

On-line supplemental data: Case Histories

Case 1, a former professional football player, developed weakness of the neck, shoulders, and fingers 8 years after the onset of mild cognitive decline and profound apathy. At the age of 64, he noted a tendency to trip while walking on uneven ground and muscle twitching in his upper extremities, lower extremities, and trunk. He had longstanding chronic neck pain with radiating discomfort in his shoulders. His past medical history was significant for multiple injuries sustained while a linebacker, including numerous concussions and multiple cervical spine injuries. There was no family history of neurodegenerative disease. According to available medical records, on neurological examination he gave a coherent history of his medical condition and his language and speech were normal. He had normal eyelid elevation and mouth and eye closure. Muscle bulk of his tongue was normal without fasciculations. He had mild weakness of neck flexion, shoulder abduction, and finger extension. His tandem gait was slightly unsteady. There were diffuse fasciculations and hyperreflexia of the lower extremities. Cervical spine magnetic resonance imaging demonstrated cervical spondylosis without spinal cord compression. Electrophysiological examination showed normal motor and sensory nerve conduction, enlarged motor units with reduced recruitment, multifocal fasciculations, and thoracic paraspinous fibrillations. The findings were interpreted as a generalized disorder of motor neurons without evidence of a polyradiculopathy. Two major teaching hospitals considered ALS the most likely diagnosis. Over the course of the next 6 months, his speech became slower and more spastic and his walking became difficult. Two years

after the onset of his symptoms, he was mute, his arms and legs were essentially motionless, there were widespread fasciculations, and he had difficulty breathing. He died at age 66 from respiratory insufficiency.

Case 2, a former professional football player, developed progressive weakness of his right arm and hand with diffuse fasciculations at the age of 47 without any cognitive abnormalities. Although he was described as having a “short fuse” throughout most of his adult life, verbal arguments or fist fights were infrequent. He did not have any significant impulse control problems but was intermittently mildly depressed. His past medical history was significant for 3 or 4 concussions sustained during his football career as a linebacker, including at least one with loss of consciousness. He had medication-controlled hypertension and hypercholesterolemia. A paternal grandmother had Alzheimer disease. Over the following months, he developed increasing shoulder and back pain, mild slurring of speech, difficulty swallowing, and excessive emotionality with weakness and atrophy of the tongue, diffuse fasciculations, hyperactive deep tendon reflexes, and bilateral Babinski signs. He was evaluated at major teaching hospitals and was diagnosed with ALS. Over the next 6 months, he developed hypophonia, progressive uselessness of his hands, difficulty breathing, and increasing depression. Two and a half years after the onset of his symptoms, he was mute, without movement in his arms, trace movement in his legs, and severe respiratory insufficiency. He died at age 49.

Case 3, a former professional boxer, developed cognitive decline at age 64. By age 65, symptoms of parkinsonism appeared and he was diagnosed with

progressive dementia with parkinsonism. At age 67, he became restless, agitated, and paranoid, with physically assaultive and wandering behaviors necessitating hospitalization. Neurological exam revealed that he was profoundly disoriented and confused, with severe memory impairment, left-right confusion, hypophonic speech, reduced facial expression, drooling, a stooped posture, and an unsteady tandem gait. There was also severe bilateral atrophy of his shoulder girdles, arms, and legs, with diffuse fasciculations. His past medical history was significant for multiple knock-outs during his 10 years as a professional boxer. In his youth he also drank alcohol excessively. A sibling had died a decade earlier with probable ALS. An EMG revealed extensive spontaneous activity and chronic denervation-reinnervation in the arms, legs, paraspinal muscles, and face without evidence of a polyneuropathy. The findings were consistent with the presence of a generalized disorder of the motor neurons, their axons, or both. He was discharged to a nursing home where he died suddenly several days later.