DEGENERATIVE DISEASE OF THE SUBTHALAMIC BODIES*†

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The literature on lesions of the subthalamic body or corpus Luysi has largely concerned itself with unilateral involvement of this nucleus as manifested clinically by the syndrome of hemiballismus. In an exhaustive review of the literature, Whittier (1) found 30 cases of hemiballismus associated with isolated lesions in the subthalamic body. In the majority these were of a vascular nature. Bilateral involvement of the subthalamic body, on the other hand, has generally been observed as a part of more diffuse pathologic conditions, for example, kernicterus and encephalitis.

In the group of heredodegenerative diseases, rare involvement of the subthalamic bodies has been reported, but again only in combination with lesions in other systems. Here belong a case of ballismus associated with cerebellar ataxia reported by Titica and van Bogaert (2), a case with Huntington's chorea by Meszaros (3), and a case with spastic paraplegia by Baumann (4). In all of these instances, the ballistic movements, as might be expected, were modified by the coexisting lesions in other systems.

The only exception appears to be the case reported clinically by Rakonitz (5) in 1933. It concerned a man who, over a ten year period, from the age of 40 to 50 years suffered from symptoms of a slowly progressive ballismus, dysarthria, and dysphagia. The most prominent neurologic signs were bilaterally symmetrical rhythmic, rapid, hurling and rotating involuntary movements, that affected most severely the head, trunk and proximal muscles of the extremities, and were accompanied by fluctuations in muscle tone. The family history showed evidence of a similar disorder in an older brother, maternal grandfather and sister of the latter. It was the opinion of Rakonitz that his was the first reported case of hereditary biballismus and that the underlying lesion was a symmetrical degeneration of the corpus Luysi. The case, however, loses some of its significance in view of the lack of pathoanatomic confirmation.

The following 3 cases are, therefore, presented as the first recorded instances of a degenerative disease of the subthalamic bodies, which has been verified postmortem.

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† Presented at the Annual Meeting of the American Association of Neuropathologists, Atlantic City, New Jersey, June 14, 1959.
CASE REPORTS

Case 1. History: A. G., a white female, aged 36, was first admitted to the hospital at the age of 34 years with a history of increasing disturbance of gait and movement over a period of 2 years. While walking, her legs would suddenly fly out from under her and she would fall flat to the ground. The purposeless movements gradually affected the upper extremities, and she would constantly drop objects, particularly when under emotional tension. As the disease progressed, she began to experience difficulty in swallowing, became more irritable and forgetful, and at times was incontinent.

Examination revealed the patient to be cooperative, well oriented but euphoric, and showing mild impairment of memory. Her speech was hesitant, and there was an occasional involuntary tremor about the mouth. The most noteworthy features were gross explosive movements of the trunk, arms and legs which appeared suddenly in a sitting position. At times, they were described as writhing with flailing of the extremities, at others as jerking movements. Towards the end of her illness they became so violent that they would shake the whole bed. The deep reflexes were hyperactive, but there were no other neurologic signs. All laboratory studies including examination of the cerebrospinal fluid, pneumoencephalography and electroencephalography were negative. Under Thorazine therapy, she improved somewhat and was discharged from the hospital. A year later, however, there was a relapse and, at this time, examination revealed continuous “choreiform” movements, emotional lability and paranoid ideation.

Her course was progressively downhill, and she died of bronchopneumonia at the age of 36 years, four years following the onset of her illness.

The clinical diagnosis was Huntington’s chorea and although there was no confirmatory family history, the mother of the patient exhibited on occasion a tremor which, however, did not persist for any significant length of time.

Pathoanatomic Findings: The brain weighed 1190 grams and appeared grossly normal with the exception of symmetrical atrophy of the subthalamic bodies.

Microscopically, the changes were restricted to the subthalamic bodies and consisted of loss of myelin (fig. la), a reduction of neurons by about 50 to 75 per cent of the normal content (fig. lc) and intense gliosis composed of a network of glial fibers and sparse astrocytes (fig. lb). The lesions were of the same intensity on both sides and tended to affect somewhat more severely the dorsomedial than the ventrolateral parts. None of the other nuclei of the extrapyramidal system, including the globus pallidus and the lenticular fasciculus, were involved. However, there were some signs of degeneration in the decussating fibers of the corpus Luysi within the supramammillary commissure and in the fiber connections with the substantia nigra.

Cases 2 and 3. These two cases were siblings, whose family history was otherwise without significance.

History: S. M., a white girl, aged 13 years, had a normal birth and early development. When she started school at the age of 6 years, it was first noted that she was slow in comprehension and that her behavior was marked by restlessness and impulsiveness. At the age of 8 years, she was observed to have “blank” spells. At this time, a psychometric test awarded her an I.Q. of 62, and the clinical impression was mental retardation and petit mal epilepsy. At the age of 11 years, she was examined in a children’s psychiatric clinic, where her condition was variously interpreted. Some examiners noted dysarthria, grimacing, and coarse, frequently flexing “choreiform” movements involving the trunk and extremities. Others emphasized autistic behavior, bizarre responses, mannerisms, tics and sudden shifts of mood from fear to apathy. An EEG disclosed a slow disorganized record with evidence of generalized paroxysmal dysrhythmia. The diagnosis varied from degenerative chorea to childhood schizophrenia. The condition of the patient continued to deteriorate. She lost much weight, became bedridden, and died in a State hospital for the mentally
Fig. 1. Case 1. (a) Demyelination of subthalamic body (S.B.) in the presence of normal myelin content of the surrounding areas. Weil stain; × 5. (b) Gliosis restricted to subthalamic body, Holzer stain; × 25. (c) Paucity of neurons in subthalamic body, more marked in dorsal than in ventral parts. Nissl stain; × 38.

retarded, of inanition and terminal bronchopneumonia. The duration of her illness was approximately 7 years.

