complex pharmacological profile, which can disrupt the balance between dopaminergic and cholinergic systems. Dopamine hypofunction and relative cholinergic overactivity are implicated in the onset of these dystonic reactions (10, 11). Additionally, aripiprazole's effects on D3 and 5-HT6/7 receptors may contribute to the development of OGC (9, 13). These mechanisms, supported by preclinical studies, suggest that aripiprazole's inhibition of the serotonin transporter can alter dopamine balance in the basal ganglia, leading to dystonia (11).

Cases in the literature indicate that aripiprazole can cause OGC, often following dose increases. Bhachech (1) reported a case where OGC developed after an increase in the aripiprazole dose, with symptoms successfully treated with promethazine. This finding underscores the need to consider unexpected side effects when treating patients with aripiprazole and the importance of close monitoring during treatment (4).

The treatment of OGC typically involves anticholinergic medications and benzodiazepines. Anticholinergic drugs help to balance the increased cholinergic activity caused by dopamine deficiency, while benzodiazepines act on gamma-aminobutyric acid A (GABA-A) receptors to alleviate symptoms (10). However, in some cases, reducing the dose or discontinuing the medication may also lead to symptom resolution (2). In our case, the discontinuation of aripiprazole led to a rapid resolution of OGC symptoms without the need for additional medication. This highlights the potential benefit of medication cessation as a treatment strategy in similar cases.

In conclusion, numerous cases of oculogyric crisis associated with aripiprazole have been reported in the literature, and our case adds to this growing body of evidence. This case underscores the importance of recognizing that aripiprazole, despite its reputation for a lower risk of extrapyramidal symptoms, can still lead to severe dystonic reactions such as OGC. Clinicians should be vigilant when prescribing aripiprazole, particularly in patients who may be at higher risk, and should not overlook the potential for EPS even with newer antipsychotic agents. Our findings suggest that aripiprazole's safety profile regarding EPS may not be as robust as previously thought, and careful monitoring is essential during treatment.

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