Clinical History: A 35 year old African-American man was referred to the Manhattan HIV Brain Bank (MHBB) with 5 years of slowly progressive gait disturbance and dysarthria. He had been diagnosed with HIV, which was sexually-acquired, around the same time his neurologic symptoms began. He was poorly adherent to antiretroviral medications, reaching a CD4+ nadir of 16. Other medical conditions included hypertension, asthma, anxiety and depression. Social history was significant for chronic cocaine dependence, several incarcerations, and periods of homelessness with extreme social alienation. In his 20s he had been a boxer, and had sustained a total of 3 knockouts. There was no known family history of neurologic disease, however both his parents had died in their 50’s (mother of cardiac disease, father of unknown causes), and he had no full siblings.

Neurologic examination at presentation revealed grossly normal mental status. Cranial nerve examination was significant for mild dysarthria, decreased facial expression, slow saccades, and mild impairment of upward gaze. Motor exam revealed normal strength and tone in his upper extremities, but in the lower limbs there was mild symmetric weakness involving both distal and proximal muscles, and mild to moderate spasticity. Vibratory sense was mildly reduced in the toes, but sensory examination was otherwise normal. Cerebellar examination was normal in the upper extremities, and limited by weakness and spasticity in the lower extremities. Gait was wide-based and unsteady. Clinical diagnostic evaluation revealed normal serum folate and B12, and negative RPR. MRI of the brain was interpreted as normal. Somatosensory evoked potentials were consistent with myelopathy. He refused a lumbar puncture. A diagnostic molecular test was performed. The patient was followed in the MHBB for the next 15 years, until his death at the age of 50. During this time his neurologic course was steadily progressive. Within two years, at age 37, he had developed nystagmus, dysmetric saccades, progressive ataxia involving the trunk, spasticity involving the upper extremities, worsening dysarthria and hypophonia, and peripheral neuropathy. Repeat MRI of the brain demonstrated a mild, diffuse cerebral and cerebellar atrophy, and more marked brainstem atrophy. By age 42, the patient was wheelchair bound, unable to bear weight on his legs. At age 43, he was institutionalized for care. At the time of his death (due to pneumonia and sepsis), he was bed bound with a tracheostomy, and was able to communicate only through blinking his eyes.

Autopsy findings: The brain weighed 1150 grams with its dural cap. The ventricular system was diffusely dilated with a fenestrated septum pellucidum, the contours of the caudate nuclei were normal. There was remarkable atrophy of the pons, pallor of the substantia nigra and multiple, ill-defined gray plaques in the cerebral and cerebellar white matter. The spinal cord was extremely atrophic.

Material submitted: 1. Images of the medial aspect of the fixed brain cut in sagittal orientation, and fixed coronal sections of a half hemisphere at the level of the caudate and globus pallidus. 2. H&E slide of the spinal cord.

Points for discussion: 1. What was the diagnostic molecular test?
2. Is the neuropathology typical of this disorder?