Paroxysmal dystonic choreoathetosis in a patient with familial ataxia

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Paroxysmal dyskinesias have been divided into two types. The most common form is paroxysmal kinesigenic choreoathetosis. This can be a familial, sporadic, or secondary disorder and is characterized by frequent, brief choreic attacks that are precipitated by sudden movement or startle. The attacks are usually controlled by anticonvulsants. The other type is paroxysmal dystonic choreoathetosis, a rare familial disorder characterized by episodes of sustained generalized dystonic contractions of muscles without loss of consciousness. No sporadic or secondary cases have been reported. Chorea and athetosis are variable features and may be absent in some patients. Four families have been described with over 59 affected members. We now describe a young man with familial ataxia who had PDC.

Case report. At age 10, this patient began to have weekly episodes of generalized muscular stiffness with brief paroxysmal dystonic choreoathetosis that was briefly controlled with acetazolamide and was almost completely eliminated by clonazepam therapy.

Paroxysmal dyskinesias also had familial ataxia. His brother was similarly affected but had rare paroxysmal episodes. No secondary or symptomatic forms of this type of paroxysmal dyskinesia have ever been reported. Episodes were briefly controlled with acetazolamide and were almost completely eliminated by clonazepam therapy.

Summary

Paroxysmal dyskinesias have been divided into two types. The most common form is paroxysmal kinesigenic choreoathetosis (PKC). This can be a familial, sporadic, or secondary disorder and is characterized by frequent, brief choreic attacks that are precipitated by sudden movement or startle. The attacks are usually controlled by anticonvulsants. The other type is paroxysmal dystonic choreoathetosis (PDC), a rare familial disorder characterized by episodes of sustained generalized dystonic contractions of muscles without loss of consciousness. No sporadic or secondary cases have been reported. Chorea and athetosis are variable features and may be absent in some patients. Four families have been described with over 59 affected members. We now describe a young man with familial ataxia who had PDC.

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dystonic extension or flexion of the fingers and wrists of both hands. In most instances, severe dysarthria would occur and progress to anarthria. Episodes lasted from 10 minutes to 4 hours. No aura or change in consciousness was ever noted by the patient or his family. The episodes were typically precipitated by fatigue, extremes in temperature, anxiety, and later by alcohol consumption.

At age 19, he developed progressive ataxia, which was exacerbated during the paroxysmal dystonic attacks. His mother, a maternal uncle, and a brother were each examined and found to have a similar form of ataxia. The maternal grandfather was said to have had poor balance and slurred speech most of his adult life. The patient's brother also had three episodes suggestive of PDC witnessed by their parents, but no other family members were known to have the paroxysms.

Neurologic examination at age 27 revealed no intellectual impairment. Slight dysarthria was apparent in spontaneous speech. Gaze-evoked nystagmus was present in all directions, and in the primary position there was slight vertical nystagmus. Motor and sensory functions were normal. A slightly wide-based gait was present, and tandem walking was difficult. Dysmetria was evident on finger-to-nose examination. Reflexes were active but symmetric.

The following laboratory studies were normal or unremarkable: serum electrolytes, thyroid screen, serum ceruloplasmin, urine for heavy metals, EEG (during and between attacks), audiogram, visual evoked responses, and CT. Electronystagmography confirmed the presence of nystagmus on lateral gaze and suggested a central origin.

During attacks, he could not stand, and all limbs were dystonic with some athetoid movements of the hands. He was also mute, could comprehend the environment, and was fully conscious. Dysmetria was present in addition to dystonia. There was no subjective feeling of vertigo or dizziness.

Phenytoin sodium, phenobarbital, and carbamazepine increased the number of PDC attacks reported by the patient. Diazepam had no effect. Based on a preliminary suspicion of periodic paralysis, serendipitous administration of acetazolamide (750 mg per day) completely eliminated the attacks. Periodic paralysis was subsequently excluded from consideration by appropriate laboratory studies that included administration of glucose and insulin and measurement of serum potassium. Acetazolamide controlled the episodes of PDC for about 8 months. When the episodes returned with the original frequency on a dosage of 1 gm acetazolamide, that medication was discontinued. Clonazepam (1 mg per day) completely eliminated the attacks of PDC; for 2½ years, he remained almost asymptomatic and returned to gainful employment. A single-blind crossover with placebo validated the efficacy of this treatment. He occasionally experienced feelings of stiffness of the arms and back at times of stress, but the major symptoms did not recur.

Discussion. Since 1940, PDC has been described in four families.1–5 This patient and his brother are unique in providing the first in association of PDC with another inheritable disease, familial ataxia. The more common PKC occurs with other neurologic disorders, but only one of the patients Lance1 described with PDC was "moderately mentally retarded from birth."

The clinical features of PDC are easily distinguished from the more common PKC.1 In general, men are more frequently affected than women, and most patients experience the onset of PDC early in life. The attacks may occur frequently but vary. For example, the brother of our patient had only three unproven episodes. The duration of attacks may be 2 minutes or 4 hours. Some patients report an aura, such as a feeling of tightness or pressure in the chest, but most experience none. Generalized dystonia usually affects the limbs and trunk as well. The pharynx is usually involved, causing dysarthria or anarthria. Precipitants include alcohol, coffee, tea, fatigue, extremes of temperature, and anxiety or stress. Lance1 reported that three of four patients improved with clonazepam and had no further episodes. Our patient improved and has remained improved on this medication for 2½ years.

Our patient might be considered an example of familial periodic ataxia, because dysmetria and ataxia worsened during the PDC episodes. The generalized dystonia and lack of subjective vertigo, however, more closely fit the clinical criteria for PDC.

Acetazolamide has been effective in periodic ataxia.6,7 The mechanism of action in this condition is unknown, but this drug has limited usefulness as an anticonvulsant, perhaps inducing systemic acidosis, which may account for its efficacy in periodic ataxia.8

Clonazepam, a benzodiazepine, is useful in some convulsive disorders, particularly myoclonic seizures.9 Clonazepam is thought to enhance polysynaptic inhibitory processes at many levels,9 but its mechanism of action has not been established.9

The etiology of the paroxysmal dyskiniesias is unknown. Lance1 suggested that they could result from any disturbance of cortical control of the neostriatum and its thalamic connections and that some complex neurotransmitter mechanisms might underlie both PKC and PDC.

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Peripheral and central nerve conduction in subacute myelo-optico-neuropathy

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Subacute myelo-optico-neuropathy (SMON) has been endemic in Japan since 1955 and is due to clioquinol intoxication. It is characterized by severe painful dysesthesia in the distal portion of the legs and perineum and spastic paraparesis with or without visual loss. It is uncertain whether the severe distal dysesthesia is a disorder of peripheral nerve or spinal cord or both. Postmortem studies demonstrated the main lesion in the distal portion of the gracile fascicle and also in the distal portion of the corticospinal tract as a result of a dying-back mechanism. Experiments on dogs fed clioquinol reproduced the characteristic clinical and pathologic alterations in the spinal cord.

Short-latency somatosensory evoked potentials (SEPs) have been useful in assessing nerve conduction through individual portions of the peripheral and central nervous system. We studied the pathophysiology of the sensory pathways in SMON by using short-latency SEP and morphometry.

Subjects and methods. We studied five patients with SMON, two men and three women, aged 50 to 80 years. The interval from onset of symptoms to the time of this investigation was 11 to 16 years. All patients had a clearly documented history of clioquinol exposure before or at the time of the onset. Two patients were severely disabled with paraplegia (spastic in one and flaccid in the other) and marked impairment of sensation for all modalities in the legs. Vibratory and joint position sense was most severely impaired, and there was marked dysalgesia on the soles of feet. One patient was moderately disabled with paraparesis and marked dysesthesia in the legs. Vibratory and joint position sense was markedly impaired in the legs, with a positive Romberg sign. Two patients were mildly disabled, although there were subjective complaints of painful paresthesia in the legs. There was no weakness in the legs, but knee jerks were hyperactive. Sensation in the legs was mildly impaired for all modalities. Ankle jerks were absent in all five patients. The arms were asymptomatic in three patients and only mildly involved with hyperactive deep reflexes in the other two. There was no sensory impairment in the upper extremities, except in one patient who showed mildly diminished tactile sensation with some dysalgesia in the hands. In none of the patients, was there sphincter impairment.

Motor nerve conduction velocity was normal in arms and legs, although peroneal or tibial conduction was just above the lower limit of normal in two patients. Sensory nerve conduction velocity of the sural nerve was normal in all three patients studied.

Short-latency SEPs were studied with median nerve stimulation in all cases and with posterior tibial nerve stimulation in three cases. Recording was carried out with the subject sitting in a reclining arm-chair in a quiet, dimly lit room. The