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CASE REPORT

# Elderly-Onset Paroxysmal Kinesigenic Dyskinesia: A Case Report

Lulu Yao · Wei Liang · Shanshan Mei · Erhe Xu · Xiaobo Huang

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## ABSTRACT

Paroxysmal kinesigenic dyskinesia (PKD) is characterized by transient and recurrent involuntary movements that are triggered by a sudden movement. Here, we report an elderly female patient with a 1-month history of paroxysmal rigidity of the right limb. As the symptoms were characterized as paroxysmal, transient, and repetitive, her condition was initially thought to be epilepsy. Subsequent examinations showed no abnormality in the continuous video-electroencephalogram (EEG) monitoring, magnetic resonance imaging (MRI), fluorodeoxyglucose (FDG)–positron emission tomography (PET)/computed tomography (CT), and genetic testing. The final diagnosis was identified as clinically diagnosed PKD, and the symptoms were well controlled after oxcarbazepine treatment. To our knowledge, this is the first report to show elderly-onset PKD. This case expands our understanding of the age of onset of PKD. However, it is necessary to differentiate PKD from reflex epilepsy and hysteria attacks. For patients with typical clinical manifestations, we should adhere to the standard diagnostic workflow for the efficient diagnosis of PKD, aiming at avoiding misdiagnosis and mistreatment.

**Keywords:** Movement disorders; Paroxysmal kinesigenic dyskinesia; Elderly-onset; PRRT2 gene; Case report

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L. Yao · W. Liang · X. Huang (✉)
Department of Traditional Chinese Medicine, Xuanwu Hospital, Capital Medical University, No. 45 Changchun Street, Xicheng District, Beijing 100053, China
e-mail: huangxiaobo@xwh.ccmu.edu.cn

S. Mei · E. Xu
Department of Neurology, Xuanwu Hospital, Capital Medical University, Beijing, China

S. Mei · E. Xu
National Clinical Research Center for Geriatric Disorders, Beijing, China

**Key Summary Points**

Paroxysmal kinesigenic dyskinesia (PKD), which commonly occurs in children and adolescents, is characterized by recurrent episodes of involuntary movements that are triggered by a sudden movement.

Elderly-onset PKD is rare and usually tends to be diagnosed as epilepsy or other types of movement disorders.

We report an elderly female patient with a 1-month history of paroxysmal rigidity of the right limb. The final diagnosis was identified as clinically diagnosed PKD, and the symptoms were well controlled after oxcarbazepine treatment.

Our case indicated that it is necessary to differentiate PKD from reflex epilepsy and hysteria attacks. Patients with typical clinical manifestations should be screened in compliance with the standard diagnostic workflow for the efficient diagnosis of PKD.

## DIGITAL FEATURES

This article is published with digital features, including a video of the patient suffering from an attack, to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.20748322.

## INTRODUCTION

Paroxysmal kinesigenic dyskinesia (PKD) is characterized by intermittent and recurrent episodes of involuntary movements that are triggered by a sudden movement, with symptoms such as chorea, dystonia, and athetosis. The incidence has been reported as 1 in 100,000 to 1 in 150,000 [1]. PKD is the most common type of paroxysmal dyskinesia, which can be categorized into familial and sporadic PKD. Familial PKD is recognized as an autosomal dominant disorder. Sporadic PKD may be secondary to other diseases [2]. As reported, the age of onset of sporadic PKD was in the 1–20 years range, with particularly high rates in children. Male individuals experienced a higher incidence of PKD than female individuals. Often the duration of symptoms was less than 1 min, and the attack frequency ranged from several times per day to 100 times per day [3]. Here, we report the case of a rare elderly-onset PKD and review relevant studies. This case expands our understanding of the age of onset of PKD.

