A Case of a Misdiagnosed Progressive Supranuclear Palsy (PSP) Patient

According to the National Institutes of Health, each year in the United States approximately 50,000 people are diagnosed with Parkinson's disease (PD). PD is the most common neurodegenerative disorder, next to Alzheimer's disease, with a lifetime risk of about 1 in 100 persons. PD is a progressive disease of the central nervous system that is more common in older adults, typically occurring after the age of 50. PD is characterized by degeneration of the basal ganglia, specifically dopamine secreting neurons of the substantia nigra pars compacta. There are motor and non-motor symptoms; motor symptoms include rest tremors, muscular (e.g., lead-pipe or cogwheel) rigidity, decreased mobility, postural instability, bradykinesia, and masked-like expression. Non-motor symptoms may include anosmia, hypophonia, anxiety, depression and fatigue, sleep issues, visual hallucinations/illusions, and cognitive deficits. PD can affect behavior and cognition, with potential impairments in verbal and visual learning and memory, attention and executive functioning, visuospatial processing, and mood. In the clinical setting, differential diagnosis is highly influenced by the physical manifestations of illness. As can be seen, it is possible to misdiagnosis the Parkinsonian-symptoms of progressive supranuclear palsy (PSP) as PD. Such is the case of Mr. Doe.

Mr. Doe, a 51-year old, right-handed, Caucasian man with 14 years of education, presented to our outpatient neurology clinic with a four-year diagnosis of PD. Symptoms included mild tremor on his right side, leg muscle stiffness, bradykinesia, impaired gait, and fatigue. He reported that two years earlier he began experiencing profound cognitive difficulties, specifically impairments in memory, verbal processing, problem solving, word-finding, spelling, speech, and comprehension. More recently his symptoms began affecting his day-to-day functioning, and he was forgetting steps necessary to complete tasks. He forgot appointments, conversations, directions, and the correct word to use when speaking. His speech was dysarthric. Mr. Doe's wife reported that on one occasion he spent nearly an hour attempting to cash a check at the bank because he could not communicate the words to the teller. His wife also added that Mr. Doe recently exhibited increased symptoms of fidgetiness and significant attentional difficulties. She noted he often forgot the name of his dog and that he was unable to hold information during conversation. He has been unable to effectively process a sequence of instructions, such as when doing the laundry. In terms of IADLs, his wife has taken charge of his medications, bill paying, and household chores. He denied any troubles with ADLs or IADLs, though this denial stemmed from the fear of losing his independence.

Further exploration of presenting concerns revealed increasing headaches and back pain, specifically in the upper back. Vision was reported to have gotten worse since 2013, with increased frequency of falling and bumping into walls or pieces of furniture. He denied any LOC or head trauma from falls. Additionally, his writing has become micrographic and he has difficulty with fine motor movements (i.e., tying shoes or a tie). Mood was reported to be waxing and waning, although he denied depression or anxiety. In addition, he denied hallucinations or delusions. Sleep was reportedly "fine"; however, he started to have increased daytime sleepiness, even though he reported roughly 10-11 hours of sleep per night. Both the patient and his wife reported that Mr. Doe had begun acting out his dreams, punching the headboard or his wife on several occasions. In addition, he stated increased frequency of nightmares/vivid dreaming since

the PD diagnosis and tremors in his legs while attempting to sleep, that he described as "feeling like pedaling while sleeping."

Mr. Doe was born and raised in a small town in New England. In terms of schooling, he received extra help in schoolwork, and was treated with Ritalin in elementary school for a short period of time. He graduated high school and attended two years of college. He worked in sales for over 20 years. Several years prior to the evaluation, he began noticing tremors and was unable to perform work duties. He has been on disability since that time.

Mr. Doe's medical history was notable for a number of sports related concussions while a rugby player during his teens to mid-adulthood. Although he reported "seeing stars" and dizziness, he denied any LOC or any changes in cognitive or emotional functioning post-concussive injury. In terms of neurotoxic exposure, he reported a history of drinking well water, though denied any reports of arsenic or PFOA (Perfluoroctanoic acid) exposure from such. There was no reported history of any remarkable alcohol or substance use. Family history was notable for heart disease (father). He noted his father may have exhibited symptoms of PD in his 80s and he passed away at the age of 84 due to a stroke.

Neuropsychological examination revealed global impairments with borderline-to-impaired performances in semantic/phonemic fluency, verbal and non-verbal memory, executive functioning (i.e., self-monitoring, set-shifting, organization, and planning), working memory, word knowledge, abstract non-verbal reasoning, visual integration, basic attention, and processing speed. Overall estimated intellectual functioning was in the borderline range, and both motor and cognitive components were equally depreciated. Mental status was impaired throughout the evaluation, and he was unable to identify the date, day, or floor of building. Throughout the evaluation he requested stimuli to be presented at eye level and would often complain of rigidity and trouble bending his neck. His eye contact was forward gaze throughout the evaluation and he evidenced trouble with vertical gaze. His gait was clumsy, and he bumped into the wall and chairs in the room.

