Sporadic paroxysmal non-kinesigenic dyskinesia: a frequently-misdiagnosed movement disorder

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ABSTRACT

Paroxysmal non-kinesigenic dyskinesia is a very rare movement disorder. Few cases have been reported in the literature so far. We present a 40-year-old man with non-kinesigenic paroxysmal dyskinesia, which was initially diagnosed as a psychogenic disorder. This case highlights the varied presentation of this condition and an excellent response to clonazepam.

Keywords: movement disorders, paroxysmal dyskinesia, paroxysmal non-kinesigenic dyskinesia, psychogenic hemiparesis

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INTRODUCTION

Paroxysmal dyskinesia consists of a spectrum of hyperkinetic movement disorders. This includes paroxysmal kinesigenic dyskinesia (PKD), paroxysmal non-kinesigenic dyskinesia (PNKD), paroxysmal hypnogenic dyskinesia (PHD) and paroxysmal exercise-induced dyskinesia (PED). The age of onset, clinical presentation, triggering factors and genetic linkage is extremely variable. The case of sporadic PNKD reported here is phenomenally similar to PKD, except for the precipitating factors.

CASE REPORT

A 40-year-old man, a non-alcoholic, presented with episodes of painful twisting movements on the right side of the body for two and a half years. Each episode comprised twisting movements of the right-sided limbs, beginning at the right lower limb, mainly at the wrist and hand, and progressing to the right upper limb and right shoulder. The movements were more marked proximally. These lasted for 2-4 minutes, and subsided spontaneously. The frequency of the attacks ranged from once a week to once a month, at irregular intervals. There was minimal post-dyskinesia weakness in the affected limbs, which was observed just after the attack and lasted for about two hours. The episodes were neither induced nor aggravated by known factors such as stress, fatigue, sleep deprivation, caffeine, heat, cold, fasting or any sudden movement. He had been on treatment and follow-up in the psychiatry department and was labelled as having a psychogenic disorder before being referred to us. There was no significant family history or instances of drug abuse. The perinatal history was not available. The symptoms never occurred during sleep. During the intervening period, neurological examination was normal.

Routine haematological and biochemical laboratory investigations were normal. Slit lamp examination of the cornea for Kayser-Fleischer ring was negative. Magnetic resonance imaging of the head and intraictal electroencephalogram were within normal limits. Electroencephalogram during the episode was not feasible. He was initially treated with carbamezapine, which did not cause any significant change in the frequency of attacks. Subsequently, he was given clonazepam, which resulted in complete elimination of the dyskinetic attacks. He has been on regular follow-up for the past ten months, and did not experience any further recurrence.

DISCUSSION

Paroxysmal dyskinesias are a heterogeneous group of disorders characterised by recurrent, sudden attacks of unilateral or bilateral involuntary movements, including dystonic postures, chorea, atheosis or ballismus without impairment of consciousness, or ictal electroencephalographical changes.[1,2] Demirkiran and Jankovic proposed four basic subtypes, viz., PKD, PNKD, PHD and PED.[3] The duration of each episode is subdivided into short (≤ five minutes) and long (> five minutes) and further divided into idiopathic or secondary subgroups.

PKD is a relatively rare form of paroxysmal movement disorder characterised by recurrent brief attacks of choreiform or dystonic movements occurring frequently during the day, and are triggered or

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exacerbated by sudden involuntary movement. Such attacks usually last from seconds to 1–2 minutes, and occasionally up to five minutes, with full recovery during the intervening period. There can be up to 100 attacks per day, but the frequency of attacks decrease with age. Age of onset is usually during childhood and early adulthood, but can range from six months to 40 years. Consciousness is preserved. Males are affected more frequently than females, with an estimated ratio of 4:1.[3] PKD can be sporadic or familial with autosomal inheritance. Genetic studies have mapped some families of PKD to chromosome 16 (16p11.2-q11.2).[4-6] Paroxysmal dyskinesias overlap with EA1 and EA2 and some epilepsy syndrome in several families. In such families, the patient may have infantile convulsions, later followed by paroxysmal dyskinesias, known as familial infantile convulsions and paroxysmal choreoathetosis (ICCA syndrome).[5,7,8] It is suspected that paroxysmal dyskinesias belong to an ever-growing list of neurological diseases which are caused by defective ion channels (channelopathies). In a recent study by Du et al, a calcium-sensitive potassium channel is located on 10q22.[9] The disorder is eminently treatable with antiepileptic drugs, such as phenytoin and carbamezapine.

In PNKD, attacks occur spontaneously, ranging in duration from 2–3 minutes to four hours. This is the major factor which differentiates PNKD from PKD. Attacks are less frequent and not precipitated by movement, but can be brought on by fatigue, anxiety or excitement, heat or cold, alcohol and caffeine, such as in coffee, tea or chocolate. It is most difficult to treat paroxysmal dyskinesia since the non-kinesigenic form does not respond to antiepileptic drugs. Clonazepam (1–2 mg) appears to be the drug of choice. Phenobarbital and sodium valproate are also known to be effective. Preliminary functional imaging studies of PNKD have shown a marked reduction in density of presynaptic dopa decarboxylase activity in the striatum, together with an increase in density of postsynaptic dopamine D2 receptors. Genetic analysis of a large multigenerational Italian family with PNKD with an autosomal pattern of inheritance, mapped the PNKD gene to chromosome 2 (2q33-q35). Also, newer studies mentioned the locus for PNKD to be on MR-1(myofibrillogenesis-1 gene).[10] This gene is a stress pathway gene. MR-1 has the similarities with the HAGH (hydroxyacylglutathione hydrolase) gene. This enzyme takes part in a pathway responsible for the detoxification of methylglyoxal, a compound which is present in the coffee and alcoholic beverages and produced as a byproduct of the stress pathway. This is evidence which suggests how important this precipitating factor can be.

