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Manic Episode Induced by Discontinuance of D-Penicillamine Treatment in Wilson's Disease

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ÖZET:

Wilson hastalığında D-Penisillamin tedavisinin kesilmesiyle indüklenen manik atak

Wilson hastalığı; değişik derecelerde hepatik, orbital ve nöropsikiyatrik hastalığa yol açan, insan bakır metabolizmasının nadir görülen otozomal resesif geçişli kalıtsal bir hastalığıdır. Nöropsikiyatrik semptomlar beyinde biriken bakırın nöronlarda, özellikle bazal ganglionlarda oluşturduğu dejenerasyona bağlıdır. Klinisyenler, manik atak ile başvuran Wilson hastasında, bakır toksisitesinin atağı tetiklemiş olabileceğini akla getirmelidir. Wilson hastalığında dirençli manik belirtiler ile karşılaşıldığında, bakır toksisitesi tedavisi sorgulanmalı ve gerekli konsültasyonlar istenmelidir. Bu yazıda, bir Wilson hastasında d-penisillamin tedavisinin kesilmesiyle ortaya çıkan manik atak sunulmuş ve psikiyatrik tedaviye d-penisillaminin eklenmesi ile klinik belirtilerdeki iyileşme vurgulanmıştır.

Anahtar sözcükler: manik atak, Wilson hastalığı, d-penisillamin

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ABSTRACT:

Manic episode induced by discontinuance of D-penicillamine treatment in Wilson's disease

Wilson's disease (WD) is a rarely seen autosomal recessive inherited genetic disease of copper metabolism, which leads to various hepatic, orbital and neuropsychiatric disorders. Neuropsychiatric symptoms are due to degeneration that results from the acccumulation of copper in the neurons of the brain, especially in the basal ganglia. Clinicians should consider that toxicity of copper might trigger the episode in a patient with WD, who displays a manic episode. When persistent manic symptoms are encountered in WD, treatment of copper toxicity should be checked and necessary consultation should be performed. In this case report, a patient with WD who developed a manic episode as a result of stopping d-penicillamine treatment is presented, and improvement of clinical symptoms when d-penicillamine was added to the psychiatric treatment is emphasized.

Keywords: manic episode, Wilson's disease; d-penicillamine

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INTRODUCTION

Wilson's disease (WD) is a rarely seen autosomal recessive genetic disease of copper metabolism, which leads to various hepatic, orbital and neuropsychiatric disorders as a result of the collection of copper in the cornea, liver and brain[1]. While some investigators have noted that psychiatric symptoms were apparent at the time of initial presentation in 65% of individuals with WD, most reports indicate a frequency in the range of 20%. It has also been noted that these symptoms were sufficiently severe to warrant psychiatric intervention in almost 50% before the diagnosis of WD was made[2]. The psychiatric manifestations of WD can be categorized into five groups of symptoms: personality changes, affective disorders, psychosis, cognitive impairment, and others. WD patients have a higher lifetime prevalence of DSM-IV major depressive disorders

(OR= 5.7, 95% CI 2.4–17.3) and bipolar disorders (OR= 12.9, 95% CI 3.6–46.3)[3]. In a cross-sectional analysis, among 50 confirmed patients with WD, distribution of the 12 patients (24%) with syndromic psychiatric diagnoses were reported as follows: bipolar affective disorder (18%), major depression (4%), and dysthymia (2%)[4].

In this case report, a patient with WD who developed a manic episode as a result of stopping d-penicillamine treatment is discussed and improvement of clinical symptoms when d-penicillamine was added to the psychiatric treatment is emphasized.

CASE REPORT

We report the case of 22-year-old female patient was diagnosed with WD when she was five. She had a depressive attack with psychotic signs for the first time when she was fifteen. When she was eighteen, she was diagnosed with bipolar affective disorder (BPAD) due to a manic episode induced by discontinuance of d-penicillamine. A year later, she was hospitalized with a second manic episode as a result of irregular treatment. She was prescribed 1000 mg/day valproic acid, 400 mg/day quetiapine, 1 mg/day risperidone, 300 mg/day d-penicillamine and 1 capsule/day zinc sulphate for maintenance therapy. The patient, who was in remission until November 2011, was referred to the emergency department by her relatives with complaints of insomnia, anger and aggressiveness to her father. In medical her history, it was learned that her complaints has begun after she could not use d-penicillamine for the last week. When her complaints increased, she also discontinued her psychiatric treatment. She was hospitalized and irritability, psychomotor agitation, increase in the speed of speech, insomnia, lack of appetite, reference and persecution ideas, grandiosity, euphoric mood and distractibility were noted in the psychiatric examination. In the neurologic examination, tremor was observed in the hands. The level of total serum copper was 11 µg/dL (normal range: 80-155 µg/dL). Valproic acid 1000 mg/day, quetiapine 300 mg/day, quetiapine XR 400 mg/day and olanzapine 20 mg/day were prescribed; d-penicillamine could not have given due to the lack of the drug for 3 weeks. In this period, her symptoms did not decrease despite the treatment of the manic episode. After delivery of the drug, treatment of WD was designed by internal medicine consultation as 600mg/day d-penicillamine. A marked decrease was seen in the symptoms of the manic episode after the addition of d-penicillamine to the treatment within 2 weeks. The patient was still in remission at the follow-up period for two years with the maintenance treatment of 1000 mg/day valproic acid, 300 mg/day quetiapine and 600 mg/day d-penicillamine.

