# PROGRESSIVE SUPRANUCLEAR PALSY (PSP): AN ATYPICAL CASE

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**Abstract:** Progressive Supranuclear Palsy (PSP), also known as Steele-Richardson-Olszewski syndrome, is recognized as one of the most common extrapyramidal neurodegenerative disorders, following in prevalence after Parkinson's disease. This condition typically manifests in individuals over the age of 40, with the highest frequency occurring between 60 to 65 years (M, 2018).
We are going to present a case of a 63-year-old female patient with difficulties with walking difficulties and sudden falls. According to her medical history, the issues began three years earlier. She also mentioned incidents of dropping objects she held and suffering a multiple falls especially when rising from a chair, causing her to fall backward. Her (initial) neurological examination revealed impairment of the upward gaze. No bulbar symptoms. Mild dysarthria. Bilateral dysdiadochokinesis. Brisk tendon reflexes. Bilateral positive Babinski sign. Impaired tandem walk, it was notable that she was walking with extended legs on a wide basis. Reduction of the synkinetic movements of the arms. Retrocolis was seen due to neck dystonia.
Her MRI showed atrophy of the mesencephalon- "the hummingbird sign". Diagnostic scales were used to distinguish the diagnosis according to the clinical phenotype, the interpretation of the score was in favor of PSP.
She was started on Levodopa/Carbidopa, later COMT inhibitor was added but no therapeutic response was seen. On later follow ups she presented with gradual worsening of her cognitive and motor symptoms. Soon she developed orthostatic hypotension. She ended up in a wheelchair 2,5 years after her diagnosis and treatment, or roughly 5,5 years after the initial symptoms.
Synucleinopathies and taupathies are characterized by distinct patterns of regional atrophy in the brain, leading to differences in the involvement of specific brain nuclei and resulting in variations in the affected neurotransmitter systems. In synucleinopathies (Peng C, 2018 Jan;) (Uemura N, 2020 Oct;), the primary focus of neurodegeneration is typically observed in the substantia nigra, brainstem, and limbic system, whereas tau-related neurodegeneration is predominantly localized within the frontal lobe structures and their connections to the basal ganglia. Midbrain atrophy is a well-established feature of Progressive Supranuclear Palsy (PSP). The distinct brainstem shape observed in MRI images of PSP patients, characterized by a reduced midbrain/pons ratio, has been coined as the "hummingbird sign" (Tsuboi Y, 2003) (Paviour DC, 2005). In contrast, when examining patients with MSA using conventional 1.5 T MRI, abnormalities may include atrophy in the lower brainstem, middle cerebellar peduncles (MCPs), cerebellum, and pons putaminal rim sign" (Thi Thuong Doan MD, 2023) (Alster P, 2022 Feb) (T., 2020 Apr;).
In the field of atypical parkinsonism, it becomes evident that there are considerable overlaps in symptom presentations, making the diagnosis of a patient particularly challenging (Jecmenica-Lukic M, 2014 Aug;). This challenge is compounded by the fact that a definitive diagnosis typically relies on histological evidence, such as the presence of Lewy bodies in neurons for Parkinson's Disease (PD), glyal cytoplasmic inclusions of alpha-synuclein in astrocytes for Multiple System Atrophy (MSA) (Gregor K Wenning, 2004), or the existence of tau-positive astrocytes in the mesencephalon and brain cortex (PSP). Therefore, careful observation and the chronological tracking of symptoms, along with the patient's response or lack to response to dopaminergic therapy, become crucial factors in the diagnostic process.
**Keywords:** Progressive supranuclear palsy, Multiple systemic atrophy, Hummingbird sign

## 1. INTRODUCTION

Progressive Supranuclear Palsy (PSP), also known as Steele-Richardson-Olszewski syndrome, is recognized as one of the most common extrapyramidal neurodegenerative disorders, following in prevalence after Parkinson's disease.

This condition typically manifests in individuals over the age of 40, with the highest frequency occurring between 60 to 65 years (M, 2018).

PSP presents with a variety of motor and cognitive symptoms that result from the accumulation of abnormal tau proteins between the cortex and the brain stem. The tau protein accumulates in nerve cells, forming aggregates that disrupt cell function and contribute to the progressive degeneration of neurons (Litvan I, 1996 Jan;) (Peng C, 2018 Jan;).

We are going to present a case of a patient who presented with PSP along with additional features.

