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Short Original Communications

Status Marmoratus and Bielschowsky Bodies

A Report of Two Cases and Review of the Literature*

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Summary. Intraneuronal inclusions, consisting of polyglucosan and having histochemical and ultrastructural features identical to Lafora body of familial myoclonic epilepsy (Unverrict-Lafora disease), have been found restricted to the lateral pallidum in five patients. Two of these patients were also found to have status marmoratus of the basal ganglia. These lateral pallidal inclusions have been named after Bielschowsky, their original discoverer.

We report two additional patients with status marmoratus and Bielschowsky bodies and suggest that these two conditions are frequent concomitant phenomena arising independently from a common cause.

Key words: Bielschowsky bodies – Lafora body – Status marmoratus – Polyglucosan – Anoxic encephalopathy

Introduction

The association of status marmoratus and intraneuronal basophilic inclusions restricted to the lateral pallidum was first described by Bielschowsky in 1912 in a patient with congenital double athetosis [1]. In his report, he remarked on the similarities of these inclusions to Lafora bodies which had then been newly described [2]. Lafora bodies are basophilic, PAS-positive cytoplasmic inclusions occurring in neurons. They are considered to be the neuropathologic hallmark of one type of familial myoclonic epilepsy, i.e., the Unverricht-Lafora disease [3]. Unlike the inclusions described by Bielschowsky, Lafora bodies in brain are seen throughout the cerebral cortex and are especially concentrated in the thalamus, globus pallidus, and substantia nigra. The presence of similar intraneuronal inclusions localized to the lateral pallida was subsequently reported by Vanderheaghen et al. [4] in two patients with slowly progressive basal ganglia dysfunction and by de León [5] in a patient with athetoid form of cerebral palsy who was found at autopsy to have status marmoratus. De León felt that these inclusions, because of their exclusive presence in the lateral pallida and occurrence in a clinical setting without myoclonic seizures, should be distinguished from Lafora bodies. He named them Bielschowsky bodies after their original discoverer. In 1975, Ule and Volk [6] reported isolated atrophy of the lateral pallida with Bielschowsky bodies in a patient with progressive choreoathetosis. Ultrastructurally, these inclusions were identical to Lafora bodies.

The finding of intraneuronal inclusions of Bielschowsky type in association with status marmoratus has only been documented in two patients. We would like to report two additional cases and discuss the possible factors which lead to the accumulation of these polyglucosans in neuronal soma and its processes.

Case Reports

Case 1

A 15-year-old Hispanic girl with significantly impaired motor and intellectual development died of sepsis. She was born after a 36-week gestation in which there had been premature rupture of membranes prior to the onset of labor. The baby was born covered with purulent material. Her Apgar index was 2, and intensive resuscitative measures were required. CSF cultures were positive for Aerobacter. She was cared for in institutions for most of her life showing no obvious development. Her last neurological evaluation was 3 days before her death. She was found to be blind, partly deaf, and diffusely rigid. She did not speak. Reflexes were 2+; Babinski responses were negative.

Case 2

A 57-year-old white woman labeled as having "cerebral palsy" since birth expired as a result of disseminated lung adenocarcinoma. A

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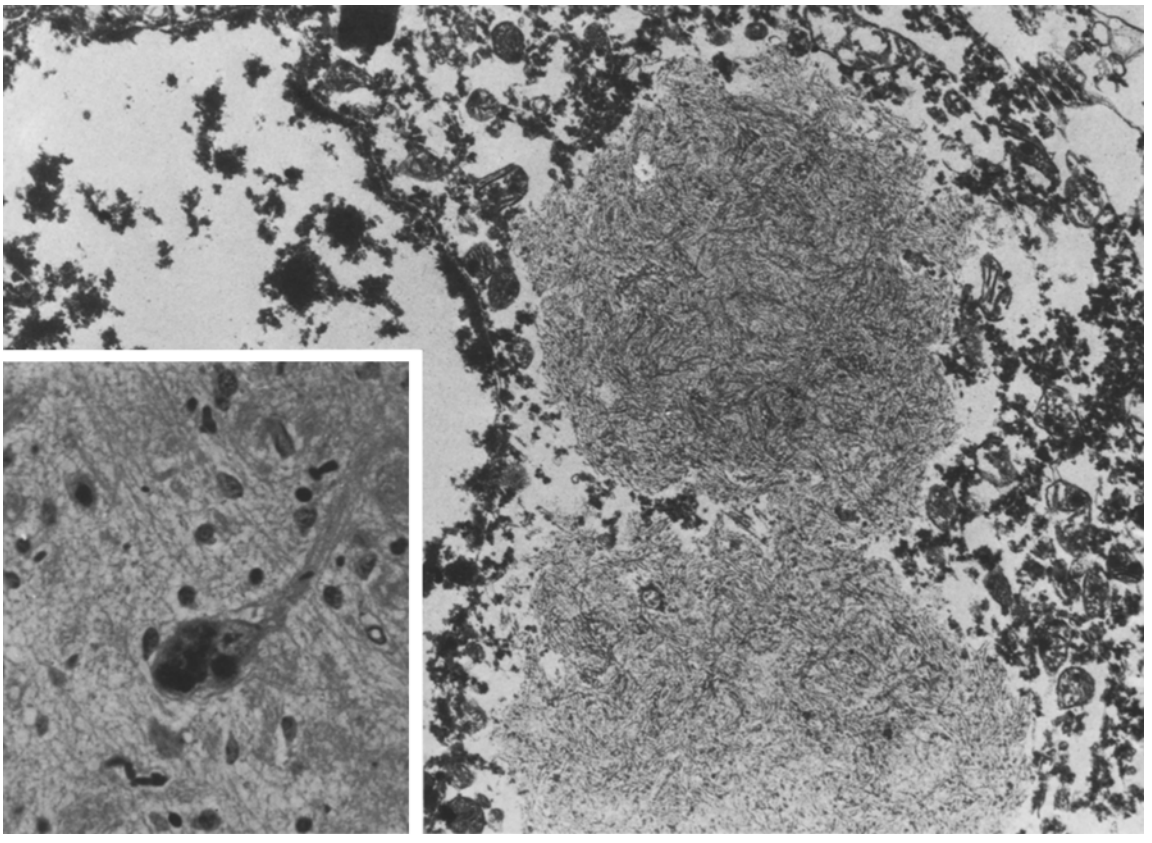