## CASE PRESENTATION

A 65-year-old woman presented with paroxysmal rigidity of the right limb for 1 month. The patient suffered right upper limb rigidity and movement restriction that was not accompanied by loss of consciousness 1 month ago. No exact reasons were confirmed. The symptoms commonly lasted for about 1 min and could remit spontaneously. Three days later, the symptoms involved the right lower limb. Subsequently, the patient experienced recurrent attacks (supplementary video showing the patient suffering from an attack manifested as right limb rigidity and movement restriction and not accompanied by loss of consciousness; the symptoms disappeared spontaneously after about 1 min). The attacks had kept occurring 10–20 times per day and were triggered by sudden movement, such as getting up or standing. Prior to the appearance of motor symptoms, the patient experienced abnormal sensations, which were depicted as tightness. She visited the neurological department of Xuanwu Hospital and underwent examinations. The results of plasma electrolyte and creatine kinase levels were normal, no myotonic discharge was observed on electromyogram (EMG) and electroencephalogram (EEG) monitoring also showed no abnormalities. As a result, the primary diagnosis was considered as epilepsy. The patient was treated with oxcarbazepine (300 mg twice daily). Two episodes occurred over the following 1 week. The patient

was hospitalized in order to undergo further examination and treatment. Prior to this complaint, the patient had a history of diabetes for more than 30 years and received insulin treatment. There was no history of stroke, Parkinson's disease, or other neurological diseases; and no history of premature delivery, brain trauma, intracranial infection, convulsions, and migraine. None of her family members showed similar symptoms.

At admission, the physical examinations showed a bilateral positive Babinski sign, and no abnormalities were found in other clinical signs. The patient's mini-mental state examination (MMSE), Montreal cognitive assessment (MoCA), and Hamilton anxiety scale (HAMA) scores were in the normal range. Blood routine, liver and kidney function, antinuclear antibodies, ceruloplasmin, and other laboratory tests were at normal levels. There were negative results of the cerebrospinal fluid (CSF) examination. No abnormality was found in the continuous video-EEG monitoring (Supplementary Material). Brain magnetic resonance imaging (MRI) showed infarcts in the right thalamic region (Fig. 1a, b). T1-weighted image revealed no obvious signal and atrophy in the hippocampus (Fig. 1c). Positron emission tomography (PET)/computed tomography (CT) showed no abnormal signal of [$^{18}$F]AV-133 in the bilateral caudate nucleus and lentiform nucleus (Fig. 1d, e), and bilateral symmetrical [$^{18}$F]fluorodeoxyglucose (FDG) uptake in the caudate nucleus and lentiform nucleus (Fig. 1f).

