

## Modafinil-Induced Psychosis: A Case Report

Özgür AYTAŞ<sup>1</sup>, Hayriye DİLEK YALVAÇ<sup>2</sup>

<sup>1</sup>Clinic of Psychiatry, Malatya State Hospital, Malatya, Turkey

<sup>2</sup>Clinic of Psychiatry, Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Ankara, Turkey

### ABSTRACT

Modafinil is used in the treatment of excessive day time sleepiness associated with several clinical conditions. It can also be used for affective stimulation for working late and/or concentrating for a long time. The reported cases of psychosis associated with modafinil use in the literature, have medical or psychiatric disorders. There is only one reported case without medical or psychiatric disorder but developed modafinil related psychosis, which is a case under simulated shift work in laboratory conditions. The cases in the literature are reported to develop mania or

psychosis with 200–400 mg/day or higher doses. The case reported in this manuscript develop psychosis with 100 mg/day dosage. This case has no previous psychiatric and medical disorder history and not being on a shift work. The aim of modafinil use in this case was reported as increasing the concentration and performance while studying. Modafinil using patients must be psychiatrically monitored for its potential psychotic effect even in previously healthy individuals and low doses.

**Keywords:** Modafinil, psychosis, attention

### INTRODUCTION

Modafinil is used for the treatment of several clinical conditions associated with daytime sleepiness (1). Although the exact mechanism has not been understood yet, it is thought to act via GABA inhibition, dopamine receptor agonist, and  $\alpha$ 1-adrenergic agonist (2). Its prescription is approved for patients who have excessive sleepiness because of shift workers' sleep disorder, obstructive sleep apnea syndrome, and narcolepsia; however, it also has various indications in our clinical practice besides the above-mentioned conditions (3). In addition to increasing alertness, it stimulates mood and increases memory performance. Modafinil is used for the treatment of disease-related fatigue syndromes, attention deficit and hyperactivity disorder, Alzheimer's disease, age-related memory disorder, depression, idiopathic hypersomnia, cognitive disorder in schizophrenia, myotonic dystrophy, Parkinson's disease, mood disorders, chronic fatigue syndrome, opiate intoxication, fatigue after anesthesia application, and jet-lag (4).

Its pharmacological profile is different, particularly from that of conventional psychostimulants. It has fewer side effects (motor hyperactivity, anxiety, irritability, and rebound effects) than conventional stimulants (5). Modafinil has similar subjective and cognitive effects with caffeine and dextroamphetamine on alertness and attention (2). A study on adult attention deficit hyperactivity disorder (ADHD) found that modafinil increased cognitive performance on domains such as attention, planning, and executive functions (6). The recommended dose range is 200–400 mg/day in single or divided doses (7).

Very few psychosis and mania cases were reported because of this medication. We present a case who was admitted to the outpatient clinic, demanding help to increase her academic performance and concentration. She was prescribed modafinil (100 mg/day) and was presented to the emergency department 5 days later with psychotic symptoms.

### CASE

An 18-year-old female who was preparing for the university entrance examinations was presented to the psychiatry clinic with a complaint of an inability to maintain attention and low study performance. Her history revealed neither a medical nor a psychiatric disorder, including substance abuse. Laboratory evaluations such as hemogram, blood biochemistry, and thyroid functions



**Correspondence Address:** Dr. Hayriye Dilek Yalvaç, Clinic of Psychiatry, Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Ankara, Turkey Phone: +90 312 434 09 90 (62 75) E-mail: hdyalvac@hotmail.com

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were within normal limits. Modafinil (100 mg/day) was prescribed and she was advised to take her drug after breakfast in the morning. She became furious and suspicious from the third day. Her symptoms rapidly aggravated and she could not sleep on the 4<sup>th</sup> day of treatment. She was forced by her relatives to go to the emergency department on the 5<sup>th</sup> day. She was agitated at her presentation to the emergency department and she said that she discontinued modafinil on the 5<sup>th</sup> day. She did not use any other drug or substance while using modafinil. Her mental status examination showed that she had a clear conscious state and was well-oriented to place, time, and person. Her hair was untidy and uncombed. Self hygiene was decreased. Her speech rate was mildly increased. Her gaze was very suspicious and furious. Motor restlessness was apparent in her movements. She had paranoid delusions. Her involuntary attention was increased. Judgment was partially impaired. Hospitalization was recommended because of the psychotic attack induced by modafinil. However, she and her relatives refused hospitalization; therefore, haloperidol (5 mg) and biperiden (2 mg) were injected intramuscularly and orally dispensable risperidon (2 mg/day) and biperiden (4 mg/day) were administered. She was asked to come to the outpatient clinic for a control examination the next day; however, she came a week later with her relatives. After receiving injections in the emergency department, she slept the full night and her symptoms improved rapidly. Paranoid delusions disappeared on the 2<sup>nd</sup> day of treatment, and irritability and agitation decreased on the 3<sup>rd</sup> day. Her sleep also improved and she was in total remission on the 6<sup>th</sup> day of treatment. Her control examination did not reveal any psychotic symptoms and treatment was discontinued because of severe sedation. The results of the control examination that was performed 1 week after cessation of drugs was totally normal.

## DISCUSSION

Modafinil has been previously studied for childhood and adult ADHD, and it is accepted as an alternative for conventional stimulants in adult ADHD (8). It is also used by people who want to study for long hours, to maintain attention for a long period, and to stimulate mood. Demand for this drug is high among high school students and people who want to increase their success in examinations and competitive sports (9). We prescribed modafinil (100 mg/day) to increase attention and academic performance. The recommended dose of modafinil is 200–400 mg/day in a single dose or two divided doses (7). Although we started a dose below the recommended limits, psychotic symptoms developed on the 3<sup>rd</sup> day of treatment. Lack of a toxicological analysis in the emergency department was a drawback. In literature, mania and psychosis cases were reported to take modafinil at a dose of 200–400 mg/day or higher. In addition, these cases had medical or psychiatric diseases or they were shift workers (10,11). One of the cases developed psychotic symptoms while she was volunteering in a study simulating shift work conditions to examine the effects of modafinil on sleep, cognitive performance, and mood. This was the only case that did not have a known medical or psychiatric illness (10). In the literature, it was reported that aggravation of psychotic symptoms was observed in some schizophrenic patients who have taken modafinil for sedative side effects of antipsychotic drugs (12,13,14). Our case did not have any physical or psychiatric illness, she did not use any drug or substance during modafinil treatment, and she was not a shift worker.

100 After cessation of modafinil and initiation of antipsychotic treatment,

her symptoms were totally remitted and then antipsychotic treatment was stopped. No psychiatric symptom was seen thereafter.

Recently, a case of a 54-year-old man who developed late onset mania after treatment with modafinil because of somatization disorder and depression was reported (1). In addition, two cases with Lewy body dementia were reported to develop agitation and psychotic symptoms after treatment with modafinil for whole day sleepiness (15).

Modafinil exerts pro-wakefulness effects by inhibiting GABA release in the forebrain through a serotonergic system mediated process (16). Modafinil also increases dopamine levels in nucleus accumbens by inhibiting GABA release. In addition, it has a weak dopamine reuptake inhibitor effect (1,16). Inhibition of both GABA release and dopamine reuptake may have roles in development of modafinil-induced psychosis.

The presented case developed psychosis with a modafinil dose of 100 mg/day. Therefore, patients who are prescribed modafinil should be carefully followed for psychosis development, even when they are previously healthy and doses are small.

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