

# Aripiprazole-induced oculogyric crisis (acute dystonia) in 11 years old girl: A case report

## 11 yaşında bir kız çocukta aripiprazole bağlı okülojirik kriz (akut distoni): Bir olgu sunumu

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### SUMMARY

Acute dystonic reaction which is described as involuntary muscle spasms and contractions including neck, chin, eye and mouth muscles is an extrapyramidal adverse effect. Acute dystonic reactions are rarely seen with atypical antipsychotics and in the pediatric population. In this study, we present a case of an aripiprazole-induced oculogyric crisis in an 11 years old girl who diagnosed with mild intellectual disability attention deficit and hyperactivity disorder, and conduct disorder. This case is important as an aripiprazole-induced oculogyric crisis caused is not an expected side effect in the child and adolescent population.

**Keywords:** Oculogyric crisis, aripiprazole, child, acute dystonia.

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### ÖZET

İstemsiz kas spazmları ve boyun, çene, göz ve ağız kaslarını içeren kasılmalar olarak tanımlanan akut distonik reaksiyon, ekstrapiramidal bir yan etkidir. Akut distonik reaksiyonlar, atipik antipsikotiklerle ve pediatrik popülasyonda nadiren görülür. Bu çalışmada, hafif zihinsel engellilik, dikkat eksikliği hiperaktivite bozukluğu ve davranış bozukluğu tanılı 11 yaşındaki bir kız çocuğunda aripiprazole bağlı okülojirik kriz olgusunu sunulmaktadır. Bu vaka, aripiprazolün neden olduğu okülojirik krizin çocuk ve ergen popülasyonda beklenen bir yan etki olmaması nedeniyle önemlidir.

**Anahtar sözcükler:** Okülojirik kriz, aripiprazol, çocuk, akut distoni.

### INTRODUCTION

The acute dystonic reaction which is described as involuntary muscle spasms and contractions including neck, chin, eye, and mouth muscles is an extrapyramidal adverse effect and one of these is the oculogyric crisis. The oculogyric crisis is

seldom reported with atypical antipsychotics such as aripiprazole<sup>1,2</sup>. Atypical antipsychotics are used for treatments of behavior disorders, diffused developmental disorder, mental retardation in childhood, stereotypic behaviors, nervousness,

hyperactivity, aggression, and self-destructive behaviors<sup>3-5</sup>. Aripiprazole is an antipsychotic agent that has a partial agonistic effect on the dopamine D2 receptor and serotonin 1A receptor and is described as a “dopaminergic system stabilizer”<sup>6-7</sup>. It is known that it does not cause extrapyramidal adverse effects by decreasing dopaminergic activity in the nigrostriatal pathway because of its partial agonistic effect<sup>7,8</sup>. In this article, the case of the oculogyric crisis induced by aripiprazole use of an 11 years old girl who was diagnosed with mild intellectual disability, attention deficit and hyperactivity disorder, and conduct disorder will be presented. We aim to draw attention to the development of the oculogyric crisis which is known to be rare during the use of aripiprazole in the pediatric population. This case is important since data on the aripiprazole-induced oculogyric crisis in the pediatric population is considerably limited. It is also noteworthy as it occurs at low doses. The patient's parents have given his written informed consent for this case report to be published.

## CASE PRESENTATION

An 11 years old female case presented to our clinic for the reasons as self-destructive behaviors harm the environment, burst of anger, aggression, and hyperactivity. She was diagnosed with mild intellectual disability at the age of 3 and was diagnosed with ADHD at the age of 6. It is learned that her ADHD treatment was started with methylphenidate 18mg/day and methylphenidate 36 mg/day has been used since last year, also she was under special education support for 8 years. A two months ago, risperidone 0.25 mg/day was started and gradually increased to 0.5 mg/day for challenging behaviors, self-mutilation, temper tantrums in addition to methylphenidate treatment. However, on the 5th day of treatment, the patient presented to the emergency department with involuntary muscle contractions on the neck. After the injection of biperiden 1x5mg intramuscular (IM) at the emergency department, the contractions were relieved approximately within 2 hours. Risperidone was stopped, and since antipsychotic therapy is required for the patient's disruptive behaviors, temper tantrums, and self-mutilation, aripiprazole 1 mg/day was immediately started and gradually increased to 2.5 mg/day. On the 3rd day of use of aripiprazole 2.5mg patient presented to the emergency department with the complaint of upper visual fixation. Any positive findings that may explain the symptoms could not be detected in a detailed physical examination, neurologic and psychiatric examinations. The results of the patient's hemogram and biochemistry tests were

normal. In terms of differential diagnosis, after the evaluation of conversion disorder, tardive dystonia, epileptic encephalopathy, anti-epileptic drug intake; she was diagnosed with the oculogyric crisis (acute dystonia). After the injection of biperiden 1x5mg (IM), the oculogyric symptoms of the patient improved completely within 3 hours.

