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CASE REPORT

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# Magnetic resonance imaging in the diagnosis of progressive supranuclear palsy: A case report and review of literature

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**Key Clinical Message**

Progressive supranuclear palsy (PSP) has many clinical features overlapping with other Parkinson syndromes and differentiation on clinical ground is difficult. This case highlights how a brain MRI can help diagnose PSP in settings with limited resources where histological diagnosis is difficult.

**Abstract**

Progressive supranuclear palsy (PSP) may be challenging to diagnose due to its widely acknowledged clinical complexity and challenges with diagnosis confirmation, particularly in resource-poor settings where the ability to obtain confirmatory tests is highly complicated, leading to an inaccurate or incomplete diagnosis of PSP. This paper discusses using brain magnetic resonance imaging (MRI) to diagnose PSP, and a review of relevant literature addresses the diagnostic value of MRI in PSP.

**KEYWORDS**

hummingbird sign, magnetic resonance imaging, Parkinson plus syndrome, progressive supranuclear palsy

## 1 | INTRODUCTION

Progressive supranuclear palsy (PSP), also known as Steele-Richardson-Olszewski syndrome, was first described in 1964.[1] PSP characteristics include vertical supranuclear palsy, postural instability with unexplained falls, akinesia and frontal cognitive dysfunction.[2]

The pathological features of PSP consist of neuronal loss, globose neurofibrillary tangles, tau-positive inclusion found in tufted astrocytes, and gliosis mainly in the basal ganglia, cerebellum, brainstem, and to a lesser extent, cerebral cortex.[3–5] Thus, the definitive diagnosis of PSP requires neuropathological examination.[6] The clinical criteria proposed by the National Institute of Neurological Disorders and Stroke and Society for PSP (NINDS-SPSP) are presently the most widely used criteria for the antemortem diagnosis of PSP.[7]

Since PSP may be linked with more than one neuropathological diagnosis, such as Alzheimer's or Parkinson disease, and because of its increasingly accepted clinical diversity, it may be challenging to identify PSP, particularly in low-resource settings.[8] Recent studies have exploited imaging properties to improve clinical diagnoses.[9,10] Furthermore, the findings of the antemortem MRI were found to correlate well with the postmortem histological findings[11] with a specificity of 99.5% and a positive predictive value of 96.1% and a specificity of 51.6%.[12] To date, a number of cases have been published

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that demonstrate the vitality of specific MRI findings in the diagnosis of PSP.[8,13–15] Neuroimaging techniques are becoming more common in Tanzania, particularly in tertiary health institutions; thus, familiarizing health practitioners with the utility of the brain MRI technique in diagnosing PSP will undoubtedly reduce the diagnostic challenge associated with the condition. The purpose of this clinical-radiological case report of PSP in a Tanzanian man is to emphasize the value of brain MRI in arriving at a diagnosis of PSP.

We present a case of PSP in a man in his early 50s who displayed the hallmark symptoms of the condition. Specific neuroradiological findