Olgu sunumu / Case report

Restless legs syndrome in a bipolar disorder patient treated with olanzapine: is there an association?

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ABSTRACT

The aim of this case report is to report a case of restless legs syndrome (RLS) in a patient with bipolar disorder (BD) caused by olanzapine and to draw attention to possible relationship between BD and RLS. A female patient was diagnosed with mixed episode of BD. Olanzapine 10 mg/day was added to the extended release valproic acid 1000 mg/d treatment that the patient was using. In the next day after the beginning of olanzapine, itching, aching and tingling sensations begun in her legs at rest. She was diagnosed as RLS caused by olanzapine. Then the dose of olanzapine gradually reduced. But the symptoms were continuing at the dose of 2.5 mg/day. RLS symptoms disappeared in the next day after discontinuation of olanzapine. RLS has comorbidity with some psychiatric and neurologic disorders such as attention deficit/hyperactivity disorder (ADHD), depressive disorders, migraine. There are studies that showed genetic relationship between BD and both migraine and ADHD. As a result there might be an association between BD and RLS. These may account for the appearance of RLS with low dose olanzapine in this case. To our knowledge there are no studies about the association between BD and RLS and further research are needed on this subject. ***(Anatolian Journal of Psychiatry 2015; 16(4):301-303)***

Key words: *restless legs syndrome, bipolar disorder, association, olanzapine*

Olanzapinle tedavi edilen bir iki uçlu bozukluk hastasında huzursuz bacaklar sendromu: Bir ilişki var mı?

ÖZET

Bu olgu sunumunun amacı iki uçlu bozukluğu (İUB) olan bir hastada olanzapinin neden olduğu huzursuz bacaklar sendromu (HBS) olgusunu bildirmek ve İUB ile HBS arasındaki olası ilişkiye dikkat çekmektir. Bir kadın hastaya İUB karma atak tanısı konuldu. Hastanın kullanmakta olduğu uzun salınımlı valproik asid 1000 mg/gün tedavisine 10 mg/gün olanzapin eklendi. Olanzapin başlandıktan sonraki gün dinlenme sırasında hastanın bacaklarında kaşınma, ağrı ve karıncalanma hissi başladı. Hastaya olanzapine bağlı HBS tanısı konuldu. Olanzapin dozu kademeli olarak azaltıldı. Ancak 2.5 mg/gün dozunda belirtiler sürüyordu. Olanzapin kesildikten bir gün sonra HBS belirtileri düzeldi. HBS, dikkat eksikliği hiperaktivite bozukluğu (DEHB), depresif bozukluklar, migren gibi bazı psikiyatrik ve nörolojik bozukluklarla birlikte görülebilir. İUB ile hem migren, hem de DEHB arasında genetik ilişki olduğunu gösteren çalışmalar vardır. Sonuç olarak İUB ve HBS arasında bir ilişki olabilir. Bizim bilgimize göre İUB ve HBS arasındaki ilişki ile ilgili çalışma yoktur ve bu konu ile ilgili ileri araştırmalara gerek vardır. ***(Anadolu Psikiyatri Derg 2015; 16(4):301-303)***

Anahtar sözcükler: *Huzursuz bacaklar sendromu, iki uçlu bozukluk, ilişki, olanzapin*

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INTRODUCTION

Restless legs syndrome (RLS) is a commonly underdiagnosed sensory-motor disorder.[1] The prevalence of RLS had been shown to vary between 2.5-29.0% in the society throughout the world in studies that use different methods.[2] The underlying pathophysiological mechanism of RLS is not fully understood. RLS is categorized into two subgroups, primary RLS and secondary RLS.[3] The frequent causes of secondary RLS are chronic diseases such as renal insufficiency, pregnancy, iron deficiency anemia, diabetic neuropathy, and Parkinson's disease. Although it is thought that primary RLS is associated with brain iron deficiency causing dopaminergic dysfunction, the etiology of primary RLS is partially understood.[4] One of the reasons of RLS is the usage of some drugs such as neuroleptics, antidepressants. The data about drug induced RLS come from case reports. RLS due to clozapine,[5] haloperidol,[6] olanzapine,[7] quetiapine,[8] and risperidone[9] was reported in a few case reports. In this report, we discuss a case of RLS in a patient with bipolar disorder (BD) caused by low dose olanzapine.