DISCUSSION

In WD, while total serum copper is decreased, free copper level is increased. In other words, the amount of copper in the circulation increases. In this way, the central nervous system is affected mostly by the copper toxicity[5]. Neuropsychiatric symptoms are due to degeneration that results from the accumulation of copper in the neurons of the brain, especially in the basal ganglia[6]. Also, thalamic and hypothalamic presynaptic dopamine and serotonin transporters decrease due to the accumulation of copper[7,8]. D-penicillamine, used in the treatment of WD, acts by increasing urinary copper excretion[5]. In the present case, the circulating copper level was increased due to the lack of d-penicillamine for the previous week. The manic episode was thought to be induced by neurodegeneration caused by high copper levels. The same cause is suggested for the first manic episode of the patient which was induced by discontinuance of d-penicillamine. Also, her clinical symptoms did not decrease despite the treatment of manic episode for 3 weeks until delivery of d-penicillamine. Her clinical symptoms have decreased from the beginning of d-penicillamine treatment together with manic episode treatment. Despite manic episode treatment, ongoing basal ganglia degeneration due

to copper toxicity may render the patient resistant to treatment. While discontinuation of d-penicillamine treatment is important in the induction of manic episode, addition of d-penicillamine to the treatment is also important in the treatment of the manic episode.

Machado et al.[9] have reported a patient with WD, who was treated only by d-penicillamine without any specific treatment for BPAD and remained non-symptomatic during the eight-year follow-up period. As we learnt from her medical history, our patient did not have any manic episodes while she took d-penicillamine regularly. D-penicillamine seems to keep the patient with BPAD and WD in remission in terms of manic episodes. Thus, we also think that neurodegeneration in the basal ganglia plays an important role in the pathophysiology of BPAD in WD.

In conclusion, clinicians should consider that toxicity of copper may trigger the episode in a patient with WD who presents with a manic episode. Moreover, when persistent manic symptoms are encountered in WD, treatment of copper toxicity should be checked and the necessary consultation should be performed.

References:

1. Tug E, Balaban YH. Wilson's Disease: A Case Report. Tigris Medical Journal-Dicle Tıp Dergisi 2007;34:57-60. (Turkish)
2. Pfeiffer RF. Wilson's Disease. Semin Neurol 2007;27:123-32. **[CrossRef]**
3. Carta MG, Sorbello O, Moro F, Bhat KM, Demelia E, Serra A, et al. Bipolar disorders and Wilson's disease. BMC Psychiatry 2012;12:52. **[CrossRef]**
4. Shanmugiah A, Sinha S, Taly AB, Prashanth LK, Tomar M, Arunodaya GR, et al. Psychiatric manifestations in Wilson's disease: a cross-sectional analysis. J Neuropsychiatry Clin Neurosci 2008;20:81-5. **[CrossRef]**
5. Yigit M, Ozkan D, Altunsoy-Sen N, Goka S, Bozdogan Z. Psychosis as the first manifestation of Wilson's disease. Klinik Psikofarmakoloji Bülteni-Bulletin of Clinical Psychopharmacology 2014;24(Spull 1):S235.
6. Koç M, Serhatlioglu S, Orhan H. Reversible cranial MRI findings in patients with psychiatric symptoms applicant Neuro-Wilson. Fırat Medical Journal 2007;12:234-6. (Turkish)
7. Carta M, Mura G, Sorbello O, Farina G, Demelia L. Quality of Life and Psychiatric Symptoms in Wilson's Disease: the Relevance of Bipolar Disorders. Clin Pract Epidemiol Ment Health 2012;8:102-9. **[CrossRef]**
8. González-Estecha M, Trasobares EM, Tajima K, Cano S, Fernández C, López JL, et al. Trace elements in bipolar disorder. J Trace Elem Med Biol 2011;25:78-83. **[CrossRef]**
9. Machado AC, Deguti MM, Caixeta L, Spitz M, Lucato LT, Barbosa ER. Mania as the first manifestation of Wilson's disease. Bipolar Disord 2008;10:447-50. **[CrossRef]**