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□ Case Report □

A familial case report of paroxysmal kinesigenic dyskinesia in three brothers

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Paroxysmal kinesigenic dyskinesia (PKD), previously referred to as movement-provoked seizures, is a rare neurological condition that is characterized by short duration dystonic or choreoathetotic movements precipitated by sudden movement, a change in position or hyperventilation. It can be difficult to distinguish this syndrome from seizures. We reported on three brothers in one family all of whom developed abnormal involuntary dystonic or choreoathetotic movement with a tingling or stiffness sensory aura. Evaluations of the patients included general physical examinations, endoclinologic, metabolic studies, chromosomal analysis, video electroencephalograms and brain MRI imaging. All of these studies were normal except for an arachnoid cyst found in one patient. All symptoms showed excellent response to oxcarbamazepine (Trileptal®) or carbamazepine. Use of the video electroencephalogram can help differentiate familial PKD from seizures. **(Korean J Pediatr 2007;50:694-697)**

Key Words : Familial, Kinesigenic, Dyskinesia, Oxcarbamazepine (Trileptal®)

Introduction

Paroxysmal kinesigenic dyskinesia (PKD) is characterized by any combination of dystonic postures, chorea, athetosis and ballism; sudden movement or startle can precipitate these movements. The attacks are usually brief, but on rare occasion can last up to five minutes[1, 2]. The etiology of PKD is idiopathic or hereditary. The inherited form has been described as autosomal dominant[1, 3]. PKD has been mapped to chromosome 16p11.2-q12.1, chromosome 16q13-q22.1 and chromosome 2q32-36 and can be sporadic[4, 5]. In this study we report a Korean family with three affected members in one generation who all had an excellent response to oxcarbazepine (Trileptal®) or carbamazepine.

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Case Report

A 13-year-old male, first noticed symptoms at age ten. The symptoms were episodic paroxysmal dystonic choreoathetotic movements in the left or right upper and lower limbs with sensations of tingling or stiffness as sensory aura. The attacks usually lasted for 10 to 35 seconds, were precipitated by sudden spontaneous movement and occurred one to two times a day. There was no loss of consciousness, eyeball deviation or cyanosis during the attack. His past medical history included a twin gestation with caesarean section delivery at 38 weeks and a birth weight of 2,700 grams. He had normal early developmental milestones and no apparent neurological conditions. His medical history was also normal, except for a febrile seizure at age three. His academic achievement was excellent.

The family history was significant. His monozygotic twin, a 13-year-old male, first noticed symptoms at age ten and his older brother, a 15-year-old male, first noticed symptoms at age eleven. His two brothers symptoms were similar to the patient (3rd son). They had normal early developmental milestones. All affected siblings were male offspring of the

same parents. The mode of transmission is consistent with autosomal dominant inheritance or X-linked dominant inheritance (Fig. 1).

Clinical evaluation included a history of the present illness, family history, medical history, and a review of systems with an emphasis on movement disorders and epilepsy. In addition, a complete blood count, serum total protein and electrophoresis, glucose, hepatic and renal function, serum calcium and calcium ion, urinalysis, alkaline phosphatase, serum copper, serum ceruloplasmin, lactic dehydrogenase, creatine kinase, and erythrocyte sedimentation rate were evaluated. Endoclinologic investigation (thyroid function and parathyroid function), metabolic investigation (serum lactate, pyruvic acid, serum ammonia, and tandem mass spectrometry), serum anti-DNA antibody, chromosomal analysis, brain MRI, and 24-hour video EEG monitoring (Table 1) were also performed.

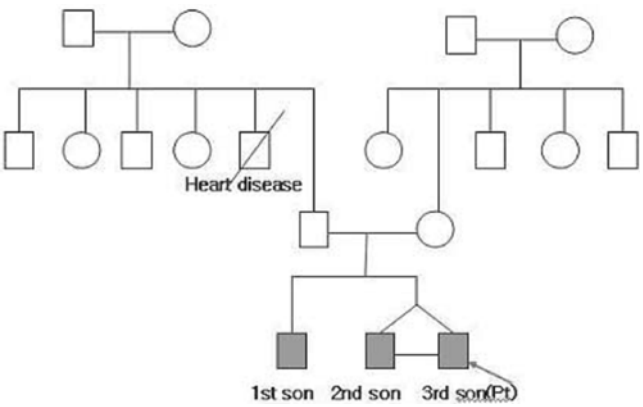

Fig. 1. Family pedigree for paroxysmal kinesigenic dyskinesia (PKD).

