CASE REPORT

Paroxysmal Dyskinesia as an Unusual and Only Presentation of Subcortical White Matter Ischaemia: A Report of Two Cases

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SUMMARY

Secondary paroxysmal dyskinesias (PxD) have been previously reported in patients with multiple sclerosis, lacunar infarcts, head trauma, metabolic disorders such as hyperglycaemia, hypocalcaemia, migraine and central nervous system (CNS) infections. The causative lesions typically involve the basal ganglia structures, medulla and rarely the spinal cord. We report two patients who presented with paroxysmal dyskinesias as the only manifestation of subcortical white-matter ischaemia. Patient 1 presented with 3-year history of paroxysmal kinesigenic dyskinesia (PKD) and patient 2 with 6-month history of paroxysmal nonkinesigenic dyskinesia (PNKD). All investigations, including CSF oligoclonal bands were negative, except for a brain MRI which showed multiple, non-enhancing subcortical white matter lacunar infarcts. Therefore, subcortical white matter ischaemia should also be included in the differential diagnosis of PxD.

KEY WORDS:
Secondary paroxysmal dyskinesias, PKD, PNKD, Lacunar infarcts, Subcortical, White-matter, Ischaemia

INTRODUCTION

Paroxysmal dyskinesias (PxD) are rare, heterogeneous involuntary movement disorders, leading to episodic dystonia, athethosis, ballism, chorea or myoclonus without loss of consciousness[1]. They are classified into four subtypes based on the precipitating factors: paroxysmal kinesigenic dyskinesia (PKD) is brief (< 2 mins) and is precipitated by sudden movements; paroxysmal nonkinesigenic dyskinesia (PNKD) lasts longer (minutes to hours), occurs during rest and is induced by stress, fatigue, alcohol or caffeine; paroxysmal exertion-induced dyskinesia (PEH) also lasts hours and is induced by exertion and paroxysmal hypnogenic dyskinesia (PNH) is induced by sleep and is now considered as a form of frontal lobe epilepsy[1].

Both sporadic and familial cases of PKD and PNKD have been described; the latter follows an autosomal dominant inheritance, with onset before 20 years of age[1]. Secondary causes include multiple sclerosis (MS), stroke, migraine, brain infections and metabolic derangements such as hyperglycaemia, hypo- or hypercalcaemia[1]. The presentation of PxD in stroke is rare and patients reported typically have lacunar infarcts involving the thalamus, subthalamus, putamen, globus pallidus and the medulla, with additional interepisodic neurological deficits[2]. To our knowledge, the presentation of paroxysmal PxD as the only manifestation of subcortical white matter ischaemia has not been described previously. We therefore describe two such patients with bilateral subcortical lacunar infarcts who presented with no other symptoms apart from PxD.

CASE HISTORIES

Case 1

A previously well, 50-year-old, Chinese lady presented with a 3-year history of intermittent hemidystonic spasms involving the right upper and lower limbs and lower face. The spasms were preceded by mild breathing difficulty and precipitated by brief movements and stress. They lasted 13 seconds, with spontaneous resolution and occurred twice monthly. Interepisodic examination revealed no neurological deficits. MRI brain showed multiple discrete, non-enhancing white-matter lesions in both centrum semiovale and occipital lobes and left corona radiata, suggestive of lacunar infarcts (Figure 1A). Cerebrospinal fluid (CSF) analysis was negative for oligoclonal bands. Brain-stem auditory evoked potentials (BAEP) and visual evoked potentials (VEP) were normal. Acetazolamide was ineffective and later changed to carbamazepine and aspirin. A reduction in the duration of attacks was noted. A repeat MRI brain two months later did not show any new lesions.

Case 2

A previously well 41-year-old Indian lady presented with a six-month history of hemidystonic spasms affecting the left arm, leg and lower jaw. The attacks occurred while resting, precipitated by fatigue and stress, preceded by an 'uncomfortable pulling sensation' in the left arm and mild 'breathing difficulty'. They lasted for 10 minutes and occurred monthly. Interepisodic examination revealed no neurological deficits. MRI brain revealed bilateral multiple discrete, white-matter lesions suggestive of lacunar infarcts (Figure 1B). A diagnosis of paroxysmal nonkinesigenic dyskinesia (PNKD) was made. Patient was commenced on aspirin.