History: R. M., aged 11 years, younger brother of patient S. M., suffered from an illness, the clinical course of which was similar to that of his sister. Thus, following a normal birth and early development, mental retardation and emotional instability became noticeable at about the age of 5 to 6 years. At the age of 8 years, he was described as hyperkinetic, fearful and having a short attention span, and was awarded an I.Q. of 54. At the age of 10 years he was showing, according to some observers, abrupt choreoathetoid movements which involved primarily the larger muscle groups. To others he appeared autistic, confused and excitable. An EEG was characterized by a slow disorganized record with spike and wave activity. The diagnosis varied from chorea to childhood schizophrenia. He too died in a
State hospital for the mentally retarded following a period of marked loss of weight, approximately 5 years after the onset of his illness.

Pathoanatomic Findings: The changes in the brain were practically identical in the 2 cases. In both, there was symmetrical atrophy of the subthalamic bodies, evidenced by an intense gliosis in the Holzer preparations (fig. 2a, c) and by a marked reduction in neurons in the Nissl stain (fig. 2b, d). There was secondary degeneration of the decussating fibers in the supramammillary commissure and of the efferent fibers to the substantia nigra, but no lesions in other extrapyramidal nuclei.

There were, however, in both cases degenerative changes in the form of paucity of neurons and reactive gliosis, in the mammillary bodies (fig. 3) and mammillothalamic tracts (fig. 2a, b), in the dorsomedial nuclei and pulvinar of the thalamus, and in the periaque-
ductal gray matter. These lesions were of moderate severity, were diffuse and unsystematized, and in the mammillary bodies were characterized by capillary proliferation.

DISCUSSION

Clinically, the 3 cases showed signs in common of a progressive extrapyramidal disorder. Although the disturbances of movement were designated as choreiform or choreoathetoid, it seemed evident that at least some of them resembled ballismus. As defined, this is a form of involuntary movement characterized by continuous violent coordinated activity of axial and proximal appendicular musculature such that the limbs are flung about. This disturbance was obvious in Case 1, where explosive and violent writhing movements of the trunk with flailing of the extremities were noted. It was suggested in Cases 2 and 3, in whom abrupt flexor movements of large muscle groups were at times described. In the latter, however, it might be suspected that the neurologic examination was inadequate since a diagnosis of childhood schizophrenia was strongly considered (that such a misinterpretation can occur has been discussed by the senior author in another communication (6)). On the other hand, the diagnosis of degenerative chorea in all of the cases could be excused on the basis that they could not be classified in any other known category.

Pathoanatomically, all three cases showed the unique finding of a symmetrical degenerative disease of the subthalamic bodies in the absence of any lesions in other nuclei of the extrapyramidal system. As has previously been mentioned,
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hitherto, such an isolated affection of this area among the degenerative diseases has not been reported. The opinion advanced by Titica and van Bogaert (2) that heredodegenerative paraballismus is not associated with isolated atrophy of the corpus Luysi but may be due rather to atrophy of the globus pallidus cannot be accepted in the light of our cases. Our findings would, in fact, confirm the contention of Mettler and his associates (7) that “choreoid hyperkinesia” results from loss of control or coordinating influence normally exercised by the corpus Luysi on the pallidum. On this basis, the movements can be abolished or reduced by destruction of the pallidum or of its efferent fibers.

The additional degenerative changes in the mammillary bodies, periventricular thalamic and periaqueductal nuclei of Cases 2 and 3 do not necessarily contradict the assumption of an isolated disorder of the subthalamic bodies. These changes closely resemble those observed in vitamin deficiency states such as underlie Wernicke’s and Korsakoff’s syndromes. In our opinion they might be attributed to the severe state of malnutrition that was present in the 2 children during the later stages of their illness. That these lesions may have contributed to the clinical picture, particularly the emotional disturbances, can only be surmised.

The hereditary basis of the disorder in our cases remains unproven in the absence of an adequate genetic study. But, while Case 1 is problematic, the familial occurrence in Cases 2 and 3 is strongly suggestive of hereditary etiology. The pathoanatomic findings in our cases makes it quite likely that the condition of hereditary biballismus reported by Rakonitz was, indeed, based on degeneration of the subthalamic bodies.

SUMMARY

1. Three cases with bilateral degeneration of the subthalamic bodies and symptoms suggestive of biballismus are reported.
2. The heredodegenerative basis of the disorder is discussed and the pertinent literature reviewed.

REFERENCES


* Case material from this paper was used by permission of the Journal.