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Secondary Paroxysmal Dyskinesias

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Abstract: Paroxysmal dyskinesias (PxDs) are involuntary, episodic movements that include paroxysmal kinesigenic (PKD), paroxysmal nonkinesigenic (PNKD), and paroxysmal hypnogenic (PHD) varieties. Although most PxDs are primary (idiopathic or genetic), we found 17 of our 76 patients with PxD (22%) to have an identifiable cause for their PxD (10 men; mean age, 41.4 years). Causes included peripheral trauma (in three patients), vascular lesions (in four), central trauma (in four), kernicterus (in two), multiple sclerosis (in one), cytomegalovirus encephalitis (in one), meningovascular syphilis (in one), and migraine (in one). The latency from insult to symptom onset ranged from days (trauma) to 18 years (kernicterus), with a mean of 3 years. Nine patients had PNKD, two had PKD, five had mixed PKD/PNKD, and one had PHD. Hemidystonia was the most common expression of the paroxysmal movement disorder, present in 11 patients. Both of the patients with PKD had symptom durations of <5 minutes. Symptom duration ranged from 10 seconds to 15 days for PNKD and from 5 minutes to 45 minutes for mixed PKD/PNKD. There were no uniformly effective therapies, but anticonvulsant drugs, clonazepam, and botulinum toxin injections were the most beneficial. Awareness of the variable phenomenology and the spectrum of causes associated with secondary PxD will allow for more timely diagnosis and early intervention. © 2002 Movement Disorder Society

Key words: chorea; dystonia; secondary; symptomatic; paroxysmal dyskinesias

Paroxysmal dyskinesias (PxD) are rare movement disorders that are involuntary and episodic and may include any combination of dystonia, ballism, chorea, or athetosis. The events may be precipitated by sudden voluntary movements (paroxysmal kinesigenic dyskinesias [PKDs]) or may occur spontaneously at rest (paroxysmal nonkinesigenic dyskinesias [PKDs]. Two less common types of PxD, precipitated by exertion and sleep, respectively, are paroxysmal exertion-induced dyskinesia (PED) and paroxysmal hypnogenic dyskinesia (PHD).[1] PKD is traditionally described as shorter in duration (seconds) and more frequent (multiple per day) than PNKD.[1–3] PKD is also thought to be more responsive to pharmacotherapy—specifically, anticonvulsant medications—than PNKD.[4–6] Symptoms may be exacerbated by multiple factors, such as anxiety, fatigue, and alcohol use in both PNKD and PKD patients. Early reports described the movements as choreic, choreoathetoid, or dystonic, but more recent reviews have argued that the less specific term *dyskinesia* is more appropriate, as the movements are often complex and may not be witnessed by the diagnosing clinician.[1,2,6]

Most cases of PxD are primary, categorized as either familial (usually autosomal dominant) or idiopathic. However, in some cases a specific cause for the PxD has been identified, such as multiple sclerosis (MS), vascular lesions, trauma, or acquired metabolic abnormalities. We reviewed the records of patients in whom we identified a specific cause of their PxD (other than familial or psychogenic) and conducted a review of the literature in order to characterize secondary PxD and examine the roles of different causes.

PATIENTS AND METHODS

Ninety-two patients diagnosed with PxD were identified in the Baylor College of Medicine Parkinson's Disease Center and Movement Disorders Clinic database, from among 12,063 patients evaluated between 1981 and 2000. Of those, 16 patients had incomplete records and were excluded from analysis. Hence, 76 records were

A videotape accompanies this article.

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reviewed for confirmation of the diagnosis of PxD, evidence of secondary causes, and demographic data. Inclusion criteria were: (1) evidence of PxD by examination and videotape review, with or without medical history; and (2) evidence of abnormal involuntary movement that was episodic in nature, sudden in onset, and not associated with a change in consciousness or seizure activity. Exclusion criteria were: (1) diagnosis of familial PxD; (2) positive family or personal history of dyskinesia or seizure disorder; and (3) evidence of a psychogenic cause. Psychogenic causes were excluded based on the presence of false sensory examinations, obvious psychiatric disorders, inconsistent neurological examinations, or other reported criteria for psychogenic movement disorders, including, in some cases, relief of symptoms with placebo.[1,7]

All patients underwent evaluation at the Parkinson's Disease Center and Movement Disorders Clinic, Baylor College of Medicine, and were categorized according to a previously reported classification.[1] PKD was diagnosed if rapid or abrupt voluntary movements precipitated the involuntary movements and PNKD was diagnosed if the involuntary movements occurred spontaneously at rest. PHD was diagnosed when patients had episodic involuntary movements during or while emerging from sleep, and PED was diagnosed when the involuntary movements followed prolonged physical exertion.

The following data were collected: diagnosis, age at onset, cause, temporal relationship between event and symptom onset, type and location of movement, frequency and duration of symptoms, precipitants, exacerbating factors, presence of auras or pain, and treatment response. Movements were categorized as dystonic, choreic, athetotic, or ballistic by the examining physician or according to patient and witness reports. The results were compared with findings reported in the literature.

RESULTS

Cause and Age at Onset

Fifty-nine patients were excluded from analysis due to diagnosis of familial or congenital PxD (31 patients), diagnosis of psychogenic PxD (21 patients), or unclear diagnosis (7 patients). Seventeen of the 76 patients reviewed (22%) had secondary PxDs. There were 10 men (mean age, 41.4 years) and 7 women (mean age, 33.5 years). Although the range of age at onset varied widely from 2.5 to 79 years, vascular causes presented when patients were older (mean age, 65 years) and trauma presented when patients were younger (mean age, 28.5 years). Causes included peripheral trauma (three patients); stroke (four patients); central trauma (four patients); kenicterus (two patients); and MS, cytomegalovirus (CMV) encephalitis, meningovascular syphilis, and migraine (one patient each; see Tables 1 and 2). Fourteen of the 17 patients diagnosed with secondary PxD had episodes that were witnessed in the Movement Disorder Clinic. The 3 patients who did not have episodes observed were diagnosed according to history and the reports of other physicians.

Diagnosis and Latency between Insult and Symptom Onset

Nine patients were diagnosed with PNKD, two with PKD, and one with PHD. Five patients had symptoms compatible with both PKD and PNKD, making classification difficult; these patients were referred to as mixed PKD/PNKD (Table 3). The mean latency from initial insult to the onset of PxD was 3 years, ranging from days (trauma) to 18 years (kernicterus; see Table 2).

Both of the patients with PKD had peripheral trauma and presented within 6 months of the trauma. The patient with PHD had a stroke 6 years prior to the onset of PxD. In three cases, the associated cause was not identified until the workup for PxD was begun; hence, the temporal relationship between insult and symptom onset could not be determined. In these cases, an anatomically related lesion was present on magnetic resonance imaging (MRI). Latency could not be calculated in two additional patients (with MS and a history of multiple neurosurgeries, hydrocephalus, and Arnold-Chiari malformation), as symptoms occurred against a background of chronic neurological deficits (Tables 1 and 2).

Types and Locations of Movements

Dystonia was the most common paroxysmal movement (occurring in 16 of 17 patients). When present, chorea, ballism, athetosis, and various hyperkinesias occurred concurrently with dystonia in all but one case (Table 3). The patient with meningovascular syphilis had pure chorea without dystonia. There was no relationship between the location or cause of neurological insult and the predominant movement type.

Consistent with previous reports,[6,8,9] the majority of patients in this series (11) had primarily unilateral distribution of involuntary movement (6 right, 5 left). Three patients had bilateral dyskinesias at onset and three had primary face and neck involvement. Seven patients had progression of their symptoms from one body area to another. Of those, one patient with mixed PKD/PNKD had progression from a unilateral to a bilateral distribution and one patient with PNKD had progression from bilateral lower to bilateral upper extremities. The remaining patients had progression within a unilateral distribution (Tables 1 and 2).

TABLE 1. *Clinical features of 17 patients with secondary paroxysmal dyskinesia sorted by suspected cause*

Suspected cause	Sex	Age at onset (yr)	Type of insult and area involved	Location of PxD symptoms
Stroke	M	56	L posterior frontal subcortical infarction on CT of brain	Neck and jaw contraction, orobuccal stereotypy, tongue protrusion
	M	68	L cerebral peduncle and brainstem, R cerebellum white matter infarcts and periventricular white matter infarcts on MRI of brain	R wrist and MCP flexion, R toe and ankle flexion, and R foot inversion
	M	58	R frontoparietal infarct on CT of brain, sleep EEG normal	L hand and elbow flexion
	F	79	R globus pallidus lacunar infarct and diffuse subcortical white matter infarcts on MRI of brain	Bilateral MCP, PIP, and DIP flexion
Peripheral trauma	M	58	Fall with disk herniation at C6–C7 on MRI of C-spine	R wrist flexion, R 1st and 2nd PIP flexion
	F	17	Blunt trauma to R leg with residual nerve damage on EMG	R foot inversion
	F	39	Trauma to L hand with fractures requiring multiple surgeries	L hand and elbow flexion, L arm adduction
Central Trauma	M	53	Neural tube defect with persistent external sac repaired; chronic hydrocephalus requiring ventricular shunting and 6 shunt revisions, 2 surgeries for repair of tethered cord, posterior fossa decompression for Arnold-Chiari defect (10 neurosurgeries), normal genetic analysis	L fingers extension and adduction; generalizes to R
	M	17	3 blunt head injuries with loss of consciousness, last injury with C1–C4 subluxation on MRI	R foot inversion and leg extension
	M	7	Anoxic brain injury at birth, grade I neonatal interventricular hemorrhage, normal genetic analysis	L arm abduction, elbow flexion and pronation, L wrist and finger flexion
	M	9	Static brain lesion—held midbrain and cerebral peduncle on MRI of brain, normal EEG during episode	R foot inversion, toe and hand flexion and face contraction
Kernicterus	F	2.5	Kernicterus—neonatal jaundice treated with light therapy, normal MRI of brain	L elbow flexion and athetosis of fingers, L face contraction, L leg extension
	M	18	Kernicterus—Rh incompatibility, significant and prolonged hemolysis requiring multiple blood transfusions; normal MRI of brain	R hand extension with chorea; posterior neck extension
Meningovascular syphilis	M	70	Meningovascular syphilis—CSF VDRL and MHA-TP positive, brainstem infarcts and R posterior parietal encephalomalacia on MRI of brain	Chorea in left arm and right leg
CMV Encephalitis	F	7	Cytomegalovirus encephalitis—confirmed by viral culture; small, poorly defined lesion in the L temporal area on MRI of brain	Bilateral knee extension, ankle and toe flexion and foot inversion, L hand flexion
Multiple sclerosis	F	44	Multiple sclerosis—diagnosed with oligoclonal bands in CSF, periventricular plaques, and classic history	R blepharospdsm, R face and neck contraction and L arm extension
Migraine	F	46	Migraine headaches with aura—increasing frequency and severity over the last several years, normal MRI of brain	L face contraction with dysarthria

CT, computed tomography; MRI, magnetic resonance imaging; MCP, metacarpophalangeal; PIP, proximal interphalangeal; DIP, distal interphalangeal; C-spine, cervical spine; MVA, motor vehicle accident; EEG, electroencephalogram; CSF, cerebrospinal fluid.

TABLE 2. *Onset of symptoms, associated neurological deficits, and responses to treatment of 17 patients with secondary paroxysmal dyskinesia sorted by suspected cause*