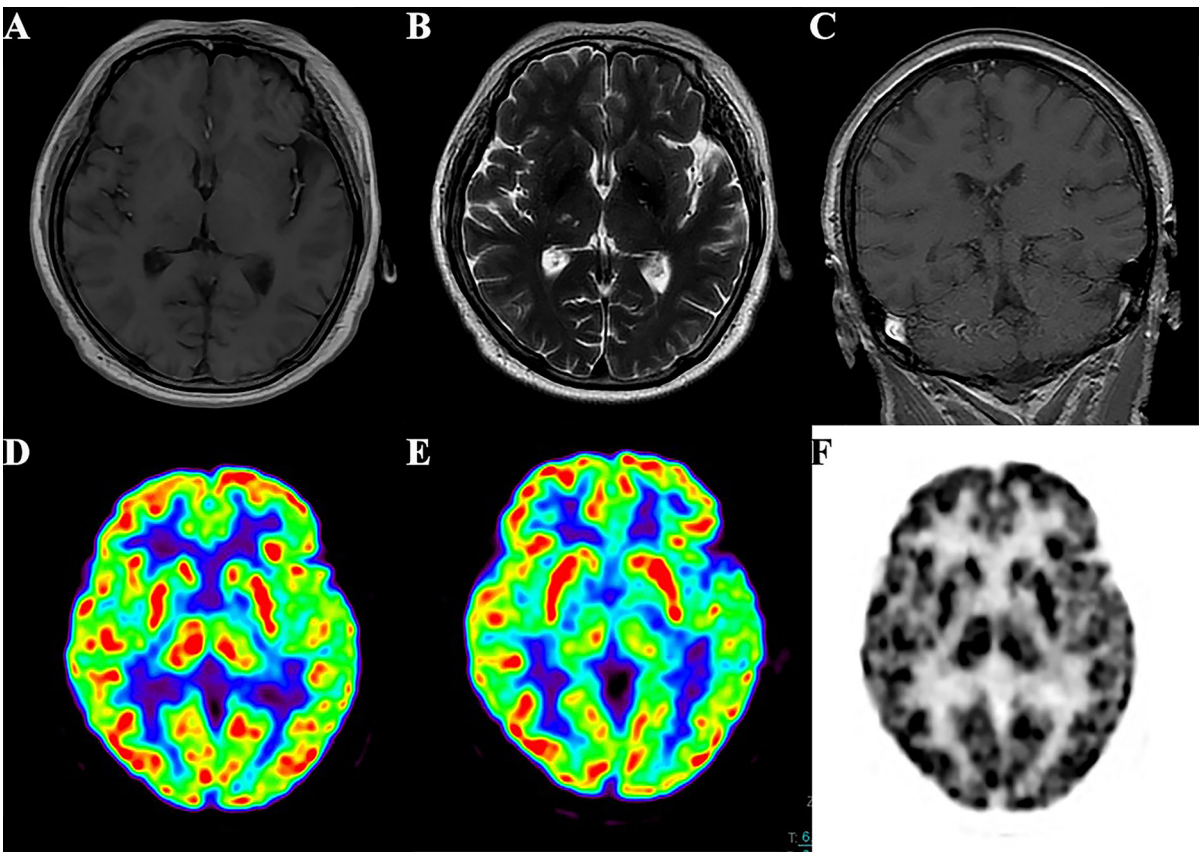


**Fig. 1** Brain MRI images did not show abnormalities associated with the disease. **a**, **b** MRI images showed the right lacunar thalamic infarctions. **c** T1-weighted coronal image showed the hippocampal uncus was normal. PET/CT showed no abnormal signal. **d**, **e** Bilateral signals of [$^{18}$F]AV-133 in the caudate nucleus and lentiform nucleus were normal. **f** Bilateral symmetrical [$^{18}$F]FDG uptake was seen in the caudate nucleus and lentiform nucleus

Genetic testing (high-throughput sequencing) presented normal results in *PRRT2*, *KCNA1*, *SLC2A1*, and *TMEM151A* genes.

According to these symptoms and clinical examination findings [4], the patient was given a final diagnosis of clinically diagnosed PKD. We continued to treat the patient with oxcarbazepine (300 mg twice daily). Unfortunately, the patient got drug eruptions and raised pruritic red macules and papules of the skin on her trunk and extremities (Supplementary Material). The rash subsided after adjustment of oxcarbazepine doses (150 mg twice daily) and combination with anti-allergic treatment. There was no recurrence in the patient's symptoms during the 3-month follow-up period. Furthermore, no symptoms of limbic dysfunction were found, such as psychiatric, behavioral, or cognitive symptoms during follow-up.

Ethical approval was obtained from the Ethics Committee of Xuanwu Hospital, Capital Medical University. Written informed consent was obtained from the patient for publication of this case report and to publish the images and video.

## DISCUSSION

PKD was first described by Kertesz in 1967 and some of the patients were found to have a clear family history [5]. Mutations in *PRRT2* gene were associated with familial PKD. Sporadic PKD may be secondary to other factors or diseases, such as multiple sclerosis, congenital myopathy, brain calcification [6], and traumatic brain injury or hyperthyroidism [7]. Familial PKD generally has more involvement in bilateral limbs and longer disease duration and is manifested in choreic movements and athetosis. Sporadic PKD usually involves a unilateral limb and shorter disease duration and is manifested as dystonia. Typical attacks are triggered by sudden voluntary movements, which usually involve changes in the speed or magnitude of movements [8]. Sensory aura is another striking clinical feature. It refers to the abnormal sensation before the movement disorder induced by the trigger factors [1]. The abnormal sensation begins distally, progresses proximally, and is often characterized as numbness, chills, and tingling. In patients with remission, aura appears isolated without subsequent dyskinesia attacks [9, 10].

The attacks experienced by this patient had definite motor triggering factors, and the duration was less than 1 min, accompanied by typical sensory aura. No disease-related abnormality was found in EMG and EEG. Considering the characteristics of acute onset, long history of diabetes, positive Babinski sign, and infarcts in the right thalamic region on MRI, we needed to exclude the diagnosis of stroke. However, the symptoms accompanied by specific events and good response to oxcarbazepine did not support the diagnosis of stroke. Although the results of genetic testing were negative, the patient met the criteria of clinically diagnosed PKD [4]. Initially, on the basis of the symptom features of paroxysmal, transient, and stereotypic, the patient was diagnosed with epilepsy, probably reflex seizures. Reflex epilepsy attacks are objectively and consistently evoked by a specific afferent stimulus, with changes in EEG activity during seizure [11]. Besides, hysteria may mimic PKD attack clinically and radiologically. It is an abnormal brain function caused by a psychological disorder rather than brain parenchyma disease, which behaves similarly to PKD. The principal difference is that hysteria fails to respond to antiepileptic therapy. In this patient, there was no epileptic discharge on EEG during a seizure, and subsequent long-term video EEG results found no abnormal activity. Moreover, this patient had a depression scale within the normal range and no clear psychological disorder. Meanwhile, the patient responded remarkably well to low-dose oxcarbazepine. Therefore, we excluded the diagnoses described above.

