

Paroxysmal kinesigenic choreoathetosis

Report of a case relieved by L-dopa

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SUMMARY A case of paroxysmal kinesigenic choreoathetosis is described. A hitherto unreported response to L-dopa is recorded and its possible relevance to the pathophysiology of the disorder is discussed.

Paroxysmal choreoathetosis is a disorder which has been known for at least 100 years (Stevens, 1966). Although the disorder is allegedly uncommon, its recognition is important as its disabling and apparently bizarre clinical features may lead to diagnostic difficulties, while its good response to anticonvulsants has been almost invariable (Lishman *et al.*, 1962; Whitty *et al.*, 1964; Kertesz, 1967; Kato and Araki, 1969; Tassinari and Fine, 1969; Burger *et al.*, 1972).

The purpose of this paper is to illustrate the stereotyped pattern of involuntary movements of this disorder and to record the response to L-dopa.

CASE REPORT

W.W.F., a 21 year old Chinese male, was referred to the Neurology Clinic as a problem of 'focal epilepsy'. The history was that at the age of 19 years he began to experience daily attacks of 'spasms' involving entirely or predominantly the right limbs. These attacks were occurring up to 20 times a day and were always precipitated by sudden movement, such as jumping out of bed or getting up from a chair. The patient recognized two grades of attacks: (1) 'small' ones which consisted merely of a transient tightening or tonic flexion of the toes, and (2) 'big' ones which began with a sudden feeling of tightness in the right toes followed, within seconds, by flexion of the toes, inversion of the foot, adduction of the arm at the shoulder, and flexion at the elbow with writhing movements (Figure). On a few occasions the involuntary movements spread to involve the left limbs as well. The duration of each episode was

about half a minute. There was no associated eye-deviation, tongue-biting, or urinary incontinence. There was no disturbance of consciousness or amnesia. The patient learned that he could prevent or abort a 'big' attack by avoiding any sudden movement or any sudden change in pace of movement. He also noticed that each episode was followed by a refractory period of several minutes during which he could indulge in any movement with impunity. His birth and developmental milestones were normal. There was no history of trauma. No similar disorder had been observed in the parents or the six siblings.

General and neurological examination between attacks revealed no abnormality. In addition to sudden voluntary movements, it was observed that sudden passive movements such as knee and hip flexion could also induce an attack. Hyperventilation and startle were not effective. Radiographs of the skull, cerebrospinal fluid, electroencephalograph (EEG) and serum calcium and phosphorus levels were normal.

The patient was initially treated with chlordiazepoxide and amitriptyline without improvement. Diphenylhydantoin 100 mg three times a day was then substituted and within two weeks the patient was completely free of 'big' attacks with a marked decrease in the frequency of 'small' ones. Whenever diphenylhydantoin was withheld, the frequency of attacks would increase after a period of a few days and reach pre-treatment level after two weeks. At one stage L-dopa in doses of 750 mg four times a day was given to the patient and found to be as effective as diphenylhydantoin. For the assessment of the response to L-dopa the patient was hospitalized. The frequency and severity (graded as 'big' and 'small') of the attacks were recorded by the patient and by us. During the first week while diphenylhydantoin was

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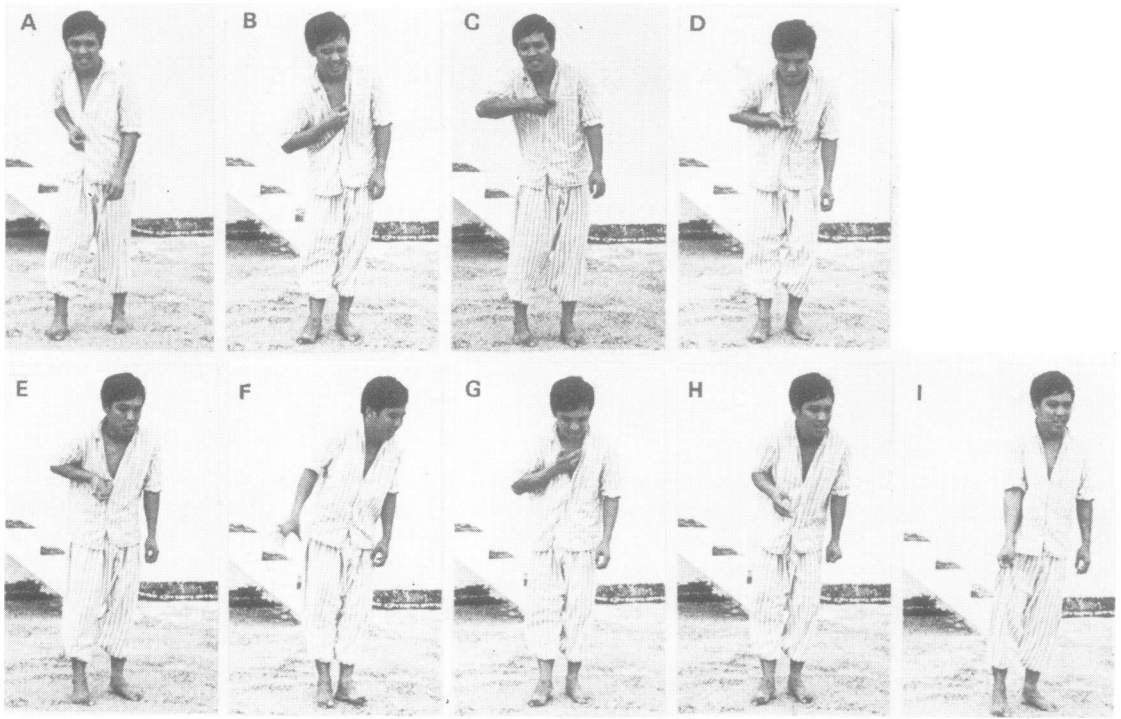