Suspected cause	Time from insult to onset of symptoms	Interepisode associated neurological deficits	Response to treatment	
			Effective	Ineffective
Stroke	3 yr	Vascular parkinsonism	Clonazepam and botulinum toxin	Bromazepam, madopar
	3 yr	Resolved L hemiparesis, hemisensory defects and dysarthria	Tetrabenazine	Carbamazepine, gabapentin, trihexyphenidyl, phenytoin, carbidopa/L-dopa, botulinum toxin, clonazepam
	6 yr	Resolved R hemiparesis	Baclofen	
	Unknown	Vascular Parkinsonism and L hemiparesis with hyperreflexia	Botulinum toxin and carbidopa/L-dopa	
Peripheral trauma	1 day	Radiculopathy	Botulinum toxin	
	4 mo	Paresthesia (tickling sensation in foot)	Carbamazepine	Pt. stopped carbamazepine and had return of symptoms; when rx. was reinitiated, sx. again resolved
	6 mo	Scoliosis (preinjury)	Carbamazepine	
Central trauma	Began 2 yr after last shunt revision; diagnosed 2 mo later (post-op 2nd tethered cord)	Neurogenic bladder since childhood, limited eye abduction bilaterally, L pronator drift, scissoring gait, abnormal sensory exam	Clonazepam	Multiple VP shunt surgeries for hydrocephalus
	2 yr	New onset severe headaches	Unknown	Haldol: generalized and increased severity
	3 yr	Baseline choreoathetosis of bilateral lower limbs, R hand chorea and dysarthria	Clonazepam	Diazepam, baclofen, gabapentin, botulinum toxin
	Unknown	Resolved R Bell's palsy, resolved R-sided weakness	Carbamazepine and gabapentin	Phenytoin, felbamate, carbidopa/L-dopa, clonazepam
Kernicterus	11 mo	Excessive drooling, mild L leg dystonia	None	Carbamazepine, clonazepam
	18 yr	Limited upward and downward gaze, hearing loss and incoordination since childhood	Trihexyphenidyl (IV diphenhydramine and diazepam for severe episodes)	Alprazolam, diazepam, carbamazepine, baclofen, cyclobenzaprine
Meningiovascular syphilis	Unknown	Vascular parkinsonism, increased tone in lower extremities, ataxia, resolved Horner's chorea minima in right arm and hand	Penicillin G and carbidopa/L-dopa	
CMV encephalitis	1 mo after diagnosis of encephalitis	chorea minima in right arm and hand	Phenobarbitol	Clonazepam, trihexyphenidyl, carbamazepine, gabapentin, depakote
Multiple sclerosis	13 yr (1st MS sx.); 4 mo (last MS sx.)	Resolving R third nerve palsy from 4 mo prior	Clonazepam, baclofen	
Migraine	6 yr since onset of migraines	Occasionally accompanied by auras such as visual changesg normal between episodes	Migraine prophylaxis/ Amitriptyline	

MS, multiple sclerosis; sx., symptoms; rx., medication; IV, intravenous; VP, ventriculoperitoneal.

TABLE 3. *Features of secondary paroxysmal dyskinesias in 17 patients sorted by suspected cause*

Suspected cause	Diagnosis	Duration	Frequency	Predominant movement
Stroke	PNKD	1–2 hr	5/day	Dystonia and stereotypy
	PNKD	15–45 sec	1/every 2 min	Dystonia
	PHD	<5 min	1/night	Dystonia
	Mixed	<5 min	1/mo → 1/week	Dystonia
Peripheral trauma	PKD	1 min	1–3/day	Dystonia
	PKD	<30 sec	5/week → 5/day	Dystonia
	Mixed	15–20 min	1/3 days → 5/day	Dystonia
Central trauma	Mixed	1–45 min	1–5/day	Dystonia
	PNKD	30 sec–2 min	3–6/day	Dystonia
	PNKD	10–15 days	1–4/yr	Dystonia
	Mixed	5–10 min	1/30 min	Dystonia
Kernicterus	PNKD	10 sec–2 min	0–20/day	Dystonia
	PNKD	1–2 hr	Multiple/day	Dystonia and chorea
Meningovascular syphilis	Mixed	10–15 min	3/day	Chorea
CMV encephalitis	PNKD	20–30 min	2/week → 2/day	Dystonia and athetosis
Multiple sclerosis	PNKD	10–5 sec	0–20/day	Dystonia
Migraine	PNKD	5 min	2–3/week	Dystonia

PNKD, paroxysmal nonkinesigenic dyskinesia; PKD, paroxysmal kinesigenic dyskinesia; PHD, paroxysmal hypnogenic dyskinesia; (→), symptoms increased in frequency.

Frequency and Duration of Paroxysmal Episodes

Both of the patients with PKD had short episodes (<5 minutes) that occurred many times per day. The variability in duration and frequency was most pronounced in the mixed PKD/PNKD and PNKD groups. The nine patients with PNKD ranged in symptom duration from 10 seconds to 15 days. Six had short episodes (seconds or minutes), two had durations of 30 minutes to 2 hours, and one had episodes lasting 10 to 15 days. Of the five patients diagnosed as having mixed PKD/PNKD, one had durations of <5 minutes, three had durations of 5–20 minutes, and in one the episodes lasted 1 to 45 minutes. Six of the PNKD patients had multiple episodes per day, two had symptoms weekly, and the patient with episodes lasting days had symptoms one to four times a year. Three of the mixed PKD/PNKD patients had symptoms daily and two had symptoms monthly or weekly (Table 3). There was no consistent relationship between duration and frequency of symptoms in these groups.