Investigations

Routine blood investigations, serum calcium, magnesium, phosphate, fasting blood glucose, tumour markers (CA 125,

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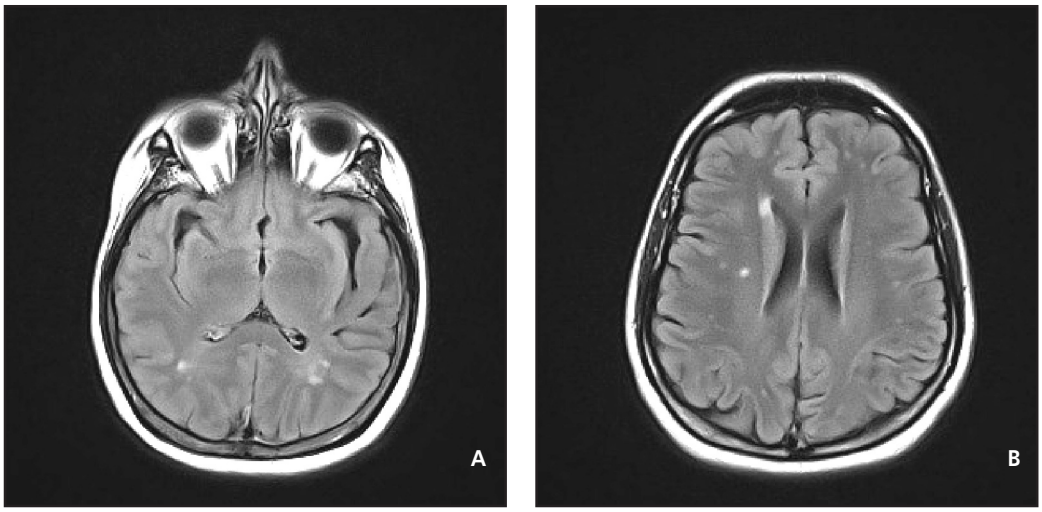

Fig. 1: FLAIR MRI T2-weighted images of patient 1 (A) and patient 2 (B) showing bilateral hyperintense subcortical white-matter lesions

CEA and alpha fetaprotein), ANA, RF, anticardiolipin (ACL) IgG and IgM antibodies, protein C, protein S and antithrombin III levels were normal or negative in both patients. Interictal and ictal electroencephalographies (EEG), echocardiography and carotid doppler studies were normal in both patients.

DISCUSSION

We have described two patients with underlying subcortical white matter ischaemia, presenting only with PxD. Patient 1 had attacks resembling PKD, with brief duration (< 1 min) and partial responsiveness to carbamazepine. Patient 2 had attacks resembling PNKD (two attacks lasting approximately 10 minutes and one attack lasting < 1 min), which occurred at rest and induced by extreme fatigue. In both patients, the attacks were preceded by a vague 'sensation' over the affected side and 'mild breathing difficulty'. An epileptic disorder was excluded in both patients, in view of the normal ictal EEGs. Importantly, MS which could also lead to paroxysmal dystonic/tonic attacks were excluded in our patients based on the negative oligoclonal bands and the absence of demyelination on brain MRI. However, 'tonic spasms' of MS are usually extremely painful and are of much longer duration.

PxD following stroke is rare and usually occurs contralateral to the infarcts with a latency of 3-6 years from the time of infarct[2]. The subtypes of PxD described are PNKD, paroxysmal hypnogenic dyskinesia (PHD) and mixed PNKD/PKD[2]. Vascular lesions typically involve the grey matter nuclei within the basal ganglia and the brainstem[2]. Interestingly, both our patients had no major identifiable risk factors for stroke or prior history suggestive of stroke. However, since transcranial Doppler ultrasound was not performed, we were unable to exclude intracranial vasculopathy in these patients.

Pure white matter involvement in secondary PxD is rare. Apart from a single case report of PxD related to an arteriovenous malformation in the subcortical parietal region[3], reports of white matter involvement in PxD are scarce. Postmortem studies in HIV-related PxD showed both subcortical grey and white matter involvement, although the former was implicated as the likely cause[4].

The mechanisms underlying PxD remain poorly understood as ictal studies have produced conflicting results. A study on a patient with PKD showed an increased ictal perfusion in the contralateral posterolateral thalamus, whereas other investigators have reported a decrease in the ictal perfusion in the contralateral basal ganglia during the attacks[1]. In both familial PKD and PNKD, genetic mutations have been identified. In PKD, mutation in the calcium-sensitive potassium channel on chromosome 16 has been identified through linkage studies. In PNKD, the myofibrillogenesis regulator-1 gene on chromosome 2, which bears similarities to another gene involved in detoxification of methylglyoxal, a compound present in coffee has been found[1]. Alternatively, animal studies have shown an increase in the extracelullar striatal dopamine levels in the during the dystonic episodes with return to baseline prior to cessation of attacks which perhaps reflects an altered regulation of dopamine release[1]. Interestingly, and perhaps more relevant to our cases, there has been a previous report of two patients with moyamoya disease presenting only paroxysmal dyskinesias[5]. The authors postulate that both hormonal and ischaemic factors may have contributed to the dyskinesias[5]. Whether the dyskinesias in our patients are due to underlying intracranial ischaemia remains to be explored.

In summary, subcortical white matter ischaemia may present only with paroxysmal dyskinesia. It is therefore crucial to recognize this rare movement disorder in such patients to avoid misdiagnosis and delay in treatment initiation to prevent further progression of infarcts.

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