PHD consists of brief and occasional painful dystonia or choreoathetoid movements occurring during non-rapid eye movement sleep. Short lasting PHD is now regarded as a form of nocturnal mesiofrontal lobe epilepsy. Lombroso suggested that electrical discharges picked up from the medial frontal lobe with depth electrode could spread to the caudate nucleus, where it is responsible for the genesis of Pdys.[11] Genetic studies have mapped the chromosome 20q13.2-13.3 (nicotinic receptor alpha 4 subunit CHRNA4).

PED consists of attacks of involuntary movements that are triggered by exertion caused by walking and running, etc. The attacks usually involve the lower limbs and are often bilateral. They may last from a few minutes to 30 minutes. PED is usually sporadic, and rarely familial, where the gene is mapped to the chromosome, 16p12-q12. Treatment with anticonvulsants and levodopa are unsatisfactory. The most common cause of secondary PED is multiple sclerosis.[12] The other aetiologies include encephalitis, AIDS, head trauma, metabolic disorders – hypoparathyroidism, thyrotoxicosis, basal ganglia calcification, and Leigh syndrome. A secondary aetiology should be suspected if the age of onset occurs in late life, and if there are atypical features.

Our case presented with paroxysmal right hemidystonia with non-involvement of the left-sided limbs. This is an unusual feature because PNKD is generally reported to be a generalised movement disorder. The patient responded dramatically to clonazepam. This case highlights the importance of the recognition of a rare paroxysmal movement disorder, which could be frequently labelled as a psychogenic condition. The patient also had weakness on the same side of the body; though it is minimal, it is yet another feature unusual to this group of disorders. The dystonic movements were not associated with a loss of consciousness, and occurred without any sudden movement. There was no other positive or negative neurological manifestation and normal intraictal electroencephalogram favoured diagnosis of PNKD over the seizure disorder. PNKD, or for that matter any kind of non-kinesigenic or kinesigenic paroxysmal movement disorder, can be initially misdiagnosed and treated as a psychogenic movement disorder, in view of its atypical and unusual clinical presentation, and a lack of awareness among physicians. The diagnosis is purely clinical and though genetics can help it may not have been feasible to do so as in our case. Since the presentation may be atypical, a thorough examination should be made before labelling a patient with the diagnosis of a psychogenic disorder.

REFERENCES

1. Bhatia KP. The paroxysmal dyskinesias. J Neurol 1999; 246:149-55.
2. Fahn S. The paroxysmal dyskinesia. In: Marsden CD, Fahn S, eds. Movement Disorder 3. Oxford: Butterworth-Heinmann, 1999:310-45.
3. Demirkiran M, Jankovic J. Paroxysmal dyskinesias: clinical features and classification. Ann Neurol 1995; 38:571-9.
4. Tomita H, Nagamitsu S, Wakui K, et al. Paroxysmal kinesigenic choreoathetosis locus maps to chromosome 16p11.2-q12.1. Am J Hum Genet 1999; 65:1688-97.
5. Online Mendelian Inheritance in Man (OMIM). National Centre For Biotechnology Information Website. John Hopkins University, McKusick VA, ed.128200: Paroxysmal kinesigenic choreoathetosis; PKC.118800. Paroxysmal nonkinesigenic choreoathetosis; PKC. 602066: Infantile convulsions and paroxysmal choreoathetosis, familial. Available at: www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?602066. Accessed March 27, 2006.
6. Szepetowski P, Rochelle J, Berquin P, et al. Familial infantile convulsions and paroxysmal choreoathetosis: a new neurological syndrome linked to the pericentromeric region of human chromosome 16. Am J Hum Genet 1997; 61:889-98.
7. Thiriaux A, de St Martin A, Vercueil L, et al. Co-occurrence of infantile epileptic seizures and childhood paroxysmal choreoathetosis in one family: clinical, EEG and SPECT characterization of episodic events. Mov Disord 2002; 17:98-104.
8. Demir E, Prud'homme JE, Topçu M. Infantile convulsions and paroxysmal choreoathetosis in a consanguineous family. Pediatr Neurol 2004; 30:349-53.
9. Du W, Bautista JF, Yang H, et al. Calcium-sensitive potassium channelopathy in human epilepsy and paroxysmal movement disorder. Nat Genet 2005; 37:733-8.
10. Lee HY, Xu Y, Huang Y, et al. The gene for paroxysmal non-kinesigenic dyskinesia encodes an enzyme in a stress response pathway. Hum Mol Genet 2004; 13:3161-70.
11. Lombroso CT. Paroxysmal choreoathetosis: an epileptic or non-epileptic disorder? Ital J Neurol Sci 1995; 16:271-7.
12. Roos RA, Wintzen AR, Vielvoye G, Polder TW. Paroxysmal kinesigenic choreoathetosis as presenting symptom of multiple sclerosis. J Neurol Neurosurg Psychiatry 1991; 54:657-8.