



# **Topiramate Induced Restless Legs Syndrome: Case Report**

## **Topiramate ile Ortaya Çıkan Huzursuz Bacaklar Sendromu: Olgu Sunumu**

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### **Summary**

Several medications can exacerbate or cause Restless Legs syndrome (RLS). Topiramate is an antiepileptic drug used to epilepsy and migraine treatment. In literature, number of case with topiramate induced RLS is very rare. Herein, we present the case with topiramate induced RLS, in which the case takes to topiramate for migraine prophylaxis. However, how topiramate causes RLS is exactly unknown. Probably, topiramate has an antidopaminergic effect. (*JTSM 2014;1:36-7*)

**Key Words:** Topiramate, restless legs syndrome, antidopaminergic effect

### **Özet**

Bazı medikal ajanlar, Huzursuz Bacaklar sendromu (HBS) oluşumuna ya da mevcut hastalık semptomlarında artmaya neden olabilirler. Topiramate, günümüzde epilepsi ve migren tedavisinde yoğun olarak kullanılan antiepileptik bir ajandır. Topiramatin neden olduğu HBS olgu sayısı literatürde oldukça azdır. Biz burada, topiramatin neden olduğu bir HBS olgusunu sunuyoruz. Bununla birlikte, topiramatin nasıl HBS'ye yol açtığı tam olarak bilinmemektedir. Olasılıkla, topiramate antidopaminergic bir etkiye sahiptir. (*JTSM 2014;1:36-7*)

**Anahtar Kelimeler:** Topiramate, huzursuz bacaklar sendromu, antidopaminergic etki

### **Introduction**

Restless Legs syndrome (RLS) is a common sensorimotor disorder that is characterized by an urge to move the legs (and, rarely, the arms as well) and peculiar, unpleasant sensations. The diagnosis is based on clinical criteria: an urge to move the legs, symptoms occurring during periods of rest; symptoms relieving by movement; and symptoms worsen in the evening or night (1). Several medications including antipsychotics, antidepressants, antihistamines, antiemetics and antiepileptics such as phenytoin, zonisamide can exacerbate or cause RLS (2). However, some antiepileptic drugs have been suggested as alternative to dopaminergic agents for RLS treatment (3,4). Topiramate (TPM) is an antiepileptic drug used in epilepsy and migraine treatment (5). We report one case with topiramate induced RLS.

### **Case**

A 29 year old woman affected by migraine without aura started to use topiramate as prophylactic treatment. It was gradually titrated up to 100 mg bid. Migraine attacks were reduced, but at the third month of treatment, she reported numbness in her legs especially during inactivity and in the evening. Her complaint was relieved by movement. There

were no similar symptoms in patient's history before migraine prophylactic treatment with topiramate. Serum studies (blood count, electrolytes, liver and renal function, thyroid hormones, iron, iron binding capacity, ferritin and vitamin B12 levels) and electroneurography were normal. We applied to International RLS rating scale (IRLS) (6) and she had moderate RLS symptoms (IRLS score 18). After 2 weeks TPM had been terminated, IRLS was repeated (IRLS score 4).

### **Discussion**

It is thought that basic pathology in RLS is dopaminergic deficiency. There are several cases with TPM induced RLS (7,8). TPM has been essentially used as a wide spectrum antiepileptic agent. However, in the other pathologies such as migraine, neuropathic pain, essential tremor and impulse control disorder, it has been effectively used. Action mechanism of TPM is multiple including gabaergic effect via GABA A receptor, antiglutamatergic effect via AMPA and kainate receptors, blockage of voltage gated sodium and calcium channels, and inhibition of carbonic anhydrase (9). It has been fully unknown relationship between TPM and dopaminergic system has not been reported before. However, in a study, TPM

has showed to reduce levodopa induced dyskinesias in MPTP lesioned primates (10). This result has suggested that TPM has antidopaminergic effect.

TPM induced RLS can be possible with regard to dopaminergic deficiency in RLS and antidopaminergic effect of TPM. Thus, we have to keep alert for RLS when using drugs like TPM with wide effect spectrum.

## References

1. Allen RP, Picchietti D, Hening WA, Trenkwalder C, Walters AS, Montplaisir J; Restless Legs Syndrome Diagnosis and Epidemiology workshop at the National Institutes of Health; International Restless Legs Syndrome Study Group. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology: a report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. *Sleep Med* 2003;4:101-19.
2. Lesage S, Hening WA. The restless legs syndrome and periodic limb movement disorder: a review of management. *Semin Neurol* 2004;24:249-59.
3. 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/ benserazide. *J Neurol* 2004;251:579-83.
4. Youssef EA, Wagner ML, Martinez JO, Hening W. Pilot trial of lamotrigine in restless legs syndrome. *Sleep Med* 2005;6:89.
5. Silberstein SD, Ben-Menachem E, Shank RP, Wiegand F. Topiramate monotherapy in epilepsy and migraine prevention. *Clin Ther* 2005;27:154-65.
6. Walters AS, LeBrocq C, Dhar A, Hening W, Rosen R, Allen RP, Trenkwalder C; International Restless Legs Syndrome Study Group. Validation of the International Restless Legs Syndrome Study Group rating scale for restless legs syndrome. *Sleep Med* 2003;4:121-32.
7. Romigi A, Izzi F, Placidi F, Sperli F, Cervellino A, Marciani MG. Topiramate-induced restless legs syndrome: A report of two cases. *J Neurol* 2007;254:1120-1.
8. Bermejo PE. Restless legs syndrome induced by topiramate: two more cases. *J Neurol* 2009;256:662-3.
9. Schank RP, Gardocki JF, Streeter AJ, Maryanoff BE. An overview of the preclinical aspects of topiramate: pharmacology, pharmacokinetics and mechanism of action. *Epilepsia* 2000;41 Suppl 1:S3-9.
10. Silverdale MA, Nicholson SL, Crossman AR, Brotchie JM. Topiramate reduces levodopa-induced dyskinesia in the MPTP-lesioned marmoset model of Parkinson's disease. *Mov Disord* 2005;20:403-9.