All investigations were normal. All patients had normal karyotypes. The brain MRI images of the patients were all

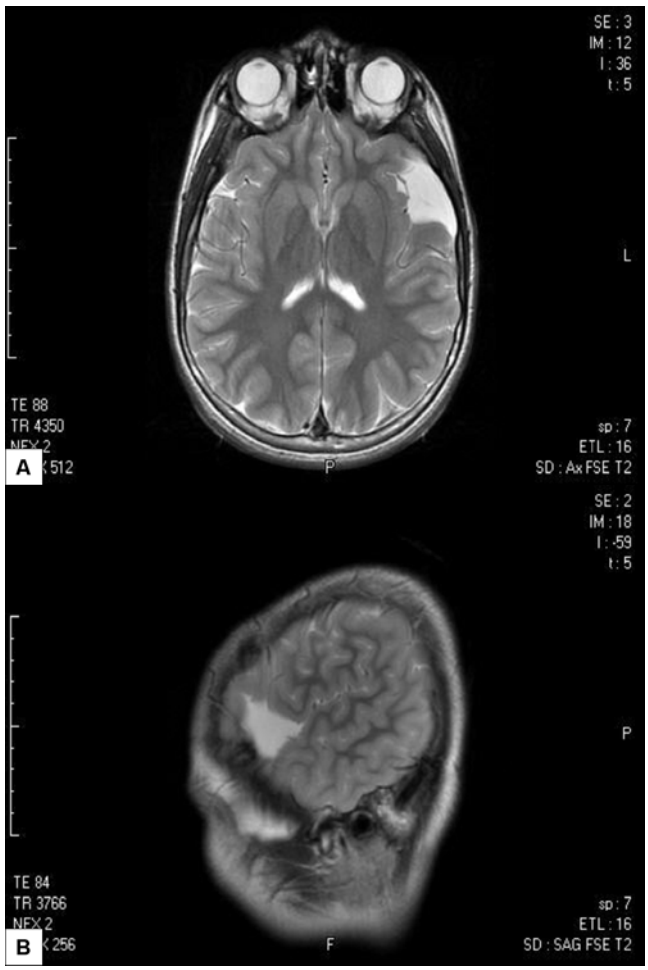

Fig. 2. Axial (A) and Sagittal (B) brain MRI images showing the arachnoid cyst in the left frontotemporal convexity area.

Table 1. Diagnostic Investigations

General investigations
(complete blood count, serum total protein and electrophoresis, hepatic and renal function tests, glucose, Immunoglobulins, complement system, prothrombin and partial thromboplastin times, serum and urinary electrolytes, serum calcium and calcium ion, lactic dehydrogenase, creatine kinase, alkaline phosphatase, serum copper, urine copper, ceruloplasmin, urinary vanillylmandelic acid, erythrocyte sedimentation rate, antistreptolysin-O titer, rheumatoid factor, TORCH titers)
Endocrinologic investigations
(serum insulin, calcitonin, parathormone, thyroid function, cortisol, adrenocorticotropic hormone)
Metabolic investigations
(serum lactate, pyruvate, arylsulfatase A and B, vitamin E, carnitine, very long chain fatty acids, ammonemia, aminoaciduria)
Autoantibodies
Magnetic nuclear resonance imaging of brain
Ophthalmologic examination (also with slit-lamp examination)
Cardiac visit, ECG, Holter-ECG
Sonography of abdomen

Abbreviations : ECG, Electrocardiogram; TORCH, Toxoplasmosis, others, rubella, cytomegalovirus, and herpes simplex virus

normal except for an arachnoid cyst in the left frontotemporal convexity of one patient (Fig. 2). The 24-hour video EEG monitoring of the patients showed paroxysmal dystonic choreoathetotic movement for 35 to 52 seconds with a tingling or stiffness sensory aura. Generalized dystonia and dystonia of the left arm and leg (Fig. 3) were identified. There was no epileptic activity on the ictal EEG.

All of the patients were treated with oxcarbazepine (Trileptal®) up to 450 mg per day. The symptoms in the patient and twin improved significantly and disappeared completely. However, the older brother did not have significant improvement of the symptoms. He was treated with carbamazepine (Tegretol-CR®) up to 600 mg and he showed excellent response.

