

# Mania Associated with Aripiprazole Treatment in Schizophrenia: a Case Report

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## ABSTRACT

### Mania associated with aripiprazole treatment in schizophrenia: a case report

Aripiprazole is a novel antipsychotic medication that is used to treat a number of psychiatric conditions, including schizophrenia, bipolar disorder, and major depressive disorder. Clinical trials have established its efficacy and favorable tolerability profile. Nevertheless, infrequent undesirable adverse events are often encountered during wide-scale everyday clinical use. There are a few mania/hypomania cases associated with second-generation antipsychotic treatment. Induction of mania, described for almost all second-generation antipsychotic, may be one of the rare adverse events of aripiprazole therapy. In this study, a female patient with chronic schizophrenia who had never presented history of mood episodes, in which manic symptoms developed after increasing aripiprazole dosage to 30mg/day and disappeared after cessation of the treatment was presented. During the second-generation antipsychotic use, clinicians should be cautious to patients's mania/hypomania symptoms.

**Key words:** Aripiprazole, hypomania, mania, schizophrenia



## ÖZET

### Şizofrenide aripiprazol kullanımı ile ilişkili mani: Bir olgu sunumu

Aripiprazol, şizofreni, bipolar bozukluk ve major depresif bozukluk gibi bir dizi psikiyatrik durumların tedavisi için kullanılan yeni bir antipsikotik ilaçtır. Klinik çalışmalarda etkinliği ve üstün tolerabilite profili belirlenmiştir. Bununla birlikte, az görülen istenmeyen yan etkilere de günlük klinik kullanım sırasında rastlanmaktadır. İkinci kuşak antipsikotik tedaviyle ilişkili az sayıda mani/hipomani olgusu bildirilmiştir. Burada aripiprazol dozunun 30mg/güne yükseltilmesinin sonrası mani belirtileri gelişen, aripiprazol tedavisinin kesilmesinin ardından mani belirtileri hızla kaybolan daha önce duygudurum dönemi öyküsü olmayan kronik şizofreni tanısı olan bir kadın olgu sunulmaktadır. İkinci kuşak antipsikotik kullanımı sırasında klinisyenler hastaların mani/hipomani belirtileri açısından dikkatli olmalıdır.

**Anahtar kelimeler:** Aripiprazol, hipomani, mani, şizofreni

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## INTRODUCTION

Aripiprazole is an atypical antipsychotic which differentiated from the other atypical antipsychotic drugs due to partial agonistic effect on presynaptic dopamine D<sub>2</sub> autoreceptor. At the same time, antagonistic effect on postsynaptic D<sub>2</sub> dopamine receptor is available (1). For this reason, aripiprazole affects like agonist in the absence of dopamine and it affects like antagonist in the presence of excessive dopamine. Aripiprazole is used to treat a number of

psychiatric conditions, including schizophrenia, bipolar disorder, and major depressive disorder. Although aripiprazole is a well tolerated antipsychotic, some side effect such as headache, insomnia, agitation, anxiety, akatizi may occur during the usage (2). While almost all second generation antipsychotics-induced mania/hypomania are reported, aripiprazol-induced mania/hypomania has been reported as very rare (3). In this article, we will discuss a case which was diagnosed with paranoid schizophrenia for 20 years and developed mania after suggesting 30mg/day aripiprazole treatment.

## CASE

M.D., 41 years old, primary school graduated, housewife, married for 20 years, mother of two, was born in Rize, still lives with her family in Rize. Patient who took her own oral antidiabetic medication in order to attempt suicide was taken to our hospital emergency services by her relatives and she hospitalized in our clinic after follow-up in the emergency department.

**History:** The patient who applied to a psychiatry outpatient clinic with the complaints of being cheated by her husband, thinking that her neighbours talk about her, thinking to harm herself, hearing voices, laughing and talking to herself, introversion and insomnia symptoms was diagnosed with paranoid schizophrenia and treated with haloperidol and biperiden 20 years ago. However, she did not use the medications on a regular basis. In the follow-up period she was hospitalized for three times and she used antipsychotics such as chlorpromazine, risperidone, haloperidol, quetiapin, flupentiksole, ziprasidone. But she saw the most benefit from risperidone. A year ago, due to the increase in similar complaints she was hospitalized in our clinic for 47 days and 6mg/day of risperidone treatment was suggested. After discharge she was suggested risperidone consta with 50mg/15day (IM). However, on outpatient monitoring her treatment was replaced with 12mg/day of paliperidone due to patient's ongoing complaints. The patient who took paliperidone for 9 months and not get well was taken to a different hospital by her relatives. Her treatment was created again as 6mg/day of risperidone and risperidone consta 50mg/15days (IM). However, because of high level of prolactin (219ng/ml), oral form of risperidone dose was decreased while aripiprazole treatment was started and increased gradually. After aripiprazole dosage of 30mg/day some symptoms like hyperactivity, increase in the amount of speech and energy and sexual interest, insomnia, costume-outfit changes were occurred. The patient observed an increase in her appetite begun to discuss with her husband about her

diet frequently. After a discussion like this she took her own oral antidiabetic drugs in order to suicide and were brought to our hospital. She hospitalized for second time.

