

# Psychopharmacology for the Clinician

The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided. The patient described in this column gave informed consent for the publication of the column.

## Oculogyric crisis: a rare type of dystonia

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A 27-year-old man was admitted to our psychiatry service with psychotic symptoms. In the months preceding admission, he had experienced ideas of reference along with persecutory delusion. He also exhibited associated behavioural and affective impairment, and his relatives reported social isolation.

On examination, we observed persecutory delusion and ideas of reference. Phenomena of thought insertion, mixed insomnia, decreased appetite, apathy, anergy, and amotivational symptomatology were also present.

The patient was antipsychotic naïve. During admission, we started paliperidone PO, titrating the dose according to the patient's symptoms until he reached the maximum dose of 18 mg/d with adequate tolerance and without notable adverse effects. Subsequently, we administered an intramuscular (IM) depot formulation, starting with 100 mg, and then 150 mg monthly for maintenance. He experienced mild akathisia, which was corrected with prolonged-release biperiden 4 mg. He had a favourable clinical course, with adequate resolution of the delusional ideation. However, after the second administration of paliperidone 150 mg IM, the patient reported sexual dysfunction, so his antipsychotic was changed after only 2 months. Aripiprazole PO was initiated at 10 mg/d, with a progressive change to an IM depot formulation of 400 mg every 28 days. The first injection of aripiprazole was administered 29 days after the last dose of paliperidone. Later, the patient reported (more evident) akathisia, which again resolved with prolonged-release biperiden 4 mg. Subsequently, the patient reported discomfort in the orolingual region, compatible with mild

orofacial dystonia. For this reason, we reduced the dose of aripiprazole IM to 300 mg, and biperiden was maintained. The patient also reported that in the later weeks, he experienced occasional episodes of involuntary gaze deviation lasting a few seconds. One of these episodes was described by his mother as a rapid and transitory deviation of both eyes to one side, with no impairment of consciousness or convulsions.

Our initial clinical suspicion was oculogyric crisis (OGC). We ordered a brain MRI and video electroencephalography (EEG), and the results of both were normal.

Aripiprazole was discontinued and replaced with olanzapine 5 mg PO, which was chosen because of its sedative profile. The patient's symptoms resolved completely.

An OGC is an uncommon type of focal dystonia that affects the extraocular muscles, producing a forced conjugate deviation of the eyes, more frequently upwards. The deviation may last from seconds to hours. The etiology of OGC is varied, the most common being the use of certain drugs that act as dopamine blockers, such as antipsychotics, antiemetics, antiepileptics and antidepressants<sup>1</sup> (Table 1). Antipsychotics, both atypical and typical, are the drugs that have been most frequently associated with OGC. The likelihood of inducing OGC theoretically depends on blocking D2 in the nigrostriatal pathway. In

a prospective investigation, OGC was reported to have an incidence of 1.8% after 3 months to 2 years of treatment with 1 or more second-generation antipsychotics.<sup>2</sup>

Oculogyric crisis could also be related to other neurologic diseases (with genetic basis or associated with other movement disorders) and with the presence of focal brain lesions, generally affecting the basal ganglia or midbrain, and therefore compromising the nigrostriatal pathway. The most important differential diagnosis is frontal lobe epilepsy. Although both OGC and frontal lobe epilepsy are associated with gaze deviation, eye deviation in epilepsy is usually associated with lateral forced head version. Other related features could be speech arrest, tonic contractions of limbs, Todd paralysis, or impairment of consciousness. MRI and EEG should be performed. Sometimes, when the ultimate cause cannot be determined, antiepileptic drugs could be started; they will lead to clinical improvement when an epileptic origin exists and will have no effect on OGC.

The appearance of acute dystonia with the use of antipsychotics is more frequent in young, male patients with primary psychotic pathology and with the use of typical antipsychotics at high doses.<sup>3</sup> However, there have been reported cases of OGC with atypical antipsychotics, including olanzapine, quetiapine and aripiprazole.<sup>4-6</sup>

**Table 1: Most frequently used drugs described as a potential cause of oculogyric crisis<sup>1</sup>**

Antipsychotics	All, both typical and atypical can induce dystonia, hence OGC
Antiemetics	Metoclopramide, clebopride, ondansetron, and droperido
Antiepileptics	Carbamazepine, lamotrigine, gabapentin, and oxcarbazepine <sup>8</sup>
Antidepressants	SSRI: fluoxetine, citalopram, fluvoxamine, escitalopram Tricyclic: imipramine
Other	Cetirizine, organophosphate poisoning, tetrabenazine, L-dopa, lithium, edrophonium, cefexime, pentazocine, nifedipine, isotretinoin, phencyclidine, and salicylate poisoning

OGC = oculogyric crisis; SSRI = selective serotonin reuptake inhibitor.

In our patient's case, OGC was associated with the use of aripiprazole. It is a new-generation antipsychotic, acting as a partial antagonist on the mesolimbic pathway, stimulating presynaptic D2 receptors, reducing dopamine secretion. At the postsynaptic level, it acts as a partial agonist on D2, producing limited effects on dopamine in the nigrostriatal pathway and, therefore, a lower rate of extrapyramidal symptoms, estimated to be 0%–1%.<sup>7</sup>

The recognition and accurate diagnosis of OGC is usually challenging because the episodes are rarely witnessed by the doctor owing to their self-limited nature.

The use of typical or atypical antipsychotics, including new-generation antipsychotics, can cause extrapyramidal symptoms. Some extrapyramidal symptoms, such as OGC, may be difficult to recognize. Therefore, it is important to know their phenomenology and pathophysiology, for the optimal clinical management and treatment.

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