A Case of the Richardson Syndrome Variant of Progressive Supranuclear Palsy With Apathy and Depression:
Clinical Evaluation and Symptomatic Treatment

David R. Spiegel, MD[a,*]; Jamie A. Parkerson, MS[a]; Perry B. Hammond, BA[a]; Rachelle L. Gonzalez, BS[a]; and Joseph W. Bannister, BS[a]

Progressive supranuclear palsy (PSP), a rare neurodegenerative condition, is the most common cause of atypical parkinsonism. Its most common phenotype, Richardson syndrome (RS), is characterized by prominent postural instability, supranuclear vertical gaze palsy, and cognitive dysfunction.[1] Additionally, neuropsychiatric features include apathy and depressive symptoms.[2]

In the absence of reliably validated biomarkers, the diagnosis is based mainly on clinical criteria. We present the case of a patient who, with lethality, had symptoms of possible/probable PSP-RS. We review the diagnostic process and neuropsychological and neuropsychiatric features of PSP-RS.

Case Report

The patient was a 66-year-old White man who was brought to the hospital after an interrupted suicide attempt. The patient had been admitted to the internal medicine department and started on venlafaxine 37.5 mg/d due to "depression" 3 weeks prior to this admission. The patient reported that his depressed symptoms developed over the past 2 months, coinciding with poor work performance. The patient denied previous psychiatric history, including alcohol and prescription/illicit substance misuse. The mental status examination was remarkable for dysarthria and delayed psychomotor processing speed.

The patient's medical history was remarkable for an 8-foot fall about 1.5 years ago, without loss of consciousness or further evaluation. About 1 month before that fall, the patient reported difficulties with balance. Subsequently, the patient and his family reported unexplainable falls until this admission.

Figure 1 provides the patient's magnetic resonance imaging results. The patient's Neuropsychiatric Inventory–Questionnaire (NPI-Q)[3] score was 12, with severe and moderate scores on apathy/indifference and depression, respectively. Table 1[4–6] provides the patient's physical, neurologic, and cognitive examination results along with the criteria of the National Institute of Neurologic Disorders and Stroke and the Society for PSP (NINDS-SPSP). Due to apathy and depression, venlafaxine was titrated to 150 mg/d. The patient was discharged after a 10-day hospitalization, with an NPI-Q score of 9. At 2-month follow-up, his NPI-Q score decreased to 4, with improvement in both apathy and depression subscales.

While the patient's diagnosis of probable PSP-RS was based on NINDS-SPSP criteria,[5] the latter evaluates 2 core functional domains (ocular motor dysfunction, postural instability). The patient also had impairments in additional domains purported by the Movement Disorder Society–PSP criteria: akinesia and cognitive dysfunction.[6]

Discussion

The order of appearance of cardinal deficits is highly variable in PSP, although classification in its first 2 years after onset may allow for a more comprehensive description of the PSP phenotypic spectrum.[7] For instance, and similar to our patient, the initial symptom in approximately two-thirds of RS patients is postural instability.[8] Shortly thereafter, falls develop within the first year of onset. Subsequently, abnormal saccades, bradykinesia, and then vertical supranuclear gaze palsy typically manifest by year 2.[7]

Alternatively, within 1 year of onset, approximately one-third of RS patients have cognitive changes, summarized as a dysexecutive frontal syndrome.[9] Bradyphrenia, a cardinal cognitive feature of PSP-RS, has been shown to progressively deteriorate throughout the course of the illness.[10]

Apathy and depression, potentially independent constructs, are commonly although not uniformly reported in PSP-RS.[11] Disruptions to cortical circuits associated with depression are reported to be far less affected than those associated with apathy.[11] Thus, the psychosocial aspects of coping with a chronic/lethal neurodegenerative disease could also explain the pathogenesis of RS patients' depressive symptoms.

While there is a dearth of evidence for treating apathy or depression in PSP, we continued and increased our patient's

[a]Department of Psychiatry and Behavioral Sciences, Eastern Virginia Medical School, Norfolk, Virginia

*Corresponding author: David R. Spiegel, MD, Department of Psychiatry and Behavioral Sciences, Eastern Virginia Medical School, 825 Fairfax Ave, Norfolk, VA 23507 (spiegedr@evms.edu).

