Lewy Bodies in the Enteric Nervous System in Parkinson’s Disease

Koichi WAKABAYASHI, Hitoshi TAKAHASHI, Shigeki TAKEDA, Eisaku OHAMA and Fusahiro IKUTA

Department of Pathology, Brain Research Institute, Niigata University, Niigata, Japan

Summary. We systematically studied the intramural nervous system of the alimentary tract in patients with Parkinson’s disease and found that Lewy bodies were distributed widely in the Auerbach’s and Meissner’s plexuses. In the central nervous system, we recognized a striking similarity between the distribution of Lewy bodies and that of monoaminergic neurons. More recently, we have demonstrated that neuronal somata immunoreactive for tyrosine hydroxylase (TH) exist in the Auerbach’s and Meissner’s plexuses of normal humans. We consider a possible relation between these TH-immunoreactive catecholaminergic neurons to the occurrence of Lewy bodies in the enteric nervous system in Parkinson’s disease. The affinity of Lewy bodies to the central and enteric neurons seems to be attributable to an unknown cell-biological characteristic apparently shared by both neurons.

Parkinson’s disease is a progressive neurological disorder of middle age or later, manifested by tremors, muscular rigidity, decreased spontaneous movements, and a variety of autonomic symptoms including those of the alimentary tract. Postmortem studies of patients with Parkinson’s disease have shown that the loss and degeneration of pigmented neurons and occurrence of concentric hyaline cytoplasmic inclusions—the Lewy bodies—in the substantia nigra and locus ceruleus are constant pathological findings in the disease (GREENFIELD and BOSANQUET, 1953; BETHLEM and DEN HARTOG JAGER, 1960). However, there have been few morphological studies on the nervous system of the alimentary tract in Parkinson’s disease, although autonomic symptoms in the alimentary tract have been well documented as constant clinical features of the disease (EADIE and TYRER, 1965; AMINOFF and WILCOX, 1971).

LEWY BODIES IN THE ENTERIC NERVOUS SYSTEM

Our recent light and electron microscope observations (WAKABAYASHI et al., 1988) indicate that cytoplasmic inclusions identified with Lewy bodies occur in the Auerbach’s and Meissner’s plexuses of the alimentary tract (for incidence and distribution see below) of some Parkinson’s disease patients. The bodies, ranging in size 3–12 µm, appear as round or elongate, homogeneous or laminated inclusions with a clear surrounding halo (Fig. 1). They are slightly argentophil in Bodian preparations and not stained with periodic acid-Schiff. In electron microscopy, the Lewy bodies consist of aggregates of filamentous substances often with an inner core composed of an electron dense material. The constituent filaments, 10–12 nm in diameter, are randomly arranged in the central portion of the body and are radially oriented in the peripheral portion (Fig. 2). The Lewy bodies observed in the enteric nerve plexuses completely coincide in structure and staining reaction with those seen in the central nervous system (GREENFIELD and BOSANQUET, 1953; DUFFY and TENNYSON, 1965).

DISTRIBUTION AND FREQUENCY OF LEWY BODIES

The occurrence of the Lewy bodies in the Auerbach’s plexus in Parkinson’s disease was first reported by QUALMAN et al. (1984), who recognized the bodies in the colon of one patient and in the esophagus of another out of 22 patients with the disease. They also found the bodies in the esophagus in 2 out of 8 patients with achalasia, a disorder of esophageal
motility. Recently, KUPSKY et al. (1987) reported the occurrence of Lewy bodies in the Auerbach's and Meissner's plexuses of the surgically resected colon and biopsied rectum of a patient with Parkinson's disease and megacolon. In our observations of seven autopsied patients with Parkinson's disease, the bodies were found in everyone and were distributed widely in the Auerbach's and Meissner's plexuses from the upper esophagus to the rectum (WAKABAYASHI et al., 1988). They occurred in neuronal cell bodies and processes and were most frequent and numerous in the Auerbach's plexus of the lower esophagus. The bodies were also found in 8 out of 24 non-parkinsonian patients of similar ages. However, they were notably small in number.

SIGNIFICANCE OF LEWY BODIES IN THE ENTERIC NERVOUS SYSTEM IN PARKINSON'S DISEASE

Since James PARKINSON's original description of Parkinson's disease (PARKINSON, 1817), the occurrence of alimentary symptoms such as dysphagia,
heartburn and constipation has been well documented for the disease (EADIE and TYRER, 1965; AMINOFF and WILCOX, 1971). Radiologically, diminished peristalsis and dilatation of the esophagus, megacolon, and dilatation of the small intestine have also been reported (LEWITAN et al., 1951; GIBBERD et al., 1974; LOGEMANN et al., 1975). However, the pathological basis for those alimentary symptoms in Parkinson's disease has remained uncertain. The alimentary tract is innervated by the Auerbach's and Meissner's plexuses and the majority of the axons observed in the plexuses have been considered to be of intrinsic origin (FURNESS and COSTA, 1980), although the tract also receives extrinsic nerve fibers of sympathetic and parasymptomatic nature. It is thus reasonable to consider that the Lewy bodies have occurred in the intrinsic neuronal components of the alimentary tract, indicating that the intramural plexuses are involved in Parkinson's disease. The extensive occurrence of the bodies in the plexuses may account for a number of the autonomic symptoms in the alimentary tract.

Lewy bodies, usually fewer in number, have been occasionally found in the central nervous system in aged non-parkinsonian patients (TOMONAGA, 1979). In our study, they were found in the alimentary tract in 8 out of 24 non-parkinsonian patients; the patients in all of these positive cases were over the age of 60. The significance of this finding appears to be analogous to that for Lewy bodies in the central nervous system, suggesting a possible relationship between the disease process of Parkinson's disease and aging.

WHAT KINDS OF NEURONS CONTAIN LEWY BODIES?

Lewy bodies were, although distributed widely in the alimentary tract, encountered most frequently and numerously in the Auerbach's plexus of the lower esophagus in Parkinson's disease. In the central nervous system, a striking similarity has been noticed between the distribution of Lewy bodies and that of the monoaminergic neurons (OHAMA and IKUTA, 1976). Recently, we have found that neuronal cell bodies immunoreactive for tyrosine hydroxylase (TH), a rate-limiting enzyme of the catecholamine synthesizing pathway, exist in the Auerbach's and Meissner's plexuses of normal humans (Fig. 3) (WA- KABAYASHI et al., 1989). Interestingly, the TH-immunoreactive neurons were most frequent in the Auerbach's plexus of the lower esophagus. At present, we are considering the possibility that these TH-immunoreactive catecholaminergic neurons may correspond to the cells containing Lewy bodies in Parkinson's disease. It seems worthwhile to examine the possible occurrence of Lewy bodies in peripheral neurons, especially of the catecholaminergic type, outside of the intestine. Now that, however, Lewy bodies have been found only in the intramural neurons of the alimentary tract, the unknown cell biological feature causing the affinity of the cell to the bodies which is shared by the central and enteric neurons deserves our attention.

Fig. 3. Tyrosine hydroxylase-immunoreactive intrinsic neurons in the Auerbach's and Meissner's plexuses of normal humans. Counterstained with hematoxylin. a. Auerbach's plexus of the lower esophagus (male, aged 56). × 490. b. Meissner's plexus of the ileum (male, aged 65). ×940
REFERENCES