A 63-year-old female patient was referred to a neurologist due to difficulties with her walking and experiencing a few sudden falls. According to her medical history, the issues began three years earlier with sensations she described as "uncertainty," "sinking," or feeling as though her body was moving backward while walking. She also mentioned incidents of dropping objects she held and suffering multiple falls that resulted in forearm fractures.

Additional information from the patient's medical history (heteroanamnesis), reveals more details: three years prior, she started experiencing sudden episodes of uncontrolled and unprovoked laughter. Gradual slowdown in her movements and a delay in verbal responses was noticed. She changed her walking pattern to a broader base with legs spread apart, and her falls increased, especially when rising from a chair, causing her to fall backward. Her family anamnesis is burdened with 3 close relatives who were diagnosed with neurodegenerative disorder, 2 first line cousins, and an uncle who were diagnosed with Parkinson's disease.

Her (initial) neurological examination revealed impairment of the upward gaze. No bulbar symptoms. Mild dysarthria. Bilateral dysdiadochokinesis. Brisk tendon reflexes. Bilateral positive Babinski sign. Impaired tandem walk, it was notable that she was walking with extended legs on a wide basis. There was reduction of the synkinetic movements of the arms. Her head was extended to the back because of retrocolis.

She was started on Levodopa/Carbidopa; the doses were elevated gradually. Later COMT inhibitor was added but no therapeutic response was seen.

On later follow ups she presented with gradual worsening of her cognitive and motor symptoms. Soon she developed orthostatic hypotension.

She was unable to walk, and ended up in a wheelchair 2,5 years after her diagnosis and treatment, or roughly 5,5 years after the initial symptoms.

## 2. METHODS AND MATERIALS

Her MRI showed global cortical atrophic changes, with atrophy of the mesencephalon- "the hummingbird sign", also on axial T2 sequence of the mesencephalon "the mickey mouse sign" was present.

As a crucial component of the diagnostic assessment, we employed a specialized questionnaire to distinguish between Progressive Supranuclear Palsy (PSP) and Multiple System Atrophy (MSA). Her assessment involved an examination of her signs and symptoms as well as an analysis of radiological markers.

## 3. RESULTS

We conducted an assessment of patients' symptoms, considering the distinctive MRI findings known as the "hummingbird sign" and the "Mickey mouse sign" (Sonthalia N, 2012 Sep). Our analysis led us to diagnose Progressive Supranuclear Palsy. It's worth noting that during the diagnostic evaluation, we also considered Multiple System Atrophy (MSA) due to the presence of some non-specific symptoms suggestive of MSA.

