

# Pallido-pyramidal syndrome treated with levodopa

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**SYNOPSIS** Two siblings are reported who developed classical signs and symptoms of Parkinsonism in the first decade of life. In addition, they had evidence of cortical spinal tract disease, thus putting them in the category of Davison's pallido-pyramidal syndrome. Both deteriorated to the point of a non-productive existence until the institution of levodopa treatment, at the ages of 18 and 20 years. The response of the extrapyramidal signs plus the lack of response of the pyramidal tract signs demonstrate the specificity of a pharmacological agent in certain areas of the nervous system. The rapid response of the female patient to very low doses of levodopa is unusual in our experience. Both patients have remained well for eight months after initiation of treatment.

Pallido-pyramidal disease, a syndrome manifested by a combination of symptoms of Parkinsonism of early onset and pyramidal tract signs, was described by Davison (1954). His five patients are the only ones reported in the literature with obvious pyramidal tract signs early in the course of the disease. No mention was made of treatment in these particular patients.

We recently evaluated a brother and sister who demonstrated signs and symptoms consistent with Davison's description of pallido-pyramidal disease. Both were treated with levodopa with excellent results. These are the sixth and seventh cases of this unusual disorder and represent the only report dealing with treatment of this disease.

## CASE 1

This 18 year old, white female was the second of five children. She was well until 8 years of age, when she developed tremors and rigidity. These became progressively worse and were followed by a gait disturbance. She volunteered that the rigidity and akinesia were more severe in the latter part of the day and were not present upon first arising. She had four brothers. The first-born male (case 2) is now 20 years old. Her three younger brothers aged 13, 11, and 8 years, are asymptomatic at the time of this report. There is no other family history of neuro-

logical disease except for a paternal cousin with Down's syndrome. There was no history of a consanguineous marriage in the family. Encephalitis was not reported in either patient.

Neurological examination revealed an alert, fully oriented patient. Memory and intellectual function were normal. Slit lamp examination revealed no Kayser-Fleischer rings. Motor examination revealed cogwheel rigidity in the upper extremities and neck. Spasticity was present in the lower extremities. Meyerson's sign was present. A 4–5 Hz coarse tremor was present at rest, but was accentuated with the hands outstretched. She demonstrated a scissors gait with poor balance. Tendon reflexes were pathologically brisk and the plantar responses were extensor bilaterally. The superficial abdominal reflexes were present. No weakness was present. The remainder of the neurological examination was normal. The following tests were normal: pneumoencephalogram, cerebral spinal fluid (cells, protein, colloidal gold, electrophoresis, and serology), erythrocyte sedimentation rate, serum total protein, albumin, calcium, phosphorus, cholesterol, glucose, uric acid, creatinine, total bilirubin, alkaline phosphatase, lactic dehydrogenase, serum glutamic oxalotransaminase, electrolytes, serum caeruloplasmin, complete blood count, radiographs of the chest and skull, electrocardiogram, liver, spleen, and brain isotopic scans, electroencephalogram, and 24 hours urine for copper.

Before beginning treatment, a marked diurnal variation in her symptoms was noted. She was asymptomatic in the morning and progressively worsened throughout the day. Amantadine hydrochloride, 100 mg twice daily, was begun. As it had

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(Accepted 21 October 1974.)

no effect after two days, this was discontinued and levodopa, 250 mg twice daily was started. Within 24 hours the patient demonstrated marked improvement in motor function. Her speed of gait increased by 300%. The levodopa was increased to 250 mg three times daily and within 48 hours her tremor, akinesia, cogwheeling, and poor balance disappeared. The hyperactive deep tendon reflexes and extensor toe signs remained present. She has been followed up for six months and has continued to have an excellent response with levodopa 250 mg four times daily. Although her extensor toe signs and hyperactive reflexes have continued, her signs of Parkinsonism have abated.

