Psychiatric symptoms of progressive supranuclear palsy: a case report and brief review

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Practice points

- Psychiatric symptoms associated with neurological conditions, including progressive supranuclear palsy, can be confusing.
- The symptoms of progressive supranuclear palsy include vertical gaze palsy, unsteady gait, falls, dysarthria, dementia, apathy, depression, personality changes, disinhibition and psychotic symptoms.
- When behavioral symptoms do not fit a typical psychiatric diagnosis, consider organic causes.
- Obtaining adequate history and records from previous physicians is of paramount importance in assisting with the diagnosis.

SUMMARY The diagnosis of early-stage progressive supranuclear palsy (PSP) can be very confusing. The psychiatric symptoms associated with neurological and medical conditions including PSP are generally not very typical and lead to diagnostic challenges. The symptoms of PSP include vertical gaze palsy, unsteady gait, falls, dysarthria, dementia, apathy, depression, personality changes, disinhibition and psychotic symptoms. In this article we report a patient who had previous diagnosis of Alzheimer’s dementia and mood disorder, and presented with hypersexual behavior and mild cognitive symptoms which on closer examination appeared to be associated with PSP. We emphasize the need for awareness of psychiatric presentations of neurological disorders and the importance of obtaining previous medical records from all clinicians.

A 63-year-old Caucasian married man, recently placed in a nursing home, was brought to the emergency room in March 2011 because he sexually assaulted his roommate. He had a history of one previous episode of similar behavior in the nursing home. His behavior problems started approximately 6 months prior to the index admission and had two brief psychiatric hospitalizations for aggressive behavior towards his family over trivial issues, such as obsessing about his batteries. The patient was also in outpatient psychiatric care in 2010 subsequent to his psychiatric hospitalization for aggressive behavior. The patient’s mother had schizophrenia. Both

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parents died in their 50s. The father died from a stroke. The patient graduated from high school and worked until retiring in 2003. The patient had a history of alcohol abuse, but had been sober for many years. The patient was placed in the nursing home after his second psychiatric hospitalization. Nursing home records indicated that the patient’s diagnoses included Alzheimer’s-type dementia; mood disorder; diabetes mellitus; hypertension; hypercholesterolemia; obesity; coronary artery disease; status post stent placement; benign prostatic hypertrophy; hypothyroidism; and intracranial aneurysms of the supraclinoid and anterior choroidal arteries. 

At the time of admission the patient was on quetiapine 100 mg daily, donepezil hydrochloride 5 mg daily, divalproex sodium 1000 mg daily, simvastatin, amlodipine, tamsulosin, levothyroxine, docusate, metformin, glyburide and lisinopril. His admitting psychiatric diagnosis was dementia, possibly secondary to Alzheimer’s disease with behavioral disturbances.

On admission to the inpatient psychiatric unit, he was alert and oriented to time, place and person. The patient’s attitude seemed indifferent and he selectively responded to questions. He was bradykinetic. His behavior was unpredictable, easily agitated and disorganized. He had aggressive potential. His speech was slow and soft and eye contact was poor. Thought process was also impoverished. He did not have any delusions, hallucinations or preoccupations. He denied being depressed but appeared apathetic with constricted affect. He denied suicidal or homicidal ideation, or mood swings. He had limited insight and judgment. His vital signs were within normal range. His physical examination was unremarkable, except for a rash on his left arm and mild swelling of his legs. A complete blood count, metabolic profile, ECG, HIV test, Mantoux test, serum rapid plasma reagin (RPR), hepatitis B surface antigen, hepatitis B core immunoglobulin G antibody, hepatitis C antibody, vitamin B₁₂ and folate levels, ceruloplasm, and computerized tomography of the head were all unremarkable. The patient had a moderately elevated triglyceride level. His thyroid-stimulating hormone level was low but thyroxine and triiodothyronine were within normal range. His urine toxicology was normal.

A Mini Mental State Examination was conducted and he scored 26 out of 30 [1]. During rounds, the patient was observed defecating on the floor in the visitor’s lounge and appeared indifferent about his behavior, and did not respond to redirection. The patient showed minimal cognitive deficits, but functional and behavioral deficits were disproportionate to the cognitive decline. We suspected a different etiology for his dementia and wanted to rule out other causes for his clinical presentation.

Subsequent examination during the week showed that the patient was seen walking around the floor with an unsteady gait. For most of the day, he chose to stay in his room. The patient was still not making eye contact and was asked if he was having difficulty with vision. The patient told us then that his neurologist diagnosed him with progressive supranuclear palsy (PSP) approximately 7 months prior to current admission. Closer examination of his vertical gaze revealed absent up and down gaze.

The patient’s wife was contacted for further information, but was unable to provide much information. We contacted the patient’s previous neurologist and obtained copies of his medical records in connection with the PSP diagnosis (noted below).