CASE

A 50 year old female patient was admitted to psychiatric evaluation with the complaints of depressed mood, anhedonia, insomnia, irritability, distractibility, increased talkativeness, excessive buying, all of which started two months ago. At the time of admission, she was using risperidon 2 mg/day, bupropion 150 mg/day, valproic acid 1000 mg/day. After psychiatric evaluation, she was diagnosed with mixed episode of bipolar disorder and risperidon 2 mg/day, bupropion 150 mg/day was discontinued and instead, olanzapine 10 mg/day was added to the treatment. At the second visit two weeks after the combined use of olanzapine and valproic acid, our patient's psychiatric condition was partially improved. However, she presented with new complaints regarding her legs which started in the next day after alteration of drug regimen. There were itching, aching and tingling sensetions in her legs while sleeping or sitting which could only be relieved by walking. According to this medical history, a 'restless legs syndrome' was diagnosed. Her medical history was noncontributory and her psychiatric history did not reveal any previous sleep-related disorder. She had no prior history or family history of leg movement disorders. She had no physical illness. Neurologic examination was normal. Laboratory tests and electromyelography (EMG) formed to investigate the situations that could cause RLS. The laboratory data did not reveal any evidence of renal failure or anemia. Her iron and ferritin levels were within normal limits. Two weeks later olanzapine dose was decreased to 5 mg/day since it was considered as the cause of RLS. At the control visit two weeks after the dose reduction she was euthymic but tingling sensation in her both legs were continuing. Then olanzapine dose was decreased to 2.5 mg/day. After 10 days she was still euthymic and feeling of restlessness in her legs were going on despite the decrease in the severity of her symptoms after dose reduction. Therefore olanzapine was discontinued. One day after the discontinuation of the drug her symptoms faded away.

DISCUSSION

For the treatment of RLS, several treatment modalities with using drugs and without medication (stay away from alcohol and caffeine, etc.) are recommended according to the severity and frequency of symptoms.[10]

In this case we consider that RLS is not a result of combined used of extended release valproic acid and olanzapine. We thought that olanzapine is responsible for the emergence of RLS. Because in some studies it was shown that extended release valproic acid can be used as an alternative to other drugs in the treatment of RLS.[11] Moreover, in some studies it was suggested that extended release of valproic acid decreases the serum levels of olanzapine in the combined use.[12] Use of the Naranjo probability scale indicated a probable relationship between RLS and olanzapine therapy for this patient.[13]

This case highlights an unusual manifestation of RLS. Despite the under extended-release valproic acid treatment, which is a known procedure to improve RLS symptomatology and to decrease olanzapine plasma levels, RLS was observed in our case. Unlike other studies, accept one case that was diagnosed as bipolar disorder type 2,[7] the RLS was occurred with low dose olanzapine (2.5 mg/day) in our report.

It was demonstrated that, a high degree of comorbidity between migraine and BPD in studies that was using different methods. However, the joint neurobiological mechanism of these disorders remains unclear.[14] It was suggested that some genes may contribute to both BPD and migraine.[15] Addition to the similarities in terms of clinical symptoms of ADHD and BD, in some

studies it was shown that there might be a common genetic structure.[16]

Dopaminerjic dysregulation is accused in the pathogenesis of BD[17] and RLS.[4]

The association between RLS and migraine has been reported in recent studies. Underlying pathophysiological mechanism of these two conditions is unclear yet.[18] Prior studies had showed that there is a genetic association between RLS and attention deficit/hyperactivity disorder (ADHD).[19]