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Table 1. National Institute of Neurologic Disorders and Stroke and Society for PSP Criteria as Applied to the Patient[a,b]

Mandatory Inclusion Criteria	Mandatory Exclusion Criteria	Supportive Criteria
Gradually progressive disorder: (+) the patient's symptoms began about ≥1 year ago Onset at age 40 years or later: (+) the patient's onset was around age 64 years	Recent history of encephalitis: denied by the patient Alien limb syndrome: denied by the patient on examination Cortical sensory deficits: not elicited on the patient's neurologic examination Local frontal or temporoparietal atrophy: not present on the patient's head MRI	Symmetric akinesia or rigidity, proximal more than distal: (+) present based on the neurologic examination Neurologic examination: (+)/(-) bilateral resting tremor
In the first year of disease onset: (+) prominent postural instability and falls were the first symptoms to be noted by the patient and his family	Hallucinations or delusions unrelated to dopaminergic therapy: the patient denied in the interview Cortical dementia of Alzheimer's type: the MoCA was administered; the patient demonstrated no short-term memory loss, and no aphasia was noted during the evaluation	Abnormal neck posture, especially retrocollis: not present during the patient's examination
Vertical (upward or downward gaze) supranuclear palsy: (+) downward gaze palsy and slowing of saccades were present on the patient's neurologic examination ≥1 years after falls developed	Prominent early unexplained dysautonomia (marked hypotension and urinary disturbances): blood pressure, including orthostatics, was normal; the patient denied urinary urgency, frequency, and nocturia without hesitancy Prominent, early cerebellar symptoms: truncal or limb ataxia were elicited on the neurologic examination	Poor or absent response of parkinsonism to levodopa therapy: no medication history or evidence that the patient was ever administered levodopa
	Neuroradiologic evidence of relevant structural abnormality (ie, basal ganglia or brain stem infarcts, lobar atrophy): not present on the patient's head MRI	Early dysphagia and dysarthria: dysarthria, but not dysphagia, present during the patient's examination
	Severe, asymmetric parkinsonian signs: on neurologic examination, the patient presented with axial bradykinesia and rigidity	Early onset of cognitive impairment including at least 2 of the following: the patient presented with apathy and decreased verbal fluency and had a MoCA score of 22 The patient had no impairment in abstract thought, utilization or imitation behavior, or frontal release signs
	**Physical examination: unremarkable, normal vital signs, without orthostatic hypotension; complete blood count, complete metabolic profile, thyroid function tests, urinalysis, and chest x-ray were unremarkable; blood alcohol and urine drug screen were negative Neurologic evaluation: mild bilateral resting tremor; reflexes were brisk throughout; flexor plantar reflex was intact	*Imaging findings: the patient's head MRI was remarkable for predominant midbrain atrophy Significant midbrain atrophy with no pons atrophy has been referred to as the "hummingbird sign" *Postsynaptic striatal dopaminergic degeneration: dopamine transporter scan showed symmetric, moderately severe, diminished radiotracer uptake in the putamen bilaterally

[a]Possible PSP: (1) presence of a gradually progressive disorder with onset at age ≥ 40 years, (2) either vertical supranuclear gaze palsy or both slowing of vertical saccades and prominent postural instability with falls in the first year of onset, (3) no evidence of other diseases that could explain these features.
[b]Probable PSP (Richardson syndrome): (1) vertical supranuclear gaze palsy, (2) prominent postural instability, (3) falls in the first year of onset, (4) other features of possible PSP.
*Supportive feature from Movement Disorder Society–PSP criteria.
**Not part of exclusion criteria but part of the medical evaluation.
Symbols: (+) = present in the patient. (+)/(-) = present in the patient but not part of diagnostic criteria.
Abbreviations: MoCA = Montreal Cognitive Assessment, MRI = magnetic resonance imaging, PSP = progressive supranuclear palsy.

venlafaxine dosage. There is evidence, especially if apathy is prominent as in our patient, that serotonin-norepinephrine reuptake inhibitors such as venlafaxine may be useful.[12]

In conclusion, presence of early gait dysfunction (described as clumsy and stiff) and postural instability is a key feature of PSP-RS that distinguishes it from other parkinsonian syndromes.[13] While there is no known treatment to slow the neurodegenerative process of PSP-RS, quality of life can be improved by evaluating and treating behavioral disorders that commonly occur.

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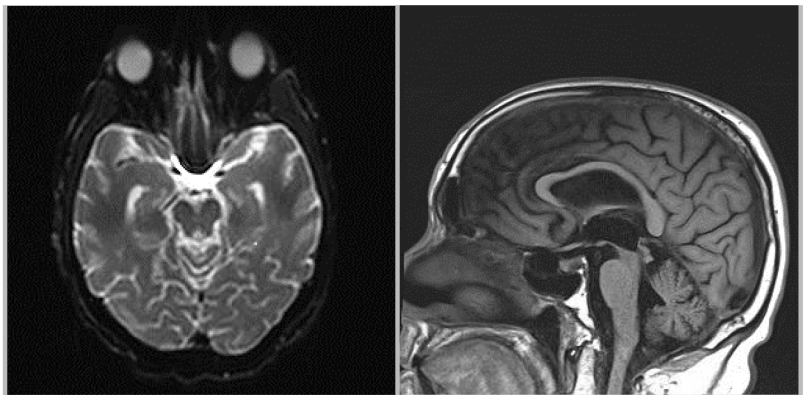
Figure 1. Magnetic Resonance Image Without Contrast With Evidence of Midbrain Atrophy: Interpeduncular Fossa to Intercollicular Groove Length of 9.06 mm on Axial Section (left) and Positive Hummingbird Sign on Sagittal Section (right)



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