Previous neurology report of September 2010

The report revealed the following information. The patient had complained of a change in mental state over a 1-year period. He reported feeling “messed up in the head” and also complained of dizziness, confusion and decreased ability to focus. He described a short period of regression of symptoms, followed by recurrence and progression of symptoms. His wife noted that the patient’s memory was declining and that he was sleeping for longer periods of time. She reported no history of agitation. He quit smoking 2 years previously, had a history of drinking beer on a daily basis, but no illicit drug use. On the Mini Mental State Examination he scored 25 out of 30 and on the Clock Drawing Test (CDT) four out of four at that time. A physical examination revealed no vertical eye movements without vision loss. There was no fever, neck pain or headache. His gait and motor examination were normal. Sensory examination revealed a mild decrease in vibratory sensation in the first toe of his left foot. His reflexes showed a mild hyper-reflexia (three out of five) for the upper limbs and patella, but ankle jerk was normal. PSP was suspected.

A lumbar puncture was performed. The only abnormal result was a high cerebrospinal fluid
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The patient was brought to the emergency department 2 weeks later, for altered mental status and hallucinations. Computed tomography and MRI of the head were unremarkable. The EEG showed mildly abnormal diffuse tracing with irregular α and β activity and moderate θ activity diffusely. This concludes the neurologist’s report. The information from this report was crucial for an accurate diagnosis in this case.

**Neuropsychological testing in March 2011 (index admission)**

The neuropsychological evaluation was completed in one session during the current hospitalization. The patient demonstrated inappropriate and disinhibited behavior as he was masturbati
ging, and continued despite the presence of the evaluator.

The patient underwent the Dementia Rating Scale-2 [2] that showed an overall level of impairment occurring in less than 1% (total score 105; 0.4%) of individuals using age corrected norms [3]. His performance on the Memory and Initiation/Preservation subscales fell within the first percentile, whereas his performance on the Attention and Construction subscale was in the second percentile. He demonstrated a relative strength on the Conceptualization subscale, performing at the ninth percentile.

The patient was administered the Complex Ideational Material and Repetition of Phrases subtests from the Boston Diagnostic Aphasia Examination [4] to assess auditory comprehension and oral expression, respectively. His performance on both subtests was intact. Whilst undergoing the Repetition of Phrases test, on more than one occasion the patient did not wait for the examiner to complete the phrase, further suggesting disinhibition and impulse control dysfunction.

The CDT was used to assess visual spatial, constructional and executive deficits. The Sunderland 10-point scoring system was used to assess the deficits [3]. The patient obtained a score of four out of ten. Despite instructions, the patient did not include numbers on the clock face. Overall, the patient demonstrated poor planning, and an impulsive response style with a behavioral pattern that was disorganized and lacked attention to detail on the CDT.

The Controlled Oral Word Association Test (F/A/S; animals) was given to assess verbal fluency when generating words to a phonemic or categorical cue [3]. Rapid verbal initiation/fluency was solidly average (total words: 22) when generating words to target letters. Semantic fluency when generating words to a categorical cue was low average (ten words).

The patient’s performance on the Trail Making Test was profoundly impaired [5]. Despite understanding the task directions, the patient failed to correctly complete either task and appeared to randomly respond indicating difficulties in cognitive flexibility and psychomotor speed.

A brief motor test was also conducted to evaluate inhibition of prepotent responses. The patient’s ability to inhibit responses during an auditory “Go, No-Go” task was slow bilaterally. He demonstrated significant difficulty inhibiting responses, committing a number of errors, more so with his dominant (right) hand (right hand <25% correct; left hand 50% correct).

This patient demonstrated profound deficits on the Trail Making Test and CDT indicating deficits in organization and cognitive flexibility, which is consistent with a diagnosis of PSP or a behavioral variant of frontotemporal dementia (FTD).

**Hospital course**

The patient’s divalproex sodium dose was increased to 500-mg orally in the morning and 1000-mg orally at night in view of a low valproic acid blood level of 30 mg/l. Quetiapine and donepezil were discontinued pending complete diagnostic evaluation. By the eighth day, the patient had shown improvement in his behavior. His repeat valproic acid level was 101 mg/l. The patient was discharged back to the nursing home where a consultation with a neuro-ophthalmologist was completed. The positive findings were
absent vertical gaze and vertical mobility of both eyes. Also noted were hypometric saccades and cogwheel pursuit horizontally with absent oculokinetik nystagmus. The report suggested the diagnosis of an early form of PSP or a variant. However, the applause test performed in the nursing home was negative [6]. The patient was able to applaud three times in rapid succession without perseveration. He had two falls in his room in the nursing home in 1 month. The valproic acid dose was reduced and the patient has been doing well since discharge.

Discussion
Psychiatric symptoms of neurological disorders and medical illnesses often pose a serious diagnostic challenge. Many investigators have noted that early stages of PSP have a similar behavioral and neuropsychological profile to FTD syndrome [7,8]. Specifically, executive impairment, apathy and disinhibition are common in patients with PSP [9]; however, cognitive impairment may be mild in the first few years after clinical onset.