#### CASE 2

This 20 year old white male, the eldest brother of case 1, was premature at birth and in an incubator for a short time. He developed normally and did well until aged 7 years when he developed tremors and rigidity. He was hospitalized at that time. A complete evaluation including a pneumoencephalogram, spinal fluid protein and cells, electroencephalogram, liver function tests, copper studies, and routine chemical analyses were all normal. A diagnosis of juvenile Parkinsonism was made and he was treated with benzotropine mesylate, with little effect. He continued to deteriorate slowly and by the time of admission here was at least at stage III Parkinsonism. He had never been gainfully employed.

Neurological examination revealed an alert 20 year old male of average intelligence. He had an antero-flexed posture with a typical Parkinsonism gait, decreased movement of the left arm, and dysarthria. He had marked cogwheel rigidity in the neck and arms with spasticity in the lower extremities. There was no focal weakness. Reflexes were pathologically hyperactive throughout with an extensor toe sign on the right and an equivocal toe sign on the left. Rapid alternating movements were done poorly, worse on the left. His laboratory studies were similar to his sister's and were all negative. The electroencephalogram was mildly abnormal, demonstrating bilateral shifting theta activity compatible with diffuse cerebral disease. A pneumoencephalogram was not repeated. Levodopa was begun and within 10 days he noted marked improvement. His akinesia and dysarthria were markedly improved, as was his cogwheel rigidity. He did retain some residual spasticity. He continued to demonstrate flexion of his posture especially in his left upper extremity. The patient has been maintained on levodopa, 500 mg five times per day, and now is gainfully employed for the first time in his life.

**DIFFERENTIAL DIAGNOSIS** Several extrapyramidal syndromes may be considered in this group. Wilson's disease was ruled out by the copper studies and the absence of Kayser-Fleischer rings. Hallervorden-Spatz disease is ruled out by the absence of dementia and movement disorder. Juvenile Huntington's chorea was excluded by the normal pneumoencephalogram and the excellent response to levodopa treatment. The lack of exposure to lead and manganese make these toxic causes unlikely.

#### DISCUSSION

Juvenile Parkinsonism was described as early as 1899 (Siehr, 1899). More recently Yamamura *et al.* (1973) presented 15 cases of paralysis agitans of early onset and reviewed the literature. There seems to be no doubt from the literature that, when it does occur in the younger age group, it is highly familial (Willige, 1911; Mjones, 1949). A dominant pattern of inheritance has been suggested in some cases (Spellman, 1962), although sporadic forms have also been reported. The signs and symptoms of the juvenile form are indistinguishable from the more common adult variety.

Juvenile Parkinson's disease was first delineated pathologically by Hunt (1917). The pathological specimen demonstrated a decrease of large cells in the globus pallidus, putamen, and caudate nucleus, but the substantia nigra was normal. Van Bogaert reported a necropsy case of juvenile-onset Parkinsonism in 1930. The clinical picture was tremor, beginning at the age of 7 years, with rigidity and pseudobulbar signs. The pathology again was restricted to the globus pallidus and consisted of atrophy and loss of cells.

Davison's five cases were characterized by pyramidal and extrapyramidal dysfunction (1954). Four cases occurred in a brother and sister in two separate families. One case, previously reported by Hunt (1917), was non-familial. In one family the brother and sister manifested the disease at the age of 17 and 18 years respectively, in the other family at 21 and 22 years of age. Onset of the disease in the non-familial case was at 13 years and she died 50 years later. Pathological study revealed degenerative changes in the globus pallidus and ansa lenticularis, with relative preservation of the putamen and caudate nuclei. The substantia

nigra was described as 'shrunken in size'. There was depigmentation of the locus caeruleus and demyelination changes were noted in the pyramids and in the crossed pyramidal tracts of the spinal cord. It thus appears that Hunt (1917) and Van Bogaert (1930) presented a pallidal syndrome with a clinical picture of Parkinsonism of the adult onset variety, and Davison's cases represented perhaps a variant, or a specific syndrome, of pallido-pyramidal disease. It is interesting that in Hunt's case 2 (1917), the patient developed extensor plantar reflexes only in later life.

Our two patients are the youngest to be reported. Others have reported juvenile Parkinsonism successfully treated with levodopa but none of these patients had extensor toe signs (Martin *et al.*, 1971; Kilroy *et al.*, 1972).

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