INTERNATIONAL JOURNAL OF EPILEPSY 2 (2015) 49–50

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.journals.elsevier.com/international-journal-of-epilepsy

Case Report

A case of paroxysmal nocturnal dystonia responsive to cyproheptadine: Is it almost always epileptic?

Mohammad Sayadnasiri[*]

Department of Clinical Sciences, Razi Hospital, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran

ARTICLE INFO

Article history:
Received 16 October 2014
Accepted 15 February 2015
Available online 11 March 2015

Keywords:
Nocturnal paroxysmal dystonia
Epilepsy
Basal ganglia

ABSTRACT

Nocturnal Paroxysmal Dystonia (NPD) is characterized by abnormal dyskinetic movements occur mostly during non-REM sleep. From introducing NPD in early 1980s, most authors have been in favour of an epileptic origin for these sleep-related episodes. Clinical characteristics of NPD including abrupt hypermotor behaviours, automatisms and vocalizations, abnormal EEG findings in some patients and therapeutic response to anti-epileptic drugs persuade clinicians to accept NPD as sleep-related epilepsy with frontal lobe origin but it seems this conclusion may not be true in all cases. We present a young adult patient with refractory NPD who responded to antihistamine cyproheptadine and propose an alternative theory to describe NPD according to the basal ganglia dysregulation. So, in such patients, other therapeutic approach should be reasonably sought.

1. Introduction

Nocturnal Paroxysmal Dystonia (NPD) is characterized by violent dyskinetic movements involving head, trunk and limbs and occurs mostly during non-REM sleep. These short lasting attacks tend to recur several times per night. PND is currently known to be a form of frontal lobe epilepsy and anti-epileptic drugs are the first line of treatment but it seems that some refractory cases of NPD are of non-epileptic origin. Here, we present a rare case responsive to antihistamine drug to propose an alternative theory based on abnormality of the basal ganglia histamine level.

2. Case presentation

A 23 years old healthy woman presented with sleep problem since more than two years ago. Her husband noticed first her abrupt awakening at mid night with violent excessive movements of extremities associated with vague vocalization lasting about 1 min. After termination of the attack, she became awake without confusion but could not recall the event. After that, these attacks have recurred 3–4 times weekly, sometimes more than one episode per night. In a videotape recorded by family at home during one attack, showed arrhythmic bizarre movements of extremities,

* University of Social Welfare and Rehabilitation Sciences, Velenjak, Daneshjoo Blv, Tehran, Iran. Tel.: +98 2177559166, +98 9373886173 (mobile); fax: +98 2133401604
E-mail address: mo.nasiri@uswr.ac.ir.
http://dx.doi.org/10.1016/j.ijep.2015.02.003

specially choreiform movements of upper limbs with repeated dystonic turning of head and neck toward right side. This attack was resolved after 30 s and the patient regained full attention to her environment. There were no triggers for this attacks and family history was also negative. Brain MRI and frequent EEG with provocation methods showed no abnormality. During last two years, she was treated with multiple anti-epileptic drugs (AED) as single or add-on therapy including carbamazepin, topiramate, levetiracetam and clonazepam but with no therapeutic response. At first visit of the patient in our center, combination therapy of carbamazepin and levetiracetam with higher doses was started but after two months, no change in sleep attack frequency was occurred. At this point, cyproheptadine (4 mg bedtime) was started for treating low appetite but patient refused to increase AED doses. Surprisingly, after two weeks she declared decrease in sleep attacks; so, cyproheptadine dose was increased to 8 mg bedtime and AEDs was tapered slowly. By continuation of cyproheptadine, sleep attacks decreased in frequency and severity more 50% and patient tolerated the drug with no significant side effects.