Precipitants, Exacerbating Factors, Auras, and Pain

Patients with kinesigenic symptoms reported rapid movements such as jumping up from a seated position, writing, holding a fork, or any purposeful hand movements, as precipitants. One patient with mixed PKD/PNKD secondary to peripheral trauma had episodes both at rest and precipitated by sudden movements or light touch to the involved area.

Patients with PNKD were more likely to report exacerbating factors (six patients) than were patients with PKD (none) or mixed PKD/PNKD (three patients). Common exacerbating factors included fatigue, stress, and temperature changes. Of the four patients who identified an aura before the paroxysmal episode, two had dyskinesias secondary to central trauma (both mixed). The remaining two patients with auras both had PNKD, associated with MS and CMV encephalitis, respectively. The dystonia was painful in five patients: In four, dyskinesias were secondary to trauma (one PKD, two PNKD, and one mixed). The fifth patient had PNKD secondary to kernicterus.

Response to Treatment

Nine of the 17 patients required only one therapy. For both of the PKD patients, a single agent (carbamazepine and botulinum toxin, respectively) resulted in symptom control. In contrast, 4 of the 9 patients with PNKD and 2 of the 5 patients with mixed PKD/PNKD experienced symptom control with a single agent. There was no consistent pattern of response to therapy based on either the cause or the type of PxD; however, the most frequently effective monotherapies were anticonvulsants (in four patients) and clonazepam (in two patients). Two PNKD patients had symptom control with tetrabenazine and trihexyphenidyl, respectively, after several other agents failed (Table 2).

Botulinum toxin relieved symptoms in 3 patients, either as a monotherapy (for 1 patient, with PKD secondary to peripheral trauma) or in combination with other agents (for 2 patients, PNKD and mixed, both secondary to stroke). Treatment of the underlying cause alleviated

symptoms in the patient with mixed PKD/PNKD secondary to meningovascular syphilis (who received intravenous penicillin) and the patient with PNKD associated with migraines (who receive migraine prophylaxis). Baclofen was effective alone for the patient with PHD secondary to stroke and with clonazepam for the patient with PNKD secondary to MS. Carbidopa combined with L-dopa was effective in 2 patients with mixed PKD/PNKD and associated vascular parkinsonism symptoms. Two patients with PNKD had not achieved symptom control despite trials of clonazepam and/or antiepileptics (Table 2). Details regarding the medications that were tried successfully or unsuccessfully are presented in Table 2.

DISCUSSION

We describe 17 patients with PxD associated with a specific cause; to our knowledge, this is the largest reported series of secondary PxD. Although PxD is itself a rare disorder, the results suggest that secondary causes may be responsible for more cases of PxD than previously recognized, accounting for 22% of all cases in this series. The goal of this study was to describe the characteristics and common causes of secondary PxD based on review of our clinic population and representative cases in the literature (Tables 1 and 2). We acknowledge the limitations of this study, which included the retrospective review of medical records and the lack of proof of a cause-and-effect relationship. With these in mind, the interpretations and observations discussed in this article must be viewed with caution.

Existing classifications focus primarily on idiopathic and familial PxD and are organized by features including duration of symptoms, precipitating factors (kinesigenic or nonkinesigenic), and cause (familial or acquired).[1,4,10,11] The secondary cases in this series did not necessarily adhere to these traditional classifications because of their marked variability in duration and frequency (Table 3). Furthermore, 29% of our patients with secondary PxD had features of both kinesigenic and nonkinesigenic dyskinesia. Finally, patients with secondary PxD appear more likely to have baseline neurological defects present between paroxysmal episodes than patients with primary PxD. Recognition of these atypical features should suggest that the cases are secondary rather than primary (idiopathic or familial). Certain characteristics of secondary PxD, however, are similar to those reported for primary PxD. Dystonia, usually observed in a unilateral or axial distribution, is the most common form of hyperkinesia in patients with primary or secondary PxD.[2,6] Consistent with classic descriptions of primary PxD,[3,4] patients with secondary PKD had frequent episodes of short duration, and patients with secondary PNKD reported exacerbating factors more frequently than did other groups.[1,3,4] Cases of secondary PxD in this series differed from reports of primary PxD is as much as there was variability of symptom duration, a wide range of ages at onset, and the overlap of kinesigenic and nonkinesigenic symptoms in five patients.