Fig. 1. Electron micrograph of neuron in lateral pallidum demonstrating the filamentous nature of Bielschowsky bodies (× 12,000). *Insert:* Lateral pallidal neuron containing multiple Bielschowsky bodies in the cytoplasm. PAS, × 100

detailed birth history was not available but the patient had been unable to walk since infancy. She could not move in bed for as long as she could remember. On neurologic examination she had garbled but appropriate speech and was oriented. She had severe limb contractures. Babinski responses were positive.

Autopsy Findings

The formalin-fixed brains in cases 1 and 2 weighed 700 and 880 g, respectively. The cerebral hemispheres were symmetric. Ulegyria was present in case 1, especially in the opercular region. The ventricular systems were moderately dilated. Sequential coronal sections revealed that both the basal ganglia and thalamus were reticulated due to interdigitating white matter bundles.

The microscopic findings in both cases were similar. The lateral pallida displayed lightly hematoxyphilic, round inclusions in the perikarya of neurons as well as in neurites (Fig. 1) (insert). They were variable in size and shape, the largest measuring 30 – 40 μm. Some were round or ovoid, others were elongated and extended in chains along cell processes. They stained deeply with PAS and resisted α-amylase digestion up to 24 h. They also stained with iodine, Best's carmine, Alcian blue, and silver stains. Toluidine blue revealed them to have metachromatic properties. Most bodies were not uniform but concentrically lamined with a dense more deeply stained central core and a paler peripheral zone. Ultrastructurally, they consisted of a feltwork of densely packed, irregular, and curved fibrils (Fig. 1). The fibrils were electron-dense and they often branched. Variable amounts of amorphous and granular material of either low or high electron density were also present. Smaller inclusions were also seen in the gliotic neuropil of the basal ganglia. They had similar histochemical and ultrastructural properties as the intraneuronal inclusions and could not be distinguished from corpora amylacea. There was marked depletion of neurons in basal ganglia and thalami which in addition had large numbers of ferruginated neurons. Myelin stain revealed randomly oriented myelinated fibers in the basal ganglia and thalami.

In case 1, in addition to the basal ganglia lesions, there were several examples of ulegyri where the cortex was thinned and gliosis was intense especially at the depths of the sulci. The white matter of the centrum semiovale, corpus callosum, and fornices was also pale and gliotic with corpora amylacea in the perivascular regions. Furthermore, the brain stem showed intense gliosis and numerous small basophilic granules in the neuropil of the periaqueductal grey, tectal plate, floor of the IVth ventricle and subpial zone. These bodies varied in size from 5 to 10 μm in diameter and had identical staining properties to those seen in the thalamus.

Discussion

The two patients described in this report, aged 15 and 57 years, had essentially a very similar clinical presentation of static psychomotor retardation. In the first patient, prematurity complicated with perinatal meningitis was well documented. In the second patient, the history suggested a non-progressive neurologic con-

dition starting in early infancy. At autopsy, both displayed status marmoratus of the basal ganglia and intraneuronal inclusions of Bielschowsky type, restricted to the lateral pallida. Numerous corpora amylacea were also seen in gliotic areas of brain.

The pathologic significance of Bielschowsky bodies is uncertain. The fact that these inclusions have now been described in four cases of status marmoratus is interesting. Status marmoratus frequently complicates difficult parturition, a situation in which impairment of placental blood flow results in hypotension, hypoxia, and acidosis. It would appear that Bielschowsky bodies represent an epiphenomenon brought about by an acute metabolic dysfunction occurring during a critical time in the perinatal period. Their presence exclusively in the basal ganglia probably reflects the higher vulnerability of the lateral pallidal cells of premature brains to this metabolic insult. The underlying mechanism which leads to accumulation of these polyglucosans in neuronal soma and its processes may be the same as that which causes status marmoratus. It is possible, therefore, that the three other cases of Bielschowsky bodies with lateral pallidal atrophy but without status marmoratus may have a similar pathogenesis.

The striking similarities in histochemistry and fine structure of Bielschowsky bodies, Lafora bodies, and corpora amylaceae suggest that all three inclusions may be more than casually related. A disturbance of carbohydrate metabolism is a likely underlying mechanism, but the factor(s) triggering their formation may be different.

Addendum

While this paper was being considered for publication, an additional paper describing the association of Bielschowsky bodies with status marmoratus appeared in Acta Neuropathol (Berl) 51:119–126 (1980) by A. Probst et al.

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