



A Case with Dyskinesia Induced by Pramipexole, Pregabalin and Gabapentin After Cardiopulmonary Resuscitation

Kardiyopulmoner Resusitasyon Sonrası Pramipeksol, Pregabalin ve Gabapentin Kullanımının Tetiklediği Diskinezi Olgusu

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Summary

Drug-induced dyskinesias can be seen occasionally in clinical practice. Here we present a 70-year-old patient who developed a noticeable dyskinesia after the use of pramipexole, gabapentin, pregabalin respectively for his restless leg syndrome. Prior to this condition, he was hospitalized in intensive care unit for the myocardial infarction that required cardiopulmonary resuscitation, and he was discharged with no neurological deficits. The case presented here is a good example indicating the importance of being vigilant for drug-induced dyskinesias after hypoxic-ischemic encephalopathy, even though everything else seems right. (*Turkish Journal of Neurology* 2013; 19:148-150)

Key Words: Hypoxic-ischemic encephalopathy, dyskinesia, pramipexole, gabapentin, pregabalin

Özet

İlaç kullanımı sonrasında ortaya çıkan hareket bozuklukları klinik pratikte zaman zaman karşılaştığımız sorunlardır. Burada kardiyopulmoner resusitasyon gerektiren bir miyokard enfarktüsünün ardından bir süre yoğun bakımda kalan, nörolojik defisiti kalmadan iyileşen ancak daha sonra huzursuz bacak sendromu tedavisi için başlanan pramipeksol, onun ardından verilen gabapentin ve pregabalin'in her birinin arkasından belirgin diskinezi gelişen 70 yaşında bir hasta sunuldu. Hipoksik ensefalopati sonrasında gelişen hareket bozuklukları bilinmektedir. Ancak bu hastada olduğu gibi her şey yolunda görünürken ilaç verilmesinin arkasından diskinezilerin gelişmesi, hipoksik ensefalopati geçirmiş hastaların takip ve tedavisinde dikkatli olunması gerektiğine işaret etmektedir. (*Türk Nöroloji Dergisi* 2013; 19:148-150)

Anahtar Kelimeler: Hipoksik-iskemik ensefalopati, diskinezi, pramipeksol, gabapentin, pregabalin

Introduction

Movement disorders developing as reactions to drugs pose important clinical problems. The most common drugs in the etiology are antipsychotic, anticonvulsant, antiemetic, antiparkinson drugs, calcium channel blockers, central nervous system (CNS) stimulants, antidepressants, sympathomimetics and lithium (1). Myoclonus, dystonia, akinetic rigidity syndromes, tremor and chorea may occur following hypoxic-ischemic brain damage, even a long time after the actual hypoxic damage (2,3). Here, we present the case of a patient who had hypoxic-ischemic encephalopathy following cardiac arrest, and later developed restless leg syndrome (RLS) and dyskinesia due to the drugs he was taking for his diabetic polyneuropathy.

Case

Seventy-year-old male patient consulted in our clinic for the feeling of restlessness in his leg and the need to constantly move it when he went to bed at night in addition to the ensuing sleeplessness. His medical history showed that he had cardiopulmonary resuscitation during the myocardial infarction he had, remained unconscious for a few days and kept in coronary intensive care unit and then was discharged. During that time, he was unable to take pramipexole (morning 0.25; noon 0.250; evening 0.5 mg) that was prescribed for his RLS complaint 3 years ago. He was conscious, cooperative and oriented in his neurological examination. His mental evaluation showed "cognitive decline in multiple areas" (he lost 2 points in attention and arithmetic, 1 point in recall and 1 point in language functions in Standardized

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Received/Geliş Tarihi: 11.02.2013 **Accepted/Kabul Tarihi:** 22.07.2013

Mini Mental Test). His upper and lower muscle strength was full and there were no involuntary movements in his motor examination. He showed glove-stocking type hypoesthesia in the sensory examination; Deep tendon reflexes were normoactive in the upper and hypoactive in the lower extremities and he did not have pathological reflexes. His medical history included diabetes mellitus, hypertension and coronary artery disease and his familial medical history was unremarkable. He had normal hemogram, blood sugar, urea, creatine, liver function tests, electrolytes, erythrocyte sedimentation speed, C-reactive protein, thyroid function tests, complete urine test and PA lung graphy. His diffusion-weighted magnetic resonance images (MRI) taken during coronary intensive care period were normal. Axial T2A flair image taken in the same period showed a few periventricular nonspecific gliotic lesions and age-related cortical atrophy (Figure 1).

The patient was started again on pramipexole which he previously found beneficial in the same doses that he used to take (3 x 0.125 mg) and scheduled for a follow-up. After a few days, however, the patient came back to our clinic and described small amplitude, irregular, jerky, generalized choreiform movement complaints apparent on the distal part of both upper extremities. The dyskinesia went away after the drug was stopped. After two months, the patient still had RLS symptoms and was diagnosed as diabetic peripheral neuropathy after an electromyography examination. He was started on pregabalin (150 mg/day) but it was stopped a day later after his dyskinesia returned. Dyskinesia completely disappeared after termination of pregabalin. After a few weeks, he came to our polyclinic again with the RLS and neuropathic pain. This time he was prescribed 3 x 300 mg gabapentin to be increased gradually over time. Again, this drug also caused serious generalized dyskinesia, which later on disappeared when the treatment was stopped. The patient expressed some relief after starting a low dose of clonazepam.

Discussion

The neurological findings and signs following cardiopulmonary arrest are directly related to the brain region where the damage is seen. Areas with higher metabolic rates and thus bigger oxygen consumption or those receiving relatively smaller amounts of total brain blood circulation are more susceptible to cerebral ischemia (4,5). Basal ganglia are also one of such areas; the movement and coordination disorders, akinetic, dystonic or hyperkinetic syndromes following cardiac arrests are often associated with damage on these areas and/or the ones that they project to (6).

