Dusunen Adam The Journal of Psychiatry and Neurological Sciences 2016;29:370-373
DOI: 10.5350/DAJPN2016290409

Case Report / Olgu Sunumu

Mania Induced by Aripiprazole Use: a Case Presentation

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ABSTRACT

Mania induced by aripiprazole use: a case presentation

Olanzapine, quetiapine and aripiprazole have been shown to be effective treatments for bipolar depression. However, induction of manic and depressive episodes with atypical antipsychotic treatments have also been described as risk. Current literature described antidepressant effects of Aripiprazole with the risk of manic shift. In this report, a case who developed manic episode with the treatment of 30mg/day of the aripiprazole will be discussed. A 35-year-old, woman, who had 12 years history of bipolar affective disorder-I (BAD-I) for 12 years, and taking paliperidone 9mg/day and lithium 1200mg/day for the last 14 months. She was admitted to outpatient clinic by her parents with complaints of fatigue, loss of pleasure and increased sleep. She was suspicious, had thoughts of getting harm form others and being a sinner, and suspecting that someone put a spell on her. She was admitted to inpatient service with the diagnosis of BAD-I depressive episode with psychotic features. Aripiprazole 30mg/day was added to current treatment regime. Consequently, increase in targeted activities, inappropriate affect, decreased need for sleep, and grandiose delusions were observed. The symptoms of mania were considered to be induced by aripiprazole, and its dose was decreased to 10mg/day. Following the dose reduction, sleepiness and her delusions were improved within the consecutive 2 weeks.

Keywords: Aripiprazole, bipolar depression, manic episode

ÖZET

Aripiprazol kullanımı ile ortaya çıkan mani: Olgu Sunumu

Bipolar depresyon tedavisinde olanzapin, ketiyapin, aripiprazol gibi bazı antipsikotik ilacların etkili oldukları gösterilmiş olup, atipik antipsikotiklerle tedavi sırasında mani ve depresyon dönemlerinin indüksiyonu da bir risk olarak tanımlanmıştır. Literatürde aripiprazol'ün antidepresan etkinliği olması ile birlikte manik kaymaya da yol açabileceği bildirilmiştir. Bu yazıda 30mg/dl dozundaki aripiprazol tedavisi ile manik kayma görülen bir olgu tartışılmıştır. 35 yaşında, kadın hasta, 12 yıldır bipolar afektif bozukluk-I (BAB-I) tanısıyla takip edilmekte olup son 14 aydır paliperidon 9mg/gün ve lityum 1200mg/gün tedavisi almaktadır. Son 3 haftadır 'güçsüzlük, hayattan keyif almama, sürekli yatma isteği sonrasında gelişen günahkar olduğunu, suçlu olduğunu, kötülük göreceğini düşünme, insanlardan şüphelenme, kendine büyü yapıldığını dile getirme' şeklinde yakınmaları ile yakını refakatinde polikliniğe başvurmuştur. Hasta, BAB- I 'psikotik özellikli depresif nöbet' tanısı ile kliniğe yatırılarak takip altına alınmıştır. Mevcut tedavisine aripiprazol 30mg/gün eklenmiştir. Aripiprazol eklendikten sonraki 15 gün içinde hastanın dışa vuran davranışlarında artma, anlamsız gülümsemeler, uyku ihtiyacında azalma, büyüklük sanrıları şeklinde yakınmaları ortaya çıkmıştır. Mani belirtilerinin aripiprazol ile indüklenmiş olacağı düşünülerek aripiprazol dozu 10mg/gün'e düşürülmüştür, sonraki 2 hafta içinde hastanın gece uykuları düzelmiş, sanrıları azalarak kaybolmuştur.

Anahtar kelimeler: Aripiprazol, bipolar depresyon, manik dönem

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Date of receipt / Geliş tarihi:
December 19, 2015 / 19 Aralık 2015

Date of the first revision letter / İlk düzeltme öneri tarihi:
December 28, 2015 / 28 Aralık 2015

Date of acceptance / Kabul tarihi:
January 19, 2016 / 19 Ocak 2016

INTRODUCTION

Bipolar affective disorder (BAD) is a serious psychiatric disorder, characterized by recurrent episodes of mania and depression and affecting 1.5% of the population (1). Bipolar depressive episodes are more repetitive, frequent and severe compared to manic episodes (2). Increasing number of research concerns the effectiveness of atypical antipsychotics in treatment of BAD is increasing. Efficacy of several atypical antipsychotics in the acute manic phase of bipolar disorder has been established. However, studies that investigated the effectiveness of antipsychotic medications in acute bipolar depression, and in the long-term prevention of recurrences are limited (3). Also, a risk of induction of manic and depressive episodes during treatment with atypical antipsychotics have also been described (4).