**Self and family history:** She was born at home as fifth child of eight in Rize. She had no problem of growth and development. Her mother is 67 years old, housewife and lives with her son and his wife. Her father died from lung cancer 15 years ago. Her mother and father's marriage is a cross-cousin marriage. She agreed with her father much more than her mother so she was affected by her father's death greatly. She reported that her mother showed more interest in her male children since her childhood. She finished first school in five years successfully and went on a religious school. She married five years ago. Her husband is five years older than her, primary school graduate and self-employed. She has two sons at the ages of twelve and seventeen. She was treated because of type 2 diabetes mellitus, obesity and hypertension. It is said that there is a family history of psychotic disorder in the grandfather and grandmother.

Neurological examination and other system examinations, hemogram and biochemical values were evaluated normally.

**Mental state examination:** She was conscious and fully oriented. There was eye contact. Self care was exaggerated. She was talking with high volume and her mood was euphoric. She was noted to have an anxious affect. Auditory and visual hallucinations were encountered. The reality testing and judgement were impaired. In the thought content there were reference, persecutory and grandiose delusions as well as delusions. Self esteem and explosive behavior had increased.

**Clinical course:** After aripiprazole treatment upgraded to 30mg/day in the last 4 days obvious changes observed in the style of clothing and behavior of the patient. According to the DSM-IV TR (4) criteria of the manic periods; euphoric mood, grandiosity, increase of self-care and amount of speech, decline in

the need of sleep, increase of spending-money and libido and movement were detected. It was reported that there was no depressive symptoms before starting aripiprazole treatment and no mixt episodic symptoms during follow-up period in our clinic in the patient who was presented to the emergency service with an unexpected suicide attempt. Young Mania Rating Scale (YMRS) was evaluated as 31 points. Aripiprazole was reduced gradually and stopped. Haloperidole was added and increased to 10mg/day. In the following period manic symptoms decreased. YMRS dropped to 7 points.

## DISCUSSION

In this paper, we presented a case with diagnosis of paranoid schizophrenia that showed manic symptoms after treatment of aripiprazole treatment of 30mg/day. Although similar cases are shown about other antipsychotics' side effects like this, the case number about aripiprazole is limited. According to a review in which case reports are evaluated between the years 2004-2010, the distribution of 28 cases with atypical antipsychotics induced mania/hypomania is like that; olanzapine-related 7 cases, ketiapin-related 5 cases, ziprasidone-related 5 cases, aripiprazole treatment-related 4 cases, amisülpirid-induced 2 cases, zotepin induced 2 cases, perospiron-induced 2 cases and paliperido-induced 1 case. It was reported that 24 cases of these are schizophrenia and 4 cases of these

are schizoaffective disorder (3). Aripiprazole is an atypical antipsychotic that acts as partial agonist on 5-HT<sub>1A</sub> and D<sub>2</sub> receptors while it acts as antagonist on 5-HT<sub>2A</sub> receptor. It was reported that there is aripiprazole-induced mania in a patient with chronic schizophrenia who has no mood disorder symptoms before (5). Aripiprazole induced mania has been reported in a male patient with resistant obsessive compulsive disorder in a case report (6). It is not clear that which mechanisms play role on this side effect but it is suggested that partial agonism 5-on HT<sub>1A</sub> and D<sub>2</sub> receptors may lead to an increase in the release of dopamine and may lead to mania (7). Another opinion about this supports that usage of partial agonism in patient who takes dopamine antagonist for a long time may increase dopaminergic activity relatively. On the other hand, that is not known exactly how or why dopaminergic hyperactivation triggers hypomania/mania without worsening psychotic symptoms. Antagonism on 5-HT<sub>2A</sub> reseptor may lead to disappearance of dopaminergic inhibition and mania (5). The mood swings because of antipsychotics use for acute phase and protective treatment of bipolar disorders are noteworthy. Even though the number of reported cases with aripiprazole is rare, we must be careful in terms of these side effects and inform patients and patient relatives about the possible mood symptoms. Further research is needed in terms of which mechanisms are acting on this side effect and determination of risk factors and predictors.

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