Adult Polyglucosan Body Disease Associated With Lewy Bodies and Tremor

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**Background:** Adult polyglucosan body disease (PGBD) is rare and typically presents with upper and lower motor neuron involvement and neurogenic bladder. Extrapyramidal features are unusual in PGBD and are presumed secondary to widespread pathology that includes the basal ganglia. There are no prior reports of Lewy bodies in PGBD.

**Objective:** To report a unique finding of Lewy bodies in a patient with PGBD.

**Report of a Case:** A 46-year-old woman initially presented with a 4-year history of resting tremor. The tremor responded to levodopa therapy. Several months later, she developed upper and lower motor neuron involvement and other clinical features of PGBD. A sural nerve biopsy specimen revealed intra-axonal polyglucosan bodies that confirmed the clinical diagnosis. Bulbar and limb weakness progressed, and she developed dementia. She died 6 years after onset. At autopsy, extensive polyglucosan body formation was found in many regions of the central nervous system. In addition, numerous α-synuclein staining Lewy bodies were observed in the substantia nigra, accompanied by marked neuron depopulation.

**Conclusions:** To our knowledge, this is the first report of adult PGBD associated with Lewy bodies and levodopa-responsive tremor. Although polyglucosan bodies were seen in substantia nigra, it is most likely that our patient had coexisting Parkinson disease.
in intrinsic hand muscles. Bradykinesia was prominent. She had mild facial and neck weakness. Asymmetric moderate distal (Medical Research Council grade 3-4) greater than proximal limb weakness affected all limbs. She had marked spasticity in all limbs, and gait was spastic. Deep tendon reflexes were diffusely brisk. Bilateral Hoffmann signs and extensor plantar responses were elicited. Sensation to all modalities was spared.

Complete blood cell count and routine blood chemistry findings were normal. Further laboratory results were normal or negative including erythrocyte sedimentation rate, antinuclear antibody level, rheumatoid factor, SSA/anti-Ro, SSB/anti-La, serum copper level, ceruloplasmin level, phytic acid level, hexosaminidase A level, lactate level, vitamin E and B12 levels, and serologic tests for syphilis and Lyme disease. Cerebrospinal fluid analysis findings were also normal. Magnetic resonance imaging of the brain revealed nonspecific foci of increased signal in subcortical white matter interpreted as microvascular ischemia. Magnetic resonance imaging of the spine was normal. Sensory and motor nerve conduction study results were normal. Needle electromyography revealed changes of diffuse chronic denervation with reinnervation. Fibrillation potentials were limited to bilateral hand muscles. Visual evoked responses were normal.

Sections of the sural nerve biopsy specimen revealed a slight loss of myelinated fibers, with no selective fascicular degeneration. Several myelinated fibers contained rounded, periodic acid–Schiff (PAS)-positive intra-axonal inclusions that, in toluidine blue-stained plastic sections, appeared as lightly metachromatic, concentrically laminated structures (Figure 1). Ultrastructurally, the deposits comprised randomly positioned filaments measuring 6.5 to 10.5 nm in diameter, typical of polyglucosan bodies (Figure 1). Gastrocnemius sections revealed evidence of denervation atrophy, manifested by the presence of angular atrophic fibers highlighted by esterase and nicotinamide adenine dinucleotide-tetrazolium reductase stains, occasional target fibers, and well-developed fiber-type grouping. No PAS-positive deposits were present in muscle to suggest type IV glycosogenosis.

Bulbar and limb weakness progressed so that she became wheelchair bound and required a feeding tube. Dementia also developed. The tremor, however, continued to respond to levodopa. She died 6 years after onset. Autopsy showed extensive polyglucosan body formation in many regions of the central nervous system, including the basal ganglia, thalamus, substantia nigra, and anterior horns (Figure 2). In addition, numerous α-synuclein–staining Lewy bodies were observed in the substantia nigra, accompanied by neuronal depopulation. There were no Lewy bodies in the cortex.

**COMMENT**

Polyglucosan body disease is a rare heterogeneous disease affecting the central and peripheral nervous system. In most cases there is upper and lower motor neuron involvement, neurogenic bladder, and cortical or subcortical dementia. Less common features include fecal incontinence, entrapment neuropathies, supranuclear gaze palsy, and skeletal and cardiac muscle dysfunction. Polyglucosan body disease is one of the few diseases that is seen with both upper and lower motor neuron signs and can simulate amyotrophic lateral sclerosis when sensory function is spared. In most cases, however, there is early sensory loss in the lower limbs to help distinguish PGBD from amyotrophic lateral sclerosis. Urinary incontinence is also a distinctive feature. The disease is inexorably progressive, and survival is variable (range, 1-20 years).

Extrapyramidal features are rarely reported in PGBD. Robertson et al described a 50-year-old woman with a speech disturbance who 1 year later developed balance problems, resting tremor of the right hand, urinary urgency, and cognitive impairment. There was no response to apomorphine hydrochloride or oral levodopa treatment. They suggested that although extrapyramidal features could be explained by a second process, PGBD may be the primary cause given the rapid evolution of other neurologic symptoms and the known accumulation of polyglucosan bodies in the brain.

Diagnosis of PGBD is based on clinical findings and confirmed by the presence of intra-axonal polyglucosan bodies in peripheral nerve or brain at autopsy. In autopsy series, polyglucosan bodies were found in processes of neurons and astrocytes. The polyglucosan bodies may also be present in cardiac and skeletal muscle, liver, and apocrine glands, suggesting a generalized storage disorder.

Polyglucosan bodies are small ellipsoid or threadlike structures, composed mainly of glucose polymers with phosphate and sulfate groups. They stain intensely on PAS preparations. Polyglucosan bodies are nonspecific and may be seen with aging. Lafora disease, type IV glyco-
The pathogenesis of PGBD remains uncertain. Some have proposed that the polyglucosan bodies interfere with axonal flow. In some patients of Jewish Ashkenazi descent who have PGBD, glycogen-branching enzyme (GBE) activity in leukocytes and peripheral nerve is reduced. Decreased GBE activity has also been reported in other adult patients with PGBD who were products of consanguineous marriages. Their offspring had partial GBE deficiency. For some patients of Jewish Ashkenazi descent with PGBD, glycogen-branching enzyme (GBE) activity in leukocytes and peripheral nerve is reduced. In addition to numerous polyglucosan bodies within the neurkilary, postmortem brain sections also demonstrated occasional polyglucosan bodies within neuronal perikarya (PAS-hematoxylin, original magnification × 400). Photomicrographs of substantia nigra demonstrating a small PAS-positive polyglucosan body adjacent to a residual pigmented neuron within the pars compacta (arrowhead). In addition, multiple PAS-negative Levy bodies are present within the cytoplasm of the pigmented neuron (arrow). Immunohistochemical stains demonstrated the expected strong α-synuclein reactivity associated with the Levy bodies but not the polyglucosan bodies. No Levy bodies were identified within the cerebral cortex (PAS-hematoxylin, original magnification × 1000).

We present the first patient with PGBD who on autopsy was found to have polyglucosan as well as Levy body formation in the substantia nigra. Her initial neurologic symptom was a levodopa-responsive tremor. Although extrapyramidal symptoms are rarely reported as a manifestation of PGBD, we suspect our patient’s tremor was related to idiopathic Parkinson disease.

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