Aripiprazole is a new-generation antipsychotic that is partially agonistic on Dopamine D2, D3 and serotonin 5HT-1A receptors, and antagonistic on serotonin 5HT-2A receptors (5). It was approved by the FDA (U.S. Food and Drugs Administration) for the maintenance treatment of BAD and acute bipolar mania. It has been described in the literature that partial agonistic activity of aripiprazole against dopamine receptors and its antagonistic activity on 5HT2A could facilitate a manic shift (6), so that caution should be exercised due to the risk of exacerbation (7). Until this time period, 5 reports of 8 cases developing 5-15mg/day aripiprazole-associated mania/hypomania have been published in the literature (8-12). In this report, a case who shifted to manic episode with 30mg/day of the aripiprazole was discussed.

CASE

A 35-year-old single woman referred to outpatient clinic with her sister for sadness, fatigue, thought related to guiltiness, suspiciousness for the past 3 weeks. In mental examination she was conscious, oriented and cooperative with limited eye contact, her speech was brief, and low in tone with prolonged response time, mood was depressed. She had auditory hallucinations. Process of thought was slowed down. Thought content includes anhedonia, hopelessness, worthlessness, somatic passivity, persecutory and reference delusions. Expressive behaviors were decreased. She was diagnosed with BAD-depressive episode with psychotic feature, and she was hospitalized. Montgomery- Asperg Depression Scale (MADRS) score was 26, Young Mania Rating Scale (YMRS) score was 2, and Hamilton Depression Scale (HAM-D) score was 19. Hemogram and biochemical measurements were within normal limits. Serum lithium level was measured as 0.7mEq/L. She was in remission with paliperidone 9mg/day and lithium 1200mg/day until the last 3 weeks.

After hospitalization, aripiprazole 10mg/day was added to current treatment, and increased to 30mg/day over 1 week. Following 15 days of the add-on therapy, increased expressed behaviors, unusual smiles, and decreased need to sleep were noticed. On the 16th day of hospitalization, her speech and thought association were accelerated, she was euphoric, and she had grandiose delusions. The scores of clinical scales was: MADRS:8, YMRS:29, HAM-D:5. Aripiprazole dose was reduced to 10mg/day, and lorazepam 2.5mg/day was added on due to mania development. Within 2 weeks following dose reduction, her sleep and delusions were improved. On 40th day of hospitalization, her speech speed slowed down, her affect was euthymic. Her thought associations and thought content were within normal limits. Clinical scales scores were: MADRS:6, YMRS:1, HAM-D 5. The patient was discharged. She was in remission for 6 months after discharge with the treatment of paliperidone 9mg/day, lithium 1200mg/day and aripiprazole 10mg/day.

DISCUSSION

Treatment of bipolar depression is one of the greatest psychopharmacologic challenges for psychiatrists. Because of that, there has been an increase in the interest on the treatment of the bipolar depression over the last 15 years (8). Lithium was shown to be insufficient in the treatment of bipolar depression (9), while olanzapine, quetiapine and aripiprazole were shown to be effective. In the present case, the patient with BAD who was admitted to clinic due to depressive symptoms with psychotic features were hospitalized. The benefits of aripiprazole were also shown in augmentation treatments of bipolar depression (11,12). On the other hand, during treatment of psychotic symptoms of a patient with aripiprazole, presence of exacerbation risk have (7). There are various hypothesis about this issue. One of them is that 5HT1A antagonism and partial D2 receptor agonism result in frontal dopamin release (13). The other hypothesis is long-term exposure to D2 antagonists trigger blockade of dopamin receptors, and add on aripiprazole as partial D2 agonist can lead to relatively higher dopamin activation (14). Our patient's history of long-term use of an antipsychotic

that can induce D2 receptor blockade might explain the manic shift after high-dose aripiprazole treatment. The dopaminergic agonism of low-dose aripiprazole and potentiated synergistic effect on serotonergic receptors can be responsible of mania/hypomania induction, a dose-dependent relationship is not reported for any of these mood swings. There has been still uncertainty about the doses of aripiprazole that have caused antimanic effect (13-16). The aripiprazole dose was between 5 to 15mg/day in published 5 reports of 8 cases. (8-12). Unlikely with the literature which reported 5-15mg/day, manic shift emerged under 30mg/dl dose in our case. Resolution of symptoms after dose reduction and mania than the previous episodes might imply dose dependent induction of mania with aripiprazole. However, it might be a part of the natural course of the disease. For clarifying the role of aripiprazole in mood disorders and the evaluation of the appropriate dose range, further controlled trials with large samples are required.

Contribution Categories	Name of Author
Follow up of the case	D.S.A.
Literature review	D.S.A., E.O., A.T.
Manuscript writing	D.S.A., E.O., A.T.
Manuscript review and revisation	D.S.A., E.O., A.T.

Conflict of Interest: Authors declared no conflict of interest.

Financial Disclosure: Authors declared no financial support.

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