The chorea or dystonia due to the encephalography following resuscitation can also be caused by cellular hypoxia in addition to global or focal hypoperfusion. As a result, inhibitory neurotransmitter levels decline and striatal cholinergic system increases following hypoxia and/or ischemia (3). There have also been reports of a hiatus between the hypoxic damage and the onset of movement disorders which can extend from months to years (7). This duration may potentially reflect the amount of time required for remyelination, inflammatory changes, ephaptic transmission, oxidative reactions, aberrant synaptic reorganization, transsynaptic

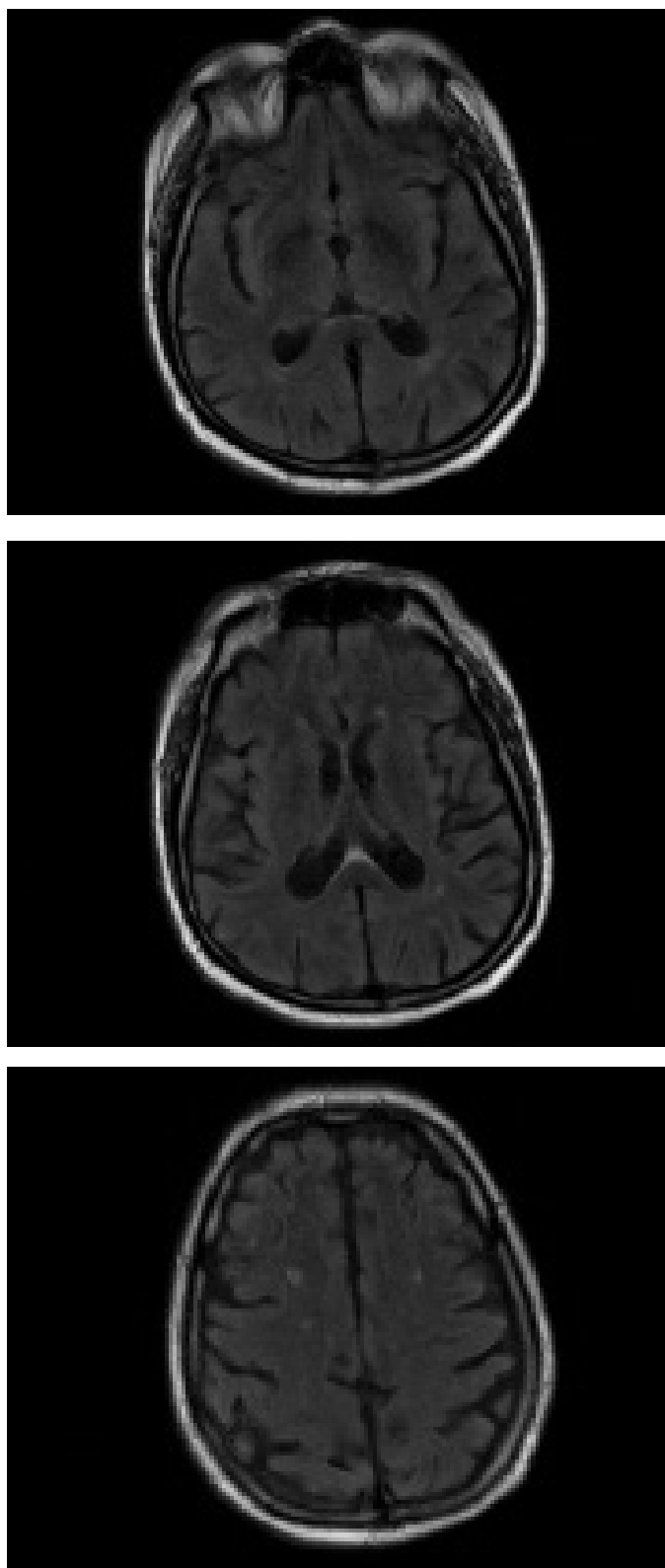


Figure 1 A, B, C. Some non-specific gliotic white matter changes and cortical atrophy seen in patient's T2-flair images.

neuronal degeneration or the formation of denervation-induced receptor oversensitivity to take place (3,7,8).

In clinical practice, dyskinesias dependent on L-DOPA are frequently reported. Those that are dependent on dopamine agonists like pramipexole are less frequent (9). Gabapentin is one of the new generation of antiepileptics and it is frequently being used in the treatment of neuropathic pain. While its activity mechanism has not been fully explored, it is known to be structurally similar to GABA. It has also been shown to increase GABA production and circulation in animal models and human brain (10). Movement disorders such as dystonia, chorea, hemichorea, bilateral ballismus, myoclonus and ataxia have been shown as a result of gabapentin use (11,12). Much like the other antiepileptics, the antidopaminergic mechanism has been the main focus in the etiology of these movement disorders (11). Both pregabalin and gabapentin structurally resemble GABA. Both molecules bind to L-type voltage-gated calcium channels and establish presynaptic neurotransmitter regulation (13). Certain movement disorders such as tremor, parkinsonism and asterixis have also been reported in pregabalin use (14,15).

The complexity of the encephalitis conditions resulting from cardiac resuscitation and the multitude of the factors at play make the understanding of the damage mechanisms extremely difficult (4,16). In this patient, it is possible that the cellular and/or neurotransmitter-level damage at the basal ganglia or other hypoxia-sensitive structures may have amplified the oversensitivity to dopaminergic and antiepileptic medicine. It is clear that a general understanding of this topic will benefit from future research. In conclusion, the emergence of dyskinesia as a result of medication suggests that movement disorders may occur in patients with a history of ischemic encephalopathy even though they might not have neurological deficits.

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