Response to treatment was difficult to interpret, as patients were not started on the same medications and had variations in dosage and duration of treatment, and assessments were subjective and not blinded. However, we did find that, like primary PKD patients, our patients responded well to anticonvulsant therapy, requiring only one agent for symptom control. Like primary PNKD patients, secondary PNKD and mixed PKD/PNKD patients were less responsive to standard treatments. Some patients benefited from botulinum toxin injections. This therapy was given only to patients who had focal paroxysmal dystonia; the injections appeared to provide meaningful relief of symptoms in one patient as a monotherapy and in two patients as an adjunct therapy.

The most common causes of secondary PxD in this study were peripheral trauma, stroke, and central trauma; additional cases were associated with kernicterus, meningovascular syphilis, CMV encephalitis, migraine, and MS. Due to referral bias, our population likely did not reflect the true prevalence of causes associated with secondary PxD in a general population. The cases presented here, however, serve to expand the list of reported causes of secondary PxD. The most common causes of secondary PxD, identified in a review of the literature, are MS, stroke or transient cerebral ischemia, trauma, metabolic abnormalities, central nervous system (CNS) infections, and anoxic brain injuries. Additional causes reported are thyrotoxicosis,[12] Arnold-Chiari malformation with syringomyelia,[13] parasagittal menigioma,[14] methylphenidate therapy,[15] progressive supranuclear palsy,[16] and spinal cord injury.[17] Early recognition of potential causes is particularly important, as symptoms may be reversed if the underlying cause is identified and treated. In order to focus on structural or metabolic causes of PxD, we excluded psychogenic PxD, although this is one of the most common causes of secondary PxD.[7] The following discussion is organized according to the most frequent causes of secondary PxD.

Multiple Sclerosis

Although we had only one patient with PxD secondary to MS, it is the most frequently cited cause of secondary PxD in the literature.[18–21] PxDs in MS are described as painful isometric muscle contractions ("tonic spasms"), often preceded by an aura and precipitated by voluntary

movement or sensory stimulation, lasting seconds to minutes and occurring many times per day.[18–21] Although lesions to the spinal cord are most commonly cited,[21] PxD in MS has been associated with lesions throughout the CNS.[22] The pathophysiological mechanism of PxD in MS is unknown; however, it has been proposed that it is related to ephaptic transmission.[19]

Vascular Events

Stroke was present in 4 patients (23.5%) in this series. The PxD symptoms developed after resolution of the stroke-related deficits, were contralateral to the infarct, and were distributed in the area affected by the stroke. Several cases in the literature make direct associations between vascular lesions in the thalamus, putamen, and medulla and the development of PxD.[23–28] These cases provide the most convincing evidence of a causal relationship between a single insult to the nervous system and the development of PxD.

Other potential cerebrovascular causes of PxD are orthostasis, transient cerebral ischemia, or both.[29–33] In these cases, PxD symptoms may be reversible with anticoagulation, revascularization, or other interventions that increase cerebral perfusion.[29,31,33] Recognition of these particular causes is crucial, as early therapeutic intervention may prevent permanent neurological deficit.

Central and Peripheral Trauma

Trauma was the most common cause of PxD in our series: central trauma occurred in 4 patients and peripheral trauma in 3 patients. The concept that brain injury can result in movement disorders has been well established.[34–36] Moreover, there are several reports of brain injury specifically associated with PxD.[37–42] In some cases there is a direct correlation between a focal neurologic insult and PxD in an anatomically related area.[40,41] In other cases, focal PxD is associated with diffuse trauma to the CNS.[38,42] As in other posttraumatic movement disorders,[43] there may be long intervals between an injury and the onset of PxD. The mechanisms of posttraumatic movement disorders are not well understood, but possible pathogenic responses to injury include inflammation, demyelination or remyelination, and synaptic reorganization. The different mechanisms may account for the variability among patients in the latency from time of injury to symptom onset.