***Figure 1- MRI showing the midbrain atrophy "the hummingbird sign"***

***Figure 2- The "Mickey mouse sign" on axial T2 sequence of the midbrain***

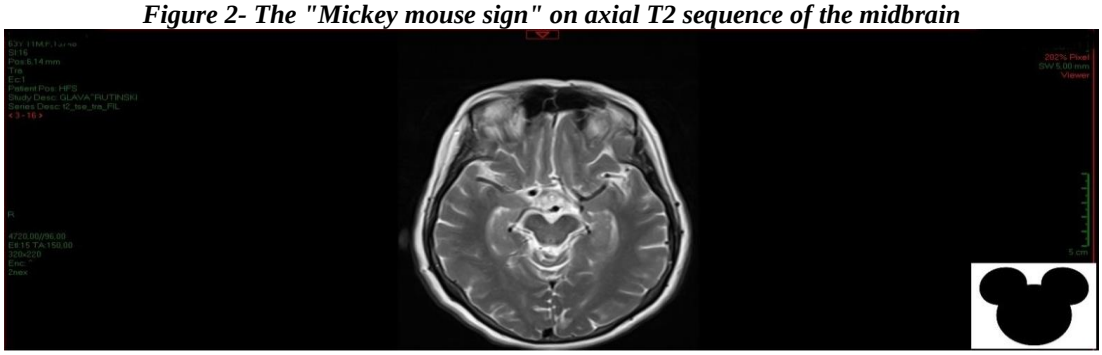

***Figure 3- PSP and MSA formula calculated results****

| **Results for Diagnosis of Progressive Supranuclear Palsy (PSP)**<br><br>Answers calculated to formulate result: | **Results for MSA Criteria**<br>Answers calculated to formulate result: |
|---|---|
| 1. Does the patient have a sporadic, progressive disorder with onset at or after the age of 40? — Yes<br>2. Are any clinical exclusion criteria present? — Yes<br>3. Are any imaging exclusion criteria present? — No<br>4. Are any laboratory exclusion criteria present? — No<br>5. Are any genetic exclusion criteria present? — No<br>6. What type of oculomotor dysfunction is present? — Vertical supranuclear gaze palsy<br>7. What type of postural instability is present? — Repeated unprovoked falls within 3 years<br>8. What type of akinesia is present? — Parkinsonism, akinetic-rigid, predominantly axial, and levodopa resistant<br>9. What type of cognitive dysfunction is present? — Frontal cognitive/behavioral presentation (apathy, bradyphrenia, dysexecutive syndrome, reduced phonemic verbal fluency, impulsiblity, disinhibition, or perseveration<br>10. Is there resistance to levodopa treatment? — Yes<br>11. Is there a hypokinetic, spastic dysarthria? — Yes<br>12. Is there dysphagia? — No<br>13. Is there photophobia? — No<br>14. Is there predominant midbrain atrophy or hypometabolism on MRI or PET? — Yes<br>15. Is there postsynaptic striatal dopaminergic degeneration on SPECT or PET? — No or not available | 1. Presence of autonomic dysfunction? — Yes<br>2. Presence of Poorly L-dopa responsive parkinsonism? — Yes<br>3. Cerebellar syndrome: Is there presence of at least one of gait ataxia, limb ataxia, cerebellar dysarthria or oculomotor features? — Yes<br>4. Supportive clinical (motor or non-motor) features? — Presence of at least 2 features<br>5. MRI marker? — No MRI marker present<br>6. Exclusion criteria? — At one least criteria present |
| | Interpretation: **MSA unlikely.** |
| **Probable PSP** – Richardson Syndrome type | |

**4. DISCUSSION**

Both PSP and MSA impact the basal ganglia, which is responsible for controlling movement. However, MSA goes beyond this, affecting the cerebellum, which influences balance and coordination, as well as the brain stem, which plays a role in regulating autonomic functions like blood pressure and bladder function. In contrast, PSP primarily affects the cortex, the upper part of the brain, leading to changes in cognitive functions and behavior (Alster P, 2022 Feb) (T., 2020 Apr;).

Midbrain atrophy is a well-established feature of Progressive Supranuclear Palsy (PSP), confirmed through radiological and pathological examinations. The distinct brainstem shape observed in MRI images of PSP patients, characterized by a reduced midbrain/pons ratio, has been coined as the "hummingbird sign" , also another radiological marker is " the Mickey mouse sign" seen on T2 axial sequence of the mesencephalon (Sonthalia N, 2012 Sep). Pathological investigations of PSP brains have revealed atrophy in the superior cerebellar peduncles (SCP). Recent MRI studies using both quantitative volumetric measurements and qualitative visual assessments have identified SCP atrophy as a valuable marker for distinguishing PSP from Multiple System Atrophy (MSA) and Parkinson's Disease (PD) (Tsuboi Y, 2003) (Paviour DC, 2005).

In contrast, when examining patients with MSA using conventional 1.5 T MRI, abnormalities may include atrophy in the lower brainstem, middle cerebellar peduncles (MCPs), cerebellum, and pons. Hyperintensities in these areas are commonly referred to as the "hot cross bun sign" when observed in the pons. Additional MRI findings in MSA-P include putaminal atrophy, T2 putaminal hyperintensity, and an abnormally high T2 linear rim surrounding the putamen, known as the "putaminal rim sign" (Thi Thuong Doan MD, 2023).

Synucleinopathies and taupathies are characterized by distinct patterns of regional atrophy in the brain, leading to differences in the involvement of specific brain nuclei and resulting in variations in the affected neurotransmitter systems. In synucleinopathies (Peng C, 2018 Jan;) (Uemura N, 2020 Oct;), the primary focus of neurodegeneration is typically observed in the substantia nigra, brainstem, and limbic system, whereas tau-related neurodegeneration is predominantly localized within the frontal lobe structures and their connections to the basal ganglia. The distinctive pathoanatomical variances form the foundation for delineating the patterns of both motor and non-motor symptoms, which serve as shared characteristics in both synucleinopathies and taupathies.