Manifestation of RLS despite the slow-release valproic acid in this case and the aforementioned relationships between BD and migraine, ADHD and migraine, ADHD and RLS to presume a possible predilection of bipolar disorder patients to RLS. Evidence showing dopaminergic dysfunction in ADHD, BPD, RLS and migraine also supports our presumption. To our knowledge there are no studies on this topic. Further studies are needed to evaluate this hypothesis

REFERENCES

1. *Ondo WG, Jancovic J. Restless legs syndrome: clinicoetiologic correlates. Neurology 1996; 47(6):1435-1441.*
2. *Rothdach AJ, Trenkwalder C, Haberstock J, Keil U, Berger K. Prevalence and risk factors of RLS in an elderly population: the MEMO study. Memory and morbidity in Augsburg elderly. Neurology 2000; 54(5):1064-1068.*
3. *Gkizlis V, Giannaki CD, Karatzaferi C, Hadjigeorgiou GM, Mihas C, Koutedakis Y, et al. Uremic versus ıdiopathic restless legs syndrome: ımpact on aspects related to quality of life. ASAIO J 2012; 58(6):607-611.*
4. *Sethi KD, Mehta SH. A clinical primer on restless legs syndrome: what we know, and what we don't know. Am J Manag Care 2012; 18(5):83-88.*
5. *Duggal HS, Mendhekar DN. Clozapine-associated restless legs syndrome. J Clin Psychopharmacol 2007; 27(1):89-90.*
6. *Horiguchi J, Yamashita H, Mizuno S, Kuramoto Y, Kagaya A, Yamawaki S, et al. Nocturnal eating/ drinking syndrome and neuroleptic-induced restless legs syndrome. Int Clin Psychopharmacol 1999; 14(1):33-36.*
7. *Aggarwal S, Dodd S, Berk M. Restless leg syndrome associated with olanzapine: a case series. Curr Drug Saf 2010; 5(2):129-131.*
8. *Buturak SV, Yazici K, Yazici AE, Tot S, Basterzi AD. Restless legs syndrome in an elderly patient induced by combined use of low dose quetiapine and citalopram. Bulletin of Clinical Psychopharmacology 2012; 22(3):271-274.*
9. *Wetter TC, Brunner J, Bronisch T. Restless legs syndrome probably induced by risperidone treatment. Pharmacopsychiatry 2002; 35(3):109-111.*
10. *Allen RP, Picchietti D, Hening WA, Trenkwalder C, Walters AS, Montplaisi J. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology. A report from the restless leg syndrome diagnosis and epidemiology workshop at the National Institute of Health. Sleep Med 2003; 4(2):101-119.*
11. *Buchfuhrer MJ. Strategies for the Treatment of Restless Legs Syndrome. Neurotherapeutics 2012; 9(4):776-790.*
12. *Eisensehr I, Ehrenberg BL, Rogge Solti S, Noachtar S. Treatment of idiopathic restless legs syndrome (RLS) with slow-release valproic acid compared with slow-release levodopa/benserazid. J Neurol 2004; 251(5):579-583.*
13. *Haslemo T, Olsen K, Lunde H, Molden E. Valproic Acid significantly lowers serum concentrations of olanzapine-an interaction effect comparable with smoking. Ther Drug Monit 2012; 34(5):512-517.*
14. *Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981; 30(2):239-245.*
15. *Minton GO, Young AH, McQuade R, Fairchild G, Ingram CD, Gartside SE. Profound changes in dopaminergic neurotransmission in the prefrontal cortex in response to flattening of the diurnal glucocorticoid rhythm: implications for bipolar disorder. Neuropsychopharmacology 2009; 34(10):2265-2274.*
16. *Khalid I, Rana L, Khalid TJ, Roehrs T. Refractory restless legs syndrome likely caused by Olanzapine. J Clin Sleep Med 2009; 5(1):68-69.*
17. *Kang SG, Lee HJ, Kim L. Restless legs syndrome and periodic limb movements during sleep probably associated with olanzapine. J Psychopharmacol 2009; 23(5):597-601.*