Late-life Onset Mania After Varenicline Use: A Case Report

Vareniklin Kullanımı Sonrası İleri Yaş Başlangıçlı Mani: Bir Olgu Sunumu

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ABSTRACT

Late-life onset manic attacks generally occur secondary to general medical conditions or drug use. Varenicline is an $\alpha 4\beta 2$ nicotinic acetylcholine receptor partial agonist, used for the cessation of smoking. In this case report, we present a 67-year-old male patient with a new-onset manic episode following varenicline treatment. The patient's manic symptoms started on the seventh day of varenicline treatment. His symptoms started on the 7th day of treatment. He was admitted to the psychiatric outpatient clinic since his symptoms did not improve despite discontinuing varenicline treatment. In the initial mental status examination, he scored 35/60 on the Young Mania Rating Scale (YMRS). On the twenty-fifth day of the hospitalization, the patient was discharged since his YMRS score improved (5/60). Varenicline may cause manic episodes in patients with bipolar disorder and in healthy individuals. An increasing number of serious psychiatric disorders are being reported due to varenicline treatment. Mental state examination before and during varenicline treatment seems necessary. (*Archives of Neuropsychiatry* 2013; 50: 372-374)

Key words: Varenicline, elderly, manic episode, bipolar disorder, psychiatry

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ÖZET

İleri yaşta başlayan manik epizot genellikle tıbbi hastalık ya da ilaç kullanımına ikincil sebeplerle ortaya çıkmaktadır. Vareniklin sigara bırakma tedavisinde kullanılan $\alpha 4\beta 2$ nikotinik reseptörlerin parsiyel agonistidir. Bu olguda daha önce psikiyatrik hastalık öyküsü bulunmayan 67 yaşındaki erkek hastada vareniklin kullanımı sonrası ilk kez ortaya çıkan manik epizot sunulmuştur. Vareniklin kullanımının yedinci gününde manik bulgular başladı. İlaç bırakılmasının birinci haftasında bulguların gerilememesi ile polikliniğimize başvuruldu. İlk ruhsal durum değerlendirmesinde Young Mani Değerlendirme Ölçeği (YMRS) 35/60 puan saptanmıştır. Hastane yatışının yirmi beşinci günü YMRS'nin 5/60 olması ile taburcu edildi. Vareniklin bipolar bozuklukta ve sağlıklı bireylerde manik epizoda yol açabilmektedir. Vareniklin tedavisi ile artan sayıda olguda ciddi psikiyatrik bozukluklar ortaya çıkmaktadır. Vareniklin tedavisine başlanmadan önce ve kullanımı sırasında ruhsal durum muayenelerinin değerlendirilmesi gerekli görünmektedir. (*Nöropsikiyatri Arşivi* 2013; 50: 372-374)

Anahtar kelimeler: Vareniklin, yaşlı , manik epizot, bipolar bozukluk, psikiyatri

Çıkar çatışması: Yazarlar bu makale ile ilgili olarak herhangi bir çıkar çatışması bildirmemişlerdir.

Introduction

Bipolar disorder is observed most commonly between the ages of 18 and 44 years with a rate of 1.4%. There are also cases of bipolar disorder with late-life onset. This rate has been reported to be 0.4% between the ages of 45 and 64 years and 0.1% above the age of 65 years (1,2). Manic episode with late-life onset generally occurs secondary to medical conditions or drug use (2,3).

Varenicline is a $\alpha 4\beta 2$ nicotinic acetylcholine receptor partial agonist which is used for the cessation of smoking (4). Depressive mood, sleep disorder, suicide, agitation, aggression and psychotic and manic findings have been found during use of varenicline (4,5,6). In 2009, American Food and Drug Administration (FDA) reported that varenicline might lead to serious neuropsychiatric findings

(6). It was emphasized that varenicline might lead to exacerbation in patients with a history of schizophrenia, bipolar disorder, major depressive disorder (7,8,9,10).

In this article, a case of manic episode which occurred for the first time following use of varenicline in a 67-old male patient who had no previous history of psychiatric disease was presented.

Case

Mr S was a 67 year-old high school graduate, retired person who had been married for 45 years and had two children. He presented to Early Diagnosis and Screening for Cancer Center 15 days before to quit smoking. He started to use varenicline at a dose of 0.5 mg/day for the first three days and 1mg/day on the