Clock drawing was significantly impaired even with 2 attempts. On his 1st attempt, he was able to draw a clock with an accurate contour; however, he evidenced spatial disorganization of numbers with mild left hemi-inattention and omission of hands. He initially drew the numbers 12-6, and then began counting backwards 5-3. On the 2nd attempt he omitted both hands and contour, with perseveration in spatial disorganization of numbers (12-6) with left hemi-inattention. Interestingly, when given a clock to read the time, he was unable to provide an accurate time and became quite fixated and distraught. Confrontation naming productions were evident for multiple semantic, visually-related, and paraphasic errors for example protractor – "proactor", "procrator." Similarly, his ability to describe a picture was telegraphic (i.e., compressed, telegram-like speech without conjunctions and articles) with grammatical errors and focuses of details were anchored on non-target items. Aphasia examination revealed mild spelling dyspraxia, auditory verbal dysgnosia, dysgraphia, dyscalculia, and constructional dyspraxia.

Commentary:

Test data and Mr. Doe's clinical presentation were consistent with Major Neurocognitive Disorder without behavioral disturbances as diagnosed under the Diagnostic and Statistical Manual of Mental Disorders- Fifth Edition (DSM-5). His impairments, however, did not demonstrate the rapid progression that would have been consistent with a differential diagnosis of Lewy Body dementia. His extensive impairments in higher order processing such as planning and abstract thinking, and his impairment in memory retrieval along with his gait impairments with multiple falls, axial rigidity, bradykinesia, and vertical gaze palsy was consistent with a clinical phenotype of Progressive Supranuclear Palsy (PSP) a motor variant of Fronto-temporal Dementia. This was also supported by evidence of a "hummingbird sign" on T1-weighted MRI of midbrain tegmental atrophy (See figure below).

PSP or Steele-Richardson-Olszewski syndrome is often misdiagnosed initially as PD, although when atypical features begin to manifest (e.g., abnormal eye movement and early behavioral changes) the differential becomes apparent. According to Adwani et al., 52% of individuals exhibit behavioral and cognitive changes early in the course of the disease. The pathology associated with PSP is not completely understood, though recent literature has speculated that formation of astrocytic lesion, tau-positive neurofibrillary tangles and neuropil threads within the brain stem and basal ganglia, underlie the characteristic pathophysiology of PSP. This presentation often leads to underestimates of true prevalence of PSP, such that Globe, Davis Schoenberg, & Duvoisin (1988) estimated a prevalence of 1.39 per 100,000 cases in the United States.

This case illustrates the importance of appropriate diagnostic interviewing and recording of behavioral observations during the course of the evaluation. Often in the work of neuropsychological and neurological case conceptualizations, hallmark symptoms can influence the differential (e.g., bradykinesia, gait instability, rigidity), which can then pose difficulty in providing effective treatment recommendations. Though PSP and PD have similar treatment recommendations, the prognoses are much different. For Mr. Doe's family, the diagnosis of PSP and progressive trajectory, the treatment was highly influenced towards the management of physical symptoms and preparing for any future medical complications (e.g., pneumonia, head injury, choking, fracture) that could potentially occur. It was important, for recommendations to have referrals for social work (health care proxy, power of attorney, and a living will), ophthalmology, physical therapy and speech therapy. Additionally, it was imperative that Mr. Doe and his family had an outlet via support group and counseling, in regard to maximizing Mr. Doe's quality of life in terms of physical, mental and social abilities. This being said, to enhance patient functional capacity for movement-based disorders, it is valuable for clinicians to supplement assessments of movement (e.g., clapping test, gait, gaze) to better identify and guide diagnostic and treatment processes.

For those interested in reading more about Progressive Supranuclear palsy and Parkinson's disease we recommend:

Adwani, S., Yadav, R., Kumar, K., Chandra, S. R., & Pal, P. K. (2016). Neuropsychological profile in early Parkinson's disease: Comparison between patients with right side onset versus left side onset of motor symptoms. Annals of Indian Academy of Neurology, 19(1), 74–78. http://doi.org/10.4103/0972-2327.167711

Armstrong, R. A. (2011), Visual signs and symptoms of progressive supranuclear palsy. Clinical and Experimental Optometry, 94: 150–160. <u>http://onlinelibrary.wiley.com/doi/10.1111/j.1444-0938.2012.00770.x/abstract</u>

Graber, J. J., & Staudinger, R. (2009). Teaching NeuroImages:" Penguin" or" hummingbird" sign and midbrain atrophy in progressive supranuclear palsy. *Neurology*, *72*(17), e81. <u>http://www.neurology.org/content/72/17/e81.full</u>

Han, D. D. Y., Pyykkonen, B. A., Shandera-Ochsner, A. L., & Schmitt, F. A. (2014). Frontotemporal Dementias. The Neuropsychology of Cortical Dementias, 221.<u>http://lghttp.48653.nexcesscdn.net/80223CF/springer-</u> static/media/samplechapters/9780826107268/9780826107268_chapter.pdf

