CAUDATO-PALLIDO-NIGRAL DEGENERATION WITH CEREBRAL ATROPHY: REPORT OF A CASE WITH PARKINSONISM AND DEMENTIA

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(Received for publication September 6, 1984)

ABSTRACT

An 86-year-old Japanese man with caudato-pallido-nigral and cerebral degeneration is reported. The patient demonstrated parkinsonism and mental deterioration of slow progression and died 7 years after the onset. Necropsy disclosed severe neuronal loss and gliosis in the substantia nigra, globus pallidus and caudate nucleus, and frontotemporal cortical atrophy with myelin pallor of the white matter. This case could not be categorized within the current nosological entities of degeneration. Its nosological classification is discussed with particular regard to the pallido-nigral degeneration.

INTRODUCTION

Coexistence of parkinsonism and dementia has been recognized in various neurological diseases such as Parkinson disease, Parkinson-dementia complex, multiinfarct dementia, Alzheimer disease, Pick disease, neurosyphilis, progressive supranuclear palsy, Huntington’s chorea (rigid form), Hallervorden-Spatz disease, and so on. We report a case of parkinsonism with dementia of late onset. Degenerative changes in the substantia nigra, globus pallidus, caudate nucleus and, to a lesser degree, in the cerebral cortex and subjacent white matter were found at necropsy. The topographical distribution of degeneration observed in this case has not been described previously.

CASE REPORT

In 1974, an 80-year-old man with no family history of neurological disease manifested mental deterioration, poor facial expression and bradykinesia of in-
sidious onset and slow progression. He had no previous history of encephalitis or exposure to carbon monoxide or manganese. In July 1975, he began to show propulsion during walking. These symptoms were slowly progressive and in September he was confined to bed. Urinary incontinence and dysphagia became apparent. He was admitted on September 14, 1975.

On admission, the patient was well developed and nourished. He had a pulse rate of 76, a respiratory rate of 17 and a blood pressure of 166/80. The findings of general physical examination were normal. On neurological examination, he showed moderate impairment of mental functions including recent and remote memories, calculation, judgement and orientation to time. He was completely confined to bed and showed symptoms of parkinsonism such as masklike face, akinesia and cogwheel rigidity which were more pronounced in the arms than in the legs. The cranial nerve function was intact and speech was normal. No weakness was noted in the extremities. Grasping, snout, sucking and palmo-mental reflexes were all positive. The muscle stretch reflexes were slightly diminished in the lower limbs. The plantar responses were equivocal. Sensory impairment and cerebellar signs were absent.

Routine laboratory examinations were normal except that urinalysis revealed mild urinary tract infection. The serum treponema pallidum hemagglutination (TPHA) test was positive at 160×. Roentgenograms of the chest and skull revealed no abnormalities. EKG demonstrated a left anterior hemiblock and occasional ventricular premature beats. Lumbar puncture yielded a clear cerebrospinal fluid under normal pressure. The glucose was normal, protein 69 mg/dl, with one lymphocytic cell/mm³. TPHA test of the cerebrospinal fluid was negative. EEG showed disorganized-waves of low or moderate amplitude. Occasionally, 5–7 Hz waves with a moderate amplitude were observed bilaterally. A computerized tomographic scan revealed moderate enlargement of the cortical sulci, especially in the frontal and temporal lobes, and mild symmetric enlargement of the lateral ventricles.

A diagnosis of parkinsonism with dementia was made. The patient's hospital course was characterized by a slow but steady deterioration in mental status and parkinsonian features. Levodopa administration, 500 mg daily, was begun and then gradually increased to a maximum of 4.5 gm per day with no apparent clinical improvement. A pill-rolling tremor was noted in both hands in July 1976 and continued until the summer of 1978. In November 1976, trihexyphenidyl, 6 mg daily, was given in addition. The patient did not respond to these medications and, in fact, continued to deteriorate. In April 1977, he fell into the condition of apallic syndrome, a state with akinesia and mutism with preservation of eye movements and blinking. He died of bronchopneumonia and ileus in November 1980 at the age of 86, about 7 years after the onset of his neurological disorder.
Pathological findings

General autopsy revealed bilateral bronchopneumonia, strangulated ileus of the sigmoid colon, and an incidental gastric carcinoma (4 cm across) at the pyloric antrum. No evidence of syphilitic aortitis or valvulitis was noted. The brain weighed 1,000 gm and showed diffuse atrophy especially in the frontal and temporal lobes (Fig. 1a). The leptomeninges were thin and transparent. The extracerebral arteries revealed only mild atheromatous changes with no significant stenosis. The cranial nerves were unremarkable. Horizontal sections of the brain showed mild dilatation of the lateral ventricles. The cerebral cortex, in general, was slightly thin and the volume of white matter was reduced to a moderate degree. The basal ganglia and thalami were unnoteworthy in gross aspect. The substantia nigra was small in size and revealed marked depigmentation (Fig. 1b).

Representative sections from each lobe of the cerebral hemisphere, hippocampus, basal ganglia, thalamus, hypothalamus, cerebellum, three levels each of the midbrain, pons and medulla, and several levels of the spinal cord were stained with hematoxylin and eosin, phosphotungustic acid hematoxylin, luxol fast blue and with Holzer and Bodian techniques.