3. Discussion

Since first definition of NPD in early 1980s, there are arguments among clinicians about origin of these sleep attacks. Hitherto, most authors consider NPD as a peculiar sleep-related epileptic seizure and AEDs are now first line treatment for most patients.[1–3] Demographic features, clinical symptoms, some EEG abnormalities and good responses to AEDs persuaded authors to reject NPD as a distinct entity and consider it a form of nocturnal frontal lobe epilepsy (NFLE) but discussion about the possibility of different causes of the same syndrome has still continued.[3,4] For the pathophysiologic origin of NPD, three hypotheses may be introduced: these attacks may be assumed a form of parasomnia and fall within this category alongside other disorders such as sleep walking; on the other hand, an epileptic phenomenon may be the explanation of these attacks and finally, one may classify them as a paroxysmal chorea-athetoid dyskinesia (PCD). Although the prevailing theory is that PND results from NFLE, some early arguments were in favour of a subcortical disease involving basal ganglia.[4] It is proposed that disturbances of the cortical control over basal ganglia and their thalamic connections result in theses paroxysmal attacks.[5] A hereditary oversensitivity of basal ganglia to dopamine or other related neurotransmitters is another explanation for paroxysmal dyskinesia in the situation such as excitement.[4] So, a similar pathophysiologic mechanism, but confined to sleep, may affect some cases of PND. According to this theory, some authors concluded that functional state of the basal ganglia of these patients may vary during the sleep–wake cycle resulting in sleep-related attacks.[5]

Clinical characteristics similar to other PCDs, lack of abnormal EEG findings during and between attacks, occurrence of secondary PCD in disorders affecting basal ganglia, unresponsiveness to multiple AEDs, and absence of family and past history of epilepsy may be opposed to the epileptic origin of these attacks.[4]

In this report, we present a case of NPD responsive to cyproheptadine, an antihistamine drug with antiserotonergic and anticholinergic effects. Williams (2012) also reported a similar case who responded to antihistamine doxylamine.[4] Although no disease entity has so far been attributed specifically to disrupted brain histaminergic pathways, we want to propose another pathophysiology for PND based on brain histamine dysfunction. Central histamine can affect motor system; as animal study showed intraventricular injection of histamine induces transient increase in locomotion activity.[6] Changes in the basal ganglia histamine level play also a pathophysiological role in movement disorders such as Parkinson or Huntington's diseases.[6] Histaminergic neurons show a circadian rhythm with increased firing during wakefulness but not during sleep.[6] So, it is estimated that in some NPD patients, such as our patients, there is an abnormal increased histaminergic activity in basal ganglia at non-REM sleep resulting in excessive abnormal movements. Although it may not be the sole underlying pathology, histamine abnormality can be considered as a precipitating factor affecting the disease susceptibility and severity.

Although, based on theses rare cases, it cannot be recommended to treat refractory cases of NPD with antihistaminergic drugs but a pathophysiologic role for basal ganglia histamine dysregulation may be considered in AED resistant cases who are probably of non-epileptic origin. Well-conducted studies are needed to document this possible mechanism.

Conflicts of interest

The author has none to declare.

REFERENCES

1. Hirsch E, Sellal F, Maton B, Rumbach L, Marescaux C. Nocturnal paroxysmal dystonia: a clinical form of focal epilepsy. *Neurophysiol Clin*. 1994;24:207–217.
2. Provini F, Plazzi G, Lugaresi E. From nocturnal paroxysmal dystonia to nocturnal frontal lobe epilepsy. *Clin Neurophysiol*. 2000;111(Suppl. 2):S2–S8.
3. Meierkord H, Fish DR, Smith SJM, Scott CA, Shorvon SD, Marsden CD. Is nocturnal paroxysmal dystonia a form of frontal lobe epilepsy? *Mov Disord*. 1992;7:38–42.
4. Williams DM. Paroxysmal hypnogenic dyskinesia responsive to doxylamine: a case report. *Case Rep Neurol Med*. 2012;2012, 484689.
5. Lugaresi E, Cirignotta F, Montagna P. Nocturnal paroxysmal dystonia. *J Neurol Neurosurg Psychiatry*. 1986;49:375–380.
6. Haas HL, Sergeeva OL, Selbach O. Histamine in the nervous system. *Physiol Rev*. 2008;88:1183–1241.