With regard to treatment, the symptoms of this patient were well controlled after oxcarbazepine treatment. However, the patient suffered severe hypersensitivity reactions after hospital discharge. Considering the lower incidence with which oxcarbazepine causes side effects compared with carbamazepine [12], we did not change the medication. The rash resolved after dose adjustment of oxcarbazepine

and combination with anti-allergic treatment, and without recurrence.

PKD was initially considered to be an ion channelopathy due to its clinical features and high sensitivity to small doses of sodium channel blockers [13, 14]. However, proline-rich transmembrane protein 2 (*PRRT2*) was the first disease-causing gene identified in 2011 by Chinese scholars, which likely explained the pathogenesis of familial PKD [15]. The incidence of *PRRT2* mutations in patients with familial PKD was between 60% and 90% [16]. It was demonstrated that *PRRT2* expression is enriched in the cerebral cortex, basal ganglia, and cerebellum. And it could modulate synaptic vesicle membrane docking and fusion through acting on presynaptic proteins, and then regulate neurotransmitter release. It is suggested that *PRRT2* gene defects may be related to synaptic dysfunction [17], and a potential mechanism in the pathogenesis of PKD. Li et al. mimicked the pathogenic process of PKD by establishing a neural differentiation system in vitro models using induced pluripotent stem cells (iPSC), and the results showed that severe defects in neural conversion were seen in iPSC [18]. This discovery suggested the important role of *PRRT2* in neurodevelopment and neuron differentiation. It also explained the cause of the younger age of onset among PKD cases. With development of the nervous system, the defects in neuron differentiation could be compensated for. As a result, attack frequency gradually decreased with age and even achieved self-remission.

Although the *PRRT2* gene was proven to be the major cause of PKD, the positive rate in patients with sporadic PKD was about 39.4% [19], suggesting that *PRRT2* gene mutations may not be the only pathogenesis of PKD. Attenuated gamma oscillation power had been observed in patients with PKD [20]. Gamma oscillation is produced in the inhibitory neurons [21], and synchronous gamma oscillation plays an important role in the regulation of sensory gating controlled by the thalamocortical circuit [18, 22]. This indicated that deficits in inhibitory functions of sensory cortices may have partially contributed to the pathogenesis of PKD. Besides, this mechanism also could explain the reason why changes in the motor status and posture could induce an attack, and is likely to be related to the appearance of sensory aura.

The age of onset of this patient was outside the age range of typical PKD, and clinical symptoms resembled the features of reflex epilepsy and hysteria, both of which increased diagnostic difficulty. PKD is a rare movement disorder, and inadequate recognition of clinical characteristics and negative results of genetic testing would probably lead to misdiagnosis. This case updates the understanding of the age of onset of PKD. For patients with typical clinical manifestations, we should adhere to the standard diagnostic workflow for the efficient diagnosis of PKD, aiming at avoiding misdiagnosis and mistreatment. Close follow-up may contribute to recognizing the whole picture of the disease and differentiating PKD from a similar disease.

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***Author Contributions.*** Lulu Yao contributed to study design, literature review, data analyses and paper drafting. Wei Liang contributed to data collection. Erhe Xu and Shanshan Mei contributed to study design and interpretation. Xiaobo Huang contributed to

paper conception, supervised data analysis and interpretation, critically reviewed the paper.

***Disclosures.*** Lulu Yao, Wei Liang, Shanshan Mei, Erhe Xu, and Xiaobo Huang declare that they do not have any personal, financial, commercial or academic conflicts of interest.

***Compliance with Ethics Guidelines.*** Written informed consent and consent for publication were provided by the patient. The study was approved by the Ethics Committee of the Xuanwu Hospital, Capital Medical University, and was performed in accordance with the Helsinki Declaration of 1964 and its later amendments.

***Data Availability.*** Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.



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