Microscopically, the cerebral cortex, in general, showed mild neuronal loss and gliosis. These changes were most prominent in the frontal and temporal lobes, but were not as prominent as one would expect from the gross appearance (Fig. 2a). Neuritic (senile) plaques and neurons with neurofibrillary tangles were not observed. No proliferation of microglial cells was seen either. The subjacent white matter exhibited a mild pallor with myelin preparation. The hippocampus revealed moderate neuronal loss, neurofibrillary tangles, and occasional neuritic plaques. No neurons were seen to contain globular intracytoplasmic argentophilic inclusions (Pick bodies). Severe neuronal loss and gliosis were noted in the entire segment of the globus pallidus (Fig. 2b) and caudate nucleus (Fig. 2c). The inner part of the putamen also showed neuronal loss and gliosis, but these changes were mild. The remainder of the putamen and thalamus contained the usual number of neurons and revealed no evidence of gliosis. The substantia nigra demonstrated severe neuronal loss with dense fibrillary gliosis both in the zona reticulata and zona compacta (Fig. 2d). Scattered extraneuronal pigment granules and occasional axonal spheroids were present. Neither Lewy bodies nor neurofibrillary tangles were encountered in the remaining neurons of the substantia nigra. The locus ceruleus contained a moderately decreased number of neurons and showed some extraneuronal pigment. These changes, however, were less prominent than those in the substantia nigra. The remainder of the brain stem including the red nucleus was unremarkable. The cerebellum and spinal cord showed no significant changes. The leptomeninges revealed no inflammatory changes. The leptomingeal and intraparenchymal blood vessels showed occa-
Fig. 1  a. Lateral view of the brain showing atrophy of the frontal and temporal lobes. b. Horizontal section through the midbrain showing atrophy and depigmentation of the substantia nigra.

Fig. 2  a. Frontal cortex showing only mild neuronal loss. ×25. b. Globus pallidus showing marked neuronal loss and gliosis. ×120. c. Caudate nucleus showing marked neuronal loss and gliosis. ×120. d. Substantia nigra showing marked neuronal loss, gliosis and scattered extraneuronal pigment granules. ×170. Hematoxylin and eosin-Luxol fast blue stain.
sional hyalinosis, but no inflammatory cell infiltrates were seen either in the vascular wall per se.

DISCUSSION

The present patient developed mental deterioration and parkinsonism of insidious onset in the late years of life. His symptoms were slowly progressive, terminating in death about 7 years after onset. The clinical presentation of masklike face, akinesia, cogwheel rigidity, propulsion and pill-rolling tremor was indistinguishable from that seen in the usual Parkinson disease, but the patient failed to respond to levodopa therapy. The pathological changes differed from those of Parkinson disease\(^1,\text{2}\) and no Lewy bodies were seen. Although the gross appearance of the atrophic frontal lobes resembled Pick disease, the most conspicuous change was severe bilateral neuronal loss and gliosis of the substantia nigra, globus pallidus and caudate nucleus. The neuronal loss and gliosis observed in the cerebral cortex in association with myelin pallor of the subjacent white matter were mild and less than might be expected from the gross atrophy of the brain. The Pick bodies, in addition, were not identified. Alzheimer neurofibrillary changes and neuritic plaques were noted only in the hippocampus. The nucleus basalis of Meynert was also unremarkable. The possibility of chronic carbon monoxide poisoning, manganese poisoning, delayed hypoxic encephalopathy as well as a variant of Creutzfeldt-Jakob disease was also considered, but could be readily ruled out based on the clinico-pathological features of the patient. Although the serum TPHA test was positive, postmortem examination showed no evidence of luetic infection either in the general organs or the central nervous system.

The topographical distribution of the lesions showed some similarity to that of a case recently reported by Matsuoka \textit{et al.}\(^3\) since the substantia nigra and globus pallidus were the most severely involved areas, and both patients presented parkinsonian features clinically. Their case, however, was different in that neurofibrillary tangles represented the main pathological feature of the globus pallidus, hippocampus, cerebral cortex and substantia nigra, instead of the simple neuronal loss and gliosis noted in our case.

The globus pallidus is the principal site among the regions affected in progressive pallidal atrophy.\(^4-\text{8}\) Its pathology in the globus pallidus resembles that observed in the present case. However, progressive pallidal atrophy is usually observed in infancy or in young adults and is clinically characterized by involuntary movements including dystonia and choreoathetosis as well as akinesia and rigidity. The substantia nigra has been reported to be less severely affected even in case of the “extended form” of the disease.\(^5,\text{7}\) The cases reported by Takahashi \textit{et al.}\(^9\) and Ohta \textit{et al.}\(^10\) both demonstrated parkinsonism, and necropsy
revealed involvement of the substantia nigra and globus pallidus. Their cases, however, were different from ours since these areas contained considerable numbers of spheroids and pigment granules.

A case with onset in the later years of life and with involvement of both the globus pallidus and substantia nigra has been reported by Contamin et al.\textsuperscript{11} Their patient showed severe progressive akinesia, "hypertonic oppositionelle", Parinaud sign and marked neck stiffness. The case reported by Kaiya et al.\textsuperscript{12} which had progressive dementia and parkinsonism of late onset and revealed pathologically pallido-nigral and thalamic degeneration, also resembles our case, although it lacked the degeneration of the caudate nucleus. They regarded the dementia as being a result of an extensive symmetrical neuronal loss of the thalamus despite that the brain weighed only 950 gm and gliosis of the cerebral cortex was observed. We consider that the dementia in our case can be explained by the presence of brain atrophy especially of the frontotemporal lobes and Alzheimer's changes in the hippocampus. Although it is difficult to categorize the present case with parkinsonism and dementia within one of the currently established forms of degenerative disease, we suggest that our case might be included in a category of degeneration of late onset involving mainly the pallido-nigral system, together with the cases reported by Contamin et al.\textsuperscript{11} and Kaiya et al.\textsuperscript{12}

REFERENCES