## DISCUSSION

In this case report, we described a case of an aripiprazole-induced oculogyric crisis (acute dystonia) in an 11 years old girl. Oculogyric crisis (OGC), reported as a rare side effect of antipsychotic agents, is characterized by tonic, usually upward, acute, or late-onset continuous ocular fixation<sup>8</sup>. The periods of OGC can take minutes or hours, it may recur or become chronic. Cases of acute- and tardive-onset OGC have been reported with olanzapine, quetiapine, clozapine, risperidone, aripiprazole, and ziprasidone<sup>9-14</sup>. Patients with OGC experience severe distress and may refuse treatment when it recurs frequently.

The nigrostriatal dopamine pathway is responsible for the underlying mechanism of this side effect. The nigrostriatal dopamine pathway projects from the substantia nigra to the putamen and caudate nucleus. Antipsychotic agents cause acute dystonia by blocking dopamine D2 receptors in caudate, putamen, and globus pallidum<sup>14</sup>. The possible mechanism for the development of less extrapyramidal side effects result from aripiprazole is that it has partial agonistic activity to dopamine D2 and serotonin 5HT1A receptors and full antagonistic activity to the 5HT2A receptor<sup>15-17</sup>. Additionally, the effect of aripiprazole on D3, 5-HT6, and 5-HT7 receptors is still not fully known and may therefore play a role in the oculogyric crisis. The number of reported cases regarding extrapyramidal adverse effects including the oculogyric crisis caused by aripiprazole is relatively low in literature since the risk of developing extrapyramidal adverse effects arising from aripiprazole is lower than the other typical antipsychotics<sup>18-19</sup>. The reported cases are mostly related to the adult population.<sup>13,15,16</sup> Our case is important as she is one of the rare cases of aripiprazole-induced oculogyric crisis (acute dystonia) reported to literature in the pediatric age group. Fountoulakis et al. reported (2006) an 18-year-old male patient with Tourette's syndrome who developed low-dose aripiprazole use and experienced an acute dystonia attack with facial muscle spasm, oculogyric crisis, and torticollis. All symptoms of their case improved after a single intramuscular injection of biperiden 5 mg<sup>13</sup>. Bhachech presented a 28-year-old paranoid schizophrenic patient who developed an oculogyric

crisis (acute dystonia) with aripiprazole dose up-titration<sup>15</sup>. Navratan et al. presented a 19-year-old obsessive-compulsive disorder patient who using fluoxetine 80 mg and aripiprazole 10 mg. On the 5th day of aripiprazole 10 mg, he developed a tightening of the neck muscles with a backward and right-sided deviation of the head along with uprolling of the eyeballs. All symptoms of their case healed, after aripiprazole was stopped, injection promethazine 50 mg intramuscularly was given immediately<sup>16</sup>. In our case, the oculogyric crisis was resolved with biperiden injection as in the case of Fountoulakis et al. Extrapyramidal side effects of antipsychotic medication it depends on the blockade of striatal D2 receptors and is usually treated with anticholinergic agents such as biperiden<sup>17,20</sup>. Limited studies of biperiden pharmacokinetics indicate that peak concentrations occur after 1–1.5 hours and the half-life is around 10 hours. Thus, it is customary in clinical practice to treat an oculogyric crisis within 3 hours after a single dose of biperiden injection<sup>21</sup>.

The recognized risk factors for the development of acute dystonia including acute oculogyric crisis include younger age, male gender, positive history of acute dystonia, family history of dystonia, beginning antipsychotic treatment with highly effective and high-dose antipsychotic drug<sup>22</sup>. Our case has risk factors for an aripiprazole-induced acute oculogyric crisis such as pediatric age and the presence of acute dystonia history. Additionally, the dysfunction of the central nervous system in cases with an intellectual disability makes it more sensitive to the toxic effects of psychotropic drugs, which may be a risk factor in our case. In patients with intellectual disability, therefore, it is recommended to initiate and use psychotropic agents at lower doses compared to the normal population<sup>23</sup>.

The prescription and use of antipsychotics in children and adults are increasing worldwide. Atypical antipsychotics are preferred more frequently due to their considerably less side effect profile<sup>24</sup>. Nonetheless, it should be careful when using antipsychotics in children and adults, and it should be kept in mind that atypical antipsychotics may lead to side effects such as acute dystonia even at low doses, especially if risk factors are present. In conclusion, our case underscores that the physicians should be careful before starting antipsychotic treatment and during patient follow-up.

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