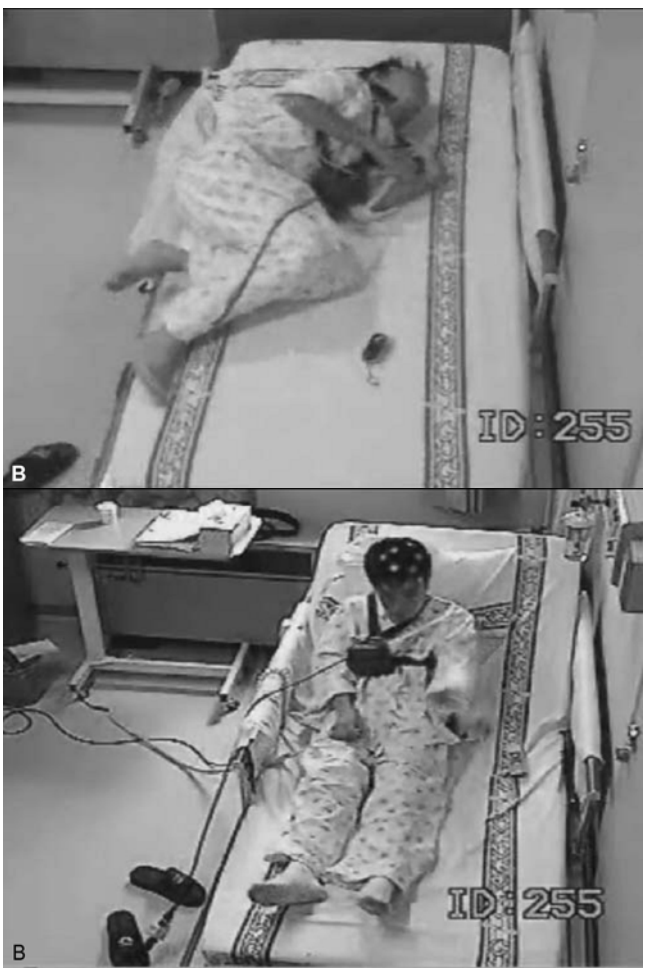

Fig. 3. 24-hr video EEG monitoring (2nd son) with attacks of paroxysmal dystonic choreoathetotic movements in his left or right upper or lower limbs, lasting 32 to 52 seconds. Video EEG monitoring did not reveal any epileptiform activity during the attacks.

Discussion

In 1940, Mount and Reback[7] reported a patient with intermittent choreodystonic attacks precipitated by alcohol, tea, coffee, tobacco, or fatigue. The condition was called paroxysmal dystonic choreoathetosis. In 1967, Kertesz[3] first used the term paroxysmal kinesigenic choreoathetosis to describe 10 cases of abnormal paroxysmal movement induced by sudden voluntary movements. In 1977, Lance[8] reviewed 100 cases and classified the paroxysmal dyskinesias into three categories, namely paroxysmal kinesigenic choreoathetosis, paroxysmal dystonic choreoathetosis and paroxysmal exercise-induced dystonia.

We identified a Korean family with three brothers who have PKD and the same parents. The proband and one sibling are monozygotic twins. History and physical examination did not differentiate PKD from epilepsy. All of the siblings had 24-hour video EEG monitoring and epilepsy was ruled out. Interestingly the twins showed unilateral dystonia during attacks and the older brother showed bilateral dystonia. The patients showed paroxysmal dystonic choreoathetotic movement lasting less than one minute with a tingling or stiffness sensory aura. Additional laboratory investigations showed no other specific etiologies for the symptoms.

Paroxysmal kinesigenic choreoathetosis or paroxysmal kinesigenic dyskinesia is a rare neurologic disorder characterized by sudden attacks of involuntary movement that are precipitated by sudden voluntary movement or changing of position. The age of onset can be as early as four months or as late as 40 years; however, most often it presents during childhood or early adult life[1, 2]. PKD can be primary and can occur as a familial autosomal dominant disorder. It has been linked to chromosome 16p11.2-q12.1, chromosome 16q 13-q22.1 and chromosome 2q32-36 but it can be sporadic[4-6]. In addition, PKD may be secondary to a variety of etiologies associated with focal or generalized brain abnormalities[9]. Therefore, thorough diagnostic investigations are needed for accurate diagnosis[10]. The pathophysiology of PKD presently remains unknown.

Some patients with PKD have reported a sensory aura prior to episodes. The sensory aura consists of paresthesia, pins and needles, stiffness, tension, or a crawling sensation in the limbs[3, 8, 9]. Our patients reported a tingling and stiffness sensory aura. Many patients with PKD have responded to treatment with anticonvulsants, particularly carbamazepine,

phenytoin, valproic acid or clonazepam[11]. Some patients with PKD respond to oxcarbazepine or levodopa[12]. Our twin patients responded to oxcarbazepine (Trileptal®) and their older brother responded to carbamazepine. The symptoms may diminish with age in both frequency and severity of episodes [4, 14, 15].

We report a Korean family with three male siblings diagnosed with PKD confirmed by 24-hour video EEG monitoring and thorough laboratory investigations.

한 글 요 약

한 가족 3형제에게서 발견 된 발작성 운동이상증 1례

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발작성 운동이상증(Paroxysmal kinesigenic dyskinesia, PKD)은 경련성 발작과 구분해야 하는 드문 신경질환으로써 1940년에 Mount와 Reback에 의해 발작성 무도무위증(paroxysmal dystonic choreoathetosis)란 용어로 처음 보고되었으며 1967년 Kertesz에 의해 처음으로 발작성 운동이상증(Dyskinesia)으로 명명 되어졌다. PKD는 아동기에서 성인기 초에 호발하며 가족성 우성 유전으로도 나타날 수 있고 chromosome 16p11.2-q12.1, 16q13-q22.1, 2q32-36과 관계 있다는 보고가 있다. 증상은 대부분 수 초 이내 멈추나 드물게 5분 이상 지속되는 경우도 있다. 증상 발현 전에 감각 이상 등의 전구 증상이 동반되는 경우가 있으며 의식소실은 동반되지 않는다. 치료는 carbamazepne, phenytoin, valproic acid, clonazepam 등의 항경련제를 투여하는데 일부에서는 oxycarbazepine이나 levodopa를 투여하기도 한다. 저자들은 한 가족의 세명의 형제에서 나타난 발작성 이상운동증을 경험하고 항경련제(Oxcarbamazepine or Carbamazepine)를 통한 좋은 치료성적을 거두었기에 보고하는 바이다.

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