Evaluating eye movements plays a major role in achieving an accurate diagnosis. When we encounter signs such as vertical gaze palsy, decreased blinking, and eye-opening apraxia, these strongly point to Progressive Supranuclear Palsy (PSP). Although vertical gaze palsy can occasionally manifest in advanced stages of Parkinson's Disease (PD), it is also found in elderly individuals without any health concerns. Notably, the impairment of bulbar movements is not a characteristic feature observed in patients with Multiple System Atrophy (MSA).

The presence of symmetric parkinsonian symptoms in the early stages, particularly the axial distribution of these symptoms, strongly suggests Atypical Parkinsonism (AP), with Progressive Supranuclear Palsy (PSP) being the most likely candidate (NR., 2016 Aug;). In Parkinson's Disease (PD), a notable feature is bradykinesia, characterized by a reduction in the speed and amplitude of repetitive movements. However, recent data indicates that the decline in speed and amplitude is even more pronounced in Multiple System Atrophy (MSA), whereas it is highly unlikely to be observed in PSP. Postural instability and falls are typically associated with the later stages of Parkinson's Disease (PD) and are indicative of disease progression. However, when falls occur within the first three years of onset and exhibit a tendency to happen frequently, it is more suggestive of Atypical Parkinsonism (AP). Furthermore, the distinct timing of these falls is not the only differentiating factor, the direction of falling also provides valuable insights. In cases of Progressive Supranuclear Palsy (PSP), patients typically fall backward, often when attempting to turn or sit in a chair. In contrast, PD patients tend to fall forward due to impairments in their locomotor patterns or motor blocks. Falls among individuals with Multiple System Atrophy (MSA) are attributed to a combination of factors, including orthostatic hypotension, impairment of their postural mechanisms, and the impact of cerebellar damage. When assessing gait patterns and postural abnormalities, a notable distinction emerges. In Parkinson's Disease (PD), patients often exhibit a 'skiing' posture with a 'magnetic' quality to their foot movements. Conversely, in Progressive Supranuclear Palsy (PSP), individuals tend to present with an extended back, hyperextended neck (attributed to nuchal dystonia), and extended legs, giving rise to descriptions such as 'walking with dignity' or likening it to the gait of a tipsy sailor. In the case of Multiple System Atrophy (MSA), the gait resembles that of PD, but with an added ataxic component. Notably, MSA patients may also display early-onset postural deformities like 'antecolis' or 'drop head,' as well as lateral body flexion known as 'the Pisa' syndrome. When examining the facial expressions of patients with Parkinson's Disease (PD), one often observes a reduced range of facial expressions, a condition referred to as 'facies hypomimica.' Conversely, in Atypical Parkinsonism (AP), a spectrum of hyperexpressive facial expressions can be observed. In the case of Multiple System Atrophy (MSA), dystonic facial expressions are common due to oro-lingual dyskinesia. Progressive Supranuclear Palsy (PSP) is characterized by a distinctive 'Mona Lisa stare,' with patients displaying a surprised facial expression, along

with vertical gaze palsy and reduced eye blinking. The presence of autonomic dysfunction serves as a distinguishing feature in patients with Multiple System Atrophy (MSA), which can also manifest to some extent in other synucleinopathies. In contrast, autonomic dysfunctions are infrequently observed in Progressive Supranuclear Palsy (PSP), and when they do occur, they are typically associated with comorbidities. Both Progressive Supranuclear Palsy (PSP) and Multiple System Atrophy (MSA) share a commonality in the early onset of cognitive and behavioral changes. Additionally, they tend to exhibit either no response or only a mild initial response to dopaminergic therapy, which diminishes rapidly as the disease progresses.

## 5. CONCLUSIONS

In the field of atypical parkinsonism, it becomes evident that there are considerable overlaps in symptom presentations, making the diagnosis of a patient particularly challenging (Jecmenica-Lukic M, 2014 Aug;). This challenge is compounded by the fact that a definitive diagnosis typically relies on histological evidence, such as the presence of Lewy bodies in neurons for Parkinson's Disease (PD), glyal cytoplasmic inclusions of alpha-synuclein in astrocytes for Multiple System Atrophy (MSA), or the existence of tau-positive astrocytes in the mesencephalon and brain cortex (PSP). Therefore, careful observation and the chronological tracking of symptoms, the interpretation of the imaging methods along with the patient's response or lack to response to dopaminergic therapy, become crucial factors in the diagnostic process.

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https://qxmd.com/calculate/- Link of the calculator used in the assessment.