Although the relationship between brain injury and resultant movement disorders is widely accepted, the notion that peripheral injury results in abnormal movements remains highly controversial.[44–46] Although the mechanism underlying peripherally induced PxD is unknown, emerging evidence suggests that peripheral lesions may result in cortical and spinal reorganization that can affect motor and sensory pathways.[47,48] Such aberrant reorganization may be at least partly responsible for the observed motor dysfunction, including PxD, following peripheral injury. Furthermore, patients who develop PxD secondary to trauma may have a predisposition to movement disorders due to genetic predilection, previous insult, or other reasons.[45] In the present series, all 3 of our patients with PxD secondary to peripheral trauma had histories of previous neurological injury, family histories of neurological disease, or both.

Metabolic Disorders

A review of the literature indicated that acquired metabolic disorders, such as hypoglycemia,[49,50] hyperglycemia,[51,52] and hypocalcemia,[53] represent the third most common cause of secondary PxD. We had no such cases in our series, likely due to referral bias, as noted above. Like transient cerebral ischemia, these are important causes to acknowledge, as appropriate therapeutic intervention can reverse symptoms.

Miscellaneous Insults to the Central Nervous System

In addition to these causes, other diverse CNS insults, including kernicterus, meningovascular syphilis, and CMV encephalitis, were associated with PxD in our series. One of our patients had PxD associated with the aura of migraine headaches. In their series on PxD, Houser and colleagues[6] noted a patient with a history of migraine headaches, but they did not consider migraine as a cause. In our patient, the PxD symptoms occurred only prior to the onset of headache; were frequently accompanied by other auras, such as visual disturbances; and were significantly relieved with migraine prophylaxis. This constellation suggests that the migraine is the cause of the PxD symptoms.

The observation that causes as diverse as those presented here result in similar symptoms suggests that PxD is the symptomatic expression of a variety of insults to the neuronal circuits that modulate movement. One unifying hypothesis emerging as a possible explanation for the pathophysiology of some cases of PxD is ion channel dysfunction. There are several paroxysmal disorders that are phenomenologically similar to PxD (episodic ataxias, hyperekplexia, and periodic paralyses) that have been linked to gene mutations resulting in ion channel abnormalities, and are thus termed channelopathies.[54,55] It is possible that variations of these ion channel defects are present in PxD. Of interest, both PxD and channelopathies (epilepsies and paroxysmal movement disorders)

respond favorably to medications that stabilize the neuronal membranes, such as anticonvulsants and acetazolamide.[55,56] The therapeutic and phenomenological overlap between paroxysmal disorders such as epilepsy, periodic paralyses, and PxD may be due to a shared ion channel defect.[55] Perhaps the causes associated with secondary PxD also interfere with the normal function of ion channels, resulting in paroxysmal, involuntary movements.

LEGENDS TO THE VIDEOTAPE

Segment 1. A 53-year-old, right-handed man mixed kinesigenic and paroxysmal nonkinesigenic dyskinesia secondary to Arnold-Chiari malformation, chronic hydrocephalus, and multiple neurosurgeries. He has dystonia manifested by extension of the first, second, and third digits and adduction and flexion of the thumb on the left hand that generalizes to the right hand. Symptoms last from 1 to 45 minutes, recur 1 to 5 times per day, and are most commonly precipitated by rapid hand movements, such as grasping a fork. Symptoms also occur at rest when his hand is held in a particular position. The episodes are preceded by a sense of tightness in his hand; they are sometimes painful and tend to be worse when he is tired or cold. He had marked symptom resolution within 1 week of starting clonazepam.

Segment 2. A 24-month-old, right-handed girl with paroxysmal nonkinesigenic dyskinesia and a history compatible with kernicterus. She had intermittent left-sided facial spasms, elbow flexion, and athetosis of the fingers by 11 months of age. This progressed to involve dystonic contractions of the trunk and extension of the left leg by 22 months of age. The episodes were initially 10 seconds in duration but over time they progressed to as long as 2 minutes. They now occur up to 20 times per day. Episodes are more likely to occur and more severe when she is crying or excited. She has had little improvement with carbamazepine or clonazepam and is now undergoing a trial of phenytoin.

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