FTD is characterized by a decline in regulation of personal or interpersonal conduct, such as socially inappropriate behaviors that are rude, irresponsible or sexually explicit, mental rigidity and emotional blunting. These impairments interfere with usual relationships with others and/or social activities, and represent a notable decline from previous level of functioning. Similarly, most patients with FTD perform poorly on tests of executive functioning, however, exhibit a relative preservation of memory. There are some patients, however, who predominantly present with personality and behavioral changes and only show nominal deficits on neuropsychological tests of executive functioning [10].

The diagnosis of early-stage PSP is very intriguing. The neurological symptoms include eye movement abnormalities, such as vertical gaze palsy (particularly downward gaze), axial parkinsonism, unsteady gait, falls, dystartria and dementia. The vertical gaze abnormalities and axial dystonia in PSP are thought to be due to the destruction of cholinergic premotor nuclei in the midbrain. The cognitive symptoms may include gradual loss of executive functions and word fluency.

Associated psychiatric symptoms may include apathy, depression, sleep disturbances, schizophreniform psychosis, personality changes, such as disinhibition, irritability, symptoms of pseudobulbar affect, such as inappropriate crying or laughing and obsessive compulsive behavior [11]. Functional hypometabolism in the medial frontal lobes and the brainstem may cause problems with sleep, arousal and attention [12]. Apathy is the most frequent neuropsychiatric symptom [13] and should be differentiated from depression. Apathy is thought to be related to a functional disconnection between the frontal cortex and paralimbic structures [14]. In a study using the Neuropsychiatric Inventory, PSP patients scored high in items related to loss of interest, motivation, decreased spontaneity and lack of enthusiasm. However, the scores were within normal limits in items related to sadness [14,15]. In another study, apathy correlated with disinhibition, lower cognitive function and aberrant motor behaviors, but not with depression [14]. A positive applause test has been noted in 71% of patients with PSP but none in FTD or Parkinson’s disease [6].

PSP was originally described by Steele et al. 1964 [16]. Estimates of the prevalence of PSP range from 1.4 per 100,000 [6] to 4–7 per 100,000 [17]. Median age of onset is approximately 63 years and median survival 6–10 years [17]. Other risk factors include male sex and hypertension [18]. A few familiar cases of PSP have been reported with an apparent autosomal dominant inheritance and reduced penetrance [19]. A microtubule-associated protein coded by a gene in chromosome 17 is thought to be associated with the pathogenesis of PSP [20], with possibly the H1 haplotype being the predisposing factor and H2 haplotype the protective factor [21]. Our patient, a 63-year-old male with hypertension, matches the epidemiological profile described. Our patient also met most of the National Institute of Neurologic Disorders and Stroke Society for PSP criteria core features of probable PSP, which include gradually progressive disorder, onset at age 40 years or later, vertical supranuclear palsy and prominent postural instability with falls in the first year of onset, and no evidence of other diseases that could explain the foregoing features [22]. The following supportive features were also met: early onset of cognitive impairment including at least two of the following; apathy, impairment in abstract thought, decreased verbal fluency, and use of imitation behavior or frontal release signs (as supported by the neuropsychological testing) [22].

Gamma amino butyric acid (GABA) transmission and benzodiazepine/GABA receptors
may be involved in the pathogenesis of PSP [28]. In view of this hypothesis, GABA agonist medications, such as zolpidem, have been used to treat motor function and voluntary saccadic eye movements in PSP patients with varied clinical improvements [24]. The beneficial effects of valproic acid, which is also a GABA agonist controlling the disinhibition symptoms in our patient, is interesting and needs further investigation. Since both zolpidem and valproic acid have the potential to increase the fall risk, use of these medications should be closely monitored in PSP patients who are already at risk for falls. Based on the cholinergic deficits in PSP, several cholinesterase inhibitors, including physostigmine, donepezil and rivastigmine, have been used to treat the cognitive symptoms of the dementia with varied responses [25–27].

Conclusion & future perspective

As a clinician, it is important to think of organic causes when the behavioral symptoms do not fit the typical psychiatric diagnosis. This report also illustrates the importance of obtaining adequate history and records from previous physicians as in our case. With advances in genetics, stem cell research and functional imaging studies, the diagnosis and treatment of degenerative diseases, including PSP, will greatly improve over the next 5–10 years.

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No writing assistance was utilized in the production of this manuscript.

References

Papers of special note have been highlighted as:

- of interest
- of considerable interest
- Describes the ‘applause sign’ that may help to differentiate progressive supranuclear palsy (PSP) from frontotemporal dementia and Parkinson’s disease.
- Provides an overall description of all subcortical dementias.
- Provides a very good discussion of the neuropsychiatric aspects of PSP.
- Helps differentiate apathy from depression.
20 Bonifate V. Progress in the genetics of progressive supra nuclear palsy: tau gene and
Discusses the advances in the genetic aspect of PSP.


3. Discusses the clinical research criteria for the diagnosis of PSP.