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following four days. On the 7th day of treatment, excessively lively mood, dynamism, increased energy, increased libido, inability to sleep, irritability when tried to be inhibited, logorrhea, grandiosity, increase in plans and projects for the future started in the patient. Although he stopped taking varenicline for the last one week his complaints continued and he referred to our outpatient clinic. He had a history of smoking for 40 years (one package a day) and rare and irregular use of Salbutamol, Budenoside and Theophylline because of a diagnosis of chronic obstructive lung disease (COLD). He had used no additional drug in the last two months. He had no history of psychiatric disease, alcohol or substance abuse, head trauma, blurred consciousness, forgetfulness, urinary and fecal incontinence. His familial history was natural. On psychological examination, he had mild untidiness in the external appearance, dynamism, increase in speech, strikingness, labile mood, euphoric affection, increase in thought production, grandiose delusions, decrease in sleep (2 hours a day) and increase in libido and in his insight, he denied that he had any behavioral change. YMRS and standardized Mini Mental Test (SMMT) scales were applied (11,12). On the first psychological evaluation, YMRS was found to be 35/60 points and SMMT was found to be 25/30 points. According to DSM-IV-TR diagnostic criteria, he was hospitalized in the psychiatry ward with a diagnosis of mood disorder related with drug use (showing manic properties). Investigations directed to medical etiology were done. Detailed systemic examination including neurological examination was found to be normal. Complete blood count, renal function tests, liver function tests, blood glucose, serum electrolytes, thyroid function tests, serum B12 vitamin, folic acid levels were within the normal limits. Cortical atrophy compatible with the age was found on brain magnetic resonance imaging. With the present data the patient was diagnosed with mood disorder related with use of varenicline (showing manic properties). As a result of Na valproate + valproic acid 750 mg (Valproate level 89 ug/ml), olanzapine 30 mg and quetiapine 300 mg treatment he was discharged when the findings regressed on the 25th day of hospitalization and YMRS was found to be 5/60.

Discussion

In the literature, cases of bipolar disorder with an onset at the age of 50 years and above are named as late-life onset cases. The incidence of bipolar disorder is 0.4% between the ages of 45 and 65 years and 0.1% above the age of 65 years (1,2). It has been reported that cases of late-onset bipolar disorder are differentiated from the young-onset cases with negative familial history, an increased rate of psychotic characteristics, an increased rate of neurological co-diagnosis and more frequent accompaniment of various medical conditions and drug use (3). Familial history was also negative in this case. Grandiose delusions accompanied the picture. As a medical condition COLD was present. Manic episode occurred as a result of drug (varenicline) use.

Late-life onset manic episodes occur secondary to medical conditions or drug use with a high rate (2,3). In this case, no medical disease which would lead to a first manic episode at an advanced age could be found. It was found that the manic episode was related with varenicline use.

Varenicline is a $\alpha 4\beta 2$ nicotinic acetylcholine receptor partial agonist. It leads to dopamine release in the mesolimbic area (6). Investigations have shown that it is a complete agonist of $\alpha 7$ nicotinic acetylcholine receptors (4). In a study performed by Rollema et al., it was found that varenicline might display antidepressant efficiency by partial agonist binding to $\alpha 4\beta 2$ nicotinic receptors in mouse swimming experiment (13). The relation between bipolar disorder and dopamine has been reported (14). The fact that varenicline leads to manic episode in bipolar disorder and in healthy individuals as observed in this case suggests that this may be related with its causing to dopamine release and its potential antidepressant efficiency.

It has been shown that varenicline causes to manic episode in bipolar patients (15,16,17). Mixed episode was found in a case of schizoaffective disorder following use of varenicline (18). Development of mania was found in an individual who had no previous history of psychiatric disease during varenicline use (19). In a case presentation presented by Francois et al., it was reported that a 65-year old male patient started to have complaints including grandiose, paranoid delusions, insomnia, logorrhea and agitation for the first time following varenicline use in the first week and his complaints continued for the last one week, though he stopped using the drug. This patient was similar to our patient in terms of the findings and clinical onset, but no information was given about the disease severity in this case. In the case presentation reported by Francois et al., it was found that the findings regressed with pharmacotherapy in one week. In contrast, manic findings did not regress in one week following discontinuation of varenicline in our patient. The symptoms only regressed at the end of the third week of mood and antipsychotic treatment. In the Pubmed and Psychiatry Index screening, this patient is the second case in the international area and the first case in Turkey.

With use of varenicline, depressive mood, sleep disorder, suicide, agitation, aggression and psychotic reactions (4,5,6,7,8,9,10) have been reported in addition to manic episode symptoms (15,16,17,18,19). FDA reported that varenicline could lead to serious neuropsychiatric symptoms in the report published in 2009; FDA emphasized that worsening might be observed in pre-existing psychiatric diseases in patients with a history of schizophrenia, bipolar disorder and major depressive disorder (6).

With use of varenicline, serious psychiatric disorders occur in an increasing number of cases or exacerbation or worsening may occur in pre-existing psychiatric diseases. Therefore, the relation between varenicline and psychiatric findings should be addressed carefully. The present psychiatric state and previous psychiatric and familial histories in patients with smoking addiction who will use varenicline should be evaluated. It appears necessary that mental state examinations should be performed before starting varenicline treatment and in the follow-up during use of the drug. Patients and families should be informed about the potential side effects in the form of psychiatric findings.

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