FIGURE. Prints (A to I) from consecutive frames taken one to five seconds apart showing representative postures during a typical 'big' attack induced by sudden movement.

continued no big attack was experienced and the small attacks occurred two to three times a day. Diphenylhydantoin was then withdrawn and the patient was observed without medication for two weeks; during this period the big attacks reappeared while the small ones increased in frequency. By the end of the second week the average daily frequency of the big and small attacks was five times and 20 times respectively. L-dopa 500 mg/day in four divided doses was commenced in the third week with increments of 125 mg per dose on every third day. Decrease in the frequency of both big and small attacks was noted on the 12th day of L-dopa therapy (2,000 mg/day) and by the 18th day (3,000 mg/day) the big attacks ceased to appear while the small attacks averaged only twice a day. Increase of L-dopa to 3,500 mg/day resulted in no further improvement. There were no side-effects except transient mild nausea on the first day of each increment. The patient was discharged with L-dopa 3,000 mg/day for six weeks, during which he continued to report freedom from big attacks and had only two to three small ones a day. As there was no difference in the degree of improvement achieved with L-dopa and with diphenylhydantoin and as the cost of L-dopa

was considerably higher, it was decided to put the patient back on diphenylhydantoin. During the interim period between discontinuation of L-dopa and reinstatement of diphenylhydantoin therapy it was noted that the attacks increased in frequency and severity. With diphenylhydantoin the patient again became free of big attacks and experienced only a few small ones a day.

Although no control study was conducted, the response to L-dopa in this patient was considered to be genuine for the following reasons: (1) the lack of spontaneous remission in the history since the onset of the disease, (2) the increase in the frequency and severity of the attacks after diphenylhydantoin withdrawal and before L-dopa therapy, and (3) the exacerbation after L-dopa withdrawal.

DISCUSSION

Gowers in 1901 mentioned two patients with paroxysmal involuntary motor disturbance induced by movement. Since then several reports on similar paroxysmal attacks have appeared in the literature under various labels. These included 'familial paroxysmal choreoathetosis'

(Mount and Reback, 1940), 'periodic dystonia' (Smith and Heersema, 1941), 'conditionally responsive extrapyramidal syndrome' (Kishimoto, 1957), and 'seizures induced by movement' (Lishman *et al.*, 1962). Despite the uniformity of the clinical features in the cases reported independently, the disorder was not universally recognized as an entity and was not uncommonly misinterpreted as having a psychogenic basis. Stevens (1966) reviewed the literature on the subject under the title of 'paroxysmal choreoathetosis' and gave the entity the emphasis it deserved. Kertesz (1967) introduced the term 'kinesigenic' to further characterize those cases whose attacks were movement-induced to differentiate them from the more uncommon cases described by Mount and Reback (1940), some of those by Lance (1963), and the family by Richards and Barnett (1968). Kato and Araki (1969) summarized the common clinical features of 56 kinesigenic cases reported in the literature. To these must be added one of the two patients described by Perez-Borja *et al.* (1968), another patient by Tassinari *et al.* (1969), and two patients by Burger *et al.* (1972).

The condition usually affects children and adolescents. Familial occurrence has been observed. Sudden movement is a regular precipitating factor. There is often an 'aura' such as paraesthesia, 'tightness', and 'tense feeling' in the limbs. The attacks occur several times a day. The involuntary movements are usually limited to one side and are dystonic, choreoathetotic, and occasionally ballistic. There is no disturbance of consciousness. Improvement on reaching adulthood is the rule.

Although the clinical features of paroxysmal kinesigenic choreoathetosis are well defined and treatment presents little problem, its pathophysiology remains uncertain. Its paroxysmal character and response to anticonvulsants have led some to consider it a form of reflex epilepsy. On the other hand, the stereotyped attacks with dystonic and choreoathetotic rather than clonic movements, the preservation of consciousness, and the lack of EEG changes in more than half the reported cases have prompted others to regard it as an extrapyramidal disorder. The response to L-dopa seems to lend support to the latter theory. The fact that L-dopa can both alleviate and produce dystonia and dyskinesia in

patients with extrapyramidal disease is now well recognized (Barbeau, 1969a, b; Cotzias *et al.*, 1969; Rosenthal *et al.*, 1972). On the other hand, L-dopa has not been shown to have any anti-convulsant property while epileptic seizures and definite EEG changes in association with L-dopa therapy have been observed (McPherson, 1970). Of the two available reports of cases of paroxysmal kinesigenic choreoathetosis that came to necropsy one showed only slight asymmetry of the substantia nigra (Stevens, 1966) and the other some melanin pigment in macrophages in the area of the locus caeruleus. Such lack of definite structural alternations would seem to indicate that the lesion is probably a biochemical one. Barbeau (1970) has suggested that dopamine has a major role to play in the basal ganglia in the regulation of postural mechanisms. Since movement involves changes in posture and the more sudden the movement the more likely it is to bring out a latent imbalance of postural mechanisms, it is tempting to speculate that paroxysmal choreoathetosis induced by sudden movement may well be due to some latent instability of extrapyramidal postural mechanisms. That this instability may be related to a relative immaturity and insufficiency of the dopaminergic system is suggested by the early age of onset and the spontaneous improvement in adulthood in most cases and the response to L-dopa in this patient.

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