Levetiracetam-Responding Paroxysmal Nonkinesigenic Dyskinesia

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Abstract
We report on a patient with 7-year history of short-lasting paroxysmal nonkinesigenic dyskinesia. The episodes occurred 100 to 125 times per day, lasted from 5 seconds to 3 minutes, and were not suppressed with sleeping, underlining the heterogeneity of phenomenology in paroxysmal dyskinesias. Neuroimaging studies showed calcifications in the basal ganglia, thalamus, brain stem, and subcortical and cerebellar regions. He was diagnosed with idiopathic hypoparathyroidism. After failure of valproate, he responded well to levetiracetam (1000 mg/d). This report revealed that intracerebral calcifications secondary to hypoparathyroidism could present as paroxysmal nonkinesigenic dyskinesia, and levetiracetam could be effective in this particular entity.

Key Words: levetiracetam, paroxysmal, dyskinesia, hypoparathyroidism

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Paroxysmal nonkinesigenic dyskinesia (PNKD) is a rare hyperkinetic movement disorder which is mostly idiopathic and unresponsive to medications.1 Levetiracetam (LEV) is a new antiepileptic drug which is used as adjunct in the treatment of partial seizures. It is the more potent S enantiomer of piracetam and generally well tolerated with a lower rate of adverse events in long-term usage.2 Effectiveness of LEV in various movement disorders including tardive dyskinesia, Huntington disease, and paroxysmal kinesigenic dyskinesia was reported previously.3–5 We report on a young man who was admitted to our institute with a 7-year history of short-lasting PNKD. He was detected to have intracerebral calcifications secondary to idiopathic hypoparathyroidism (IHP), and PNKD was well responded to LEV therapy.

CASE REPORT
A 25-year-old man was admitted to our institute with the complaint of abnormal movement episodes in his extremities for 7 years. These involuntary movements were composed of brief rapid purposeless movements of the distal parts of his extremities and a bit slower movements with larger amplitude in the proximal parts. They occurred in form of attacks that lasted from 10 seconds to 5 minutes both while awake and asleep. There was no associated alteration of consciousness during the episodes. He was misdiagnosed as having epilepsy in another medical center, and sodium valproate treatment was given. The dosage was increased to 1500 mg/d, but the attacks were not suppressed during the 5-year follow-up period. Repeat electroencephalography studies did not reveal any epileptiform discharge during this period. The frequency of attacks has increased over the years from once in a day to 130 in a day. His neurological examination was completely normal. He had no history of convulsion or developmental delay in childhood. There was no family history of neurological disease.

The attacks were observed in the examination room spontaneously. They mostly occurred as unilateral choreatoathetotic spasm; sometimes, they occurred bilaterally. The athetoid movements were observed both in the upper and lower extremities; sometimes, these occurred bilaterally, causing a great disability. Choreiform movements were also seen in the distal parts of the involved extremities simultaneously. Sometimes, dystonic spasms on the neck muscles accompanied these choreatoathetotic attacks. Sudden body movements (jumping, standing up or starting to run immediately, and holding up the hands) did not provoke these episodes.

He had frequent PNKD attacks during the inpatient clinical follow-up. Prolonged electroencephalography recordings during and after the attacks did not reveal any abnormality. The duration was between 5 seconds and 3 minutes. The attacks were seen 108, 121, and 116 times, respectively, during the first 3 days. Consciousness was never altered. The episodes were also recorded during sleeping, their frequency did not change with sleeping. He would be awakened by the event, but he would quickly return to sleep.

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Computerized tomography of the brain revealed bilateral massive calcifications in the basal ganglia, thalamus, brain stem, and subcortical and cerebellar regions (Fig. 1). Serum calcium level was low (4.5 mg/dL) and intact parathyroid hormone level was undetectable (<3 pg/L) in serum. Further laboratory investigations including complete blood cell count, sedimentation rate, renal and liver function tests, thyroid hormone levels, growth hormone, cortisol, ceruloplasmin levels, and viral markers did not reveal any abnormality. He was diagnosed with HPP, and elementary calcium replacement and 1α-hydroxyvitamin D3 were started. Hypocalcemia was resolved at the end of first week.

Upon the failure of valproate treatment, it was ceased, and oxcarbazepine (600 mg/d) was introduced on the fourth day of hospitalization. However, it was stopped upon drug eruption on the second day. The attacks were seen 124 and 110 times, respectively, within these 2 days. In the sixth day, LEV (1000 mg/d) treatment was introduced. Two attacks were observed within 2 hours after the intake of the pills, and no more attack was observed within the next 5-day follow-up. After the serum calcium level was normalized and the patient was informed, LEV intake was interrupted for 2 days to confirm if the improvement is caused by LEV. The attacks were seen 105 and 121 times, respectively, within these 2 days. Reintake of LEV resulted in complete relief again. The patient did not report any new attack within 2 months after discharge.

**DISCUSSION**

Paroxysmal dyskinesias (PDs) are characterized with recurrent involuntary movement attacks in which abnormal movements are absent between the episodes. In 1977, Lance classified PDs into 3 main types. In paroxysmal dystonic choreoathetosis or paroxysmal nonkinesigenic choreoathetosis, the attacks last from 10 minutes to 4 hours and are precipitated by alcohol, caffeine, fatigue, or emotional stress. Nonkinesigenic character indicates that abnormal movements are not induced with sudden body movements and could be seen spontaneously even at rest as in our case. However, the attacks

![Bilateral massive calcifications in subcortical region, basal ganglia, brain stem, and cerebellar regions.](image)

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occur in longer durations and with much less frequency than the ones of our subject. In paroxysmal kinesigenic choreoathetosis (PKC), the episodes are provoked by sudden movements and suppressed with sleeping. They could be seen more than 100 times per day, usually as unilateral choreoathetosis spasms lasting seconds to 5 minutes. The temporal aspects of the episodes in our case are more similar with PKC. However, the attacks are not provoked by sudden movements and sometimes occur bilaterally and during sleeping period. In paroxysmal exercise-induced dystonia, the attacks are provoked by prolonged exercise and last between 5 and 30 minutes. Therefore, the PD of our case was not similar to any classic type in Lance’s classification.

In 1995, Demirkiran and Jankovic proposed a new classification based chiefly on precipitating events, duration of attacks, and etiology. Paroxysmal kinesigenic dyskinesia (PKD), and paroxysmal exertion-induced dyskinesia were further divided into short-lasting (5 minutes or less) and long-lasting forms (more than 5 minutes). Depending on etiology, each patient was further distinguished as either idiopathic or secondary. However, there is also limited number of reports in the current literature about the patients representing the proposed subcategories. Our case could be considered within short-lasting secondary PKD.

Multiple sclerosis, stroke, hypoxia, trauma, encephalitis, hyperthyroidism, hypoglycemia, and basal ganglia calcifications were identified as causing PD. Paroxysmal dyskinesia, as a sign of IHP, has also been rarely described. To date, 5 cases of IHP have been reported to present with PKC, whereas only 2 reports associated it with PNKC. Our case responded well to an antiepileptic (LEV) excellently, and sleeping did not relieve the dyskinesia in opposition to previous reports.

An impaired function of the basal ganglia causing an impairment of the indirect pathway of the thalamocortical basal ganglionic circuitry is suggested to underlie the PD and choreic phenomena. Positron emission tomography and single photon emission computed tomography studies also impress the abnormalities of perfusion and metabolism in the basal ganglia of these patients. In an IHP patient with PKC, Volonte et al reported ventral striatum hypometabolism that regressed after the disappearance of the clinical symptoms with normalization of serum calcium level. They suggested that hypocalcemia, not calcium deposits, is responsible for the altered function of the basal ganglia. This might have also been true for our case, and LEV might be thought as exerting its antidyskinetic effect by regulating calcium current in basal ganglia neurons as in other regions presumed in studies with experimental models of epilepsy. However, the PNKD in this patient continued even after hypocalcemia got resolved. Indeed, idiopathic basal ganglia calcification itself (without IHP or hypocalcemia) was also reported as presenting with PNKC, and a PET study in a large family with PNKC showed no abnormalities in the basal ganglia. Considering the effectiveness of other several antiepileptic drugs (valproic acid and clonazepam) in enhancing GABAergic neurotransmission in PNKD, we presumed that the effect of LEV could be achieved by regulating the γ-aminoic acid pathway as previously shown in vitro and in vivo. Remembering the effectiveness of LEV in various disorders in which the choreoathetotic movements occur (e.g., PKC, tardive dyskinesia, and Huntington disease), γ-aminobutyric acid pathway could be the common side of action of LEV in these movement disorders. However, further detailed studies are warranted to clarify this issue.

In conclusion, further classifications distinguishing the phenomenology of the attacks are needed to define the sporadic cases better. It may also be valuable in choosing the treatment and predicting the response. The IHP is a readily manageable condition that should be considered in the paroxysmal movement disorder, and
the use of LEV is suggested in the treatment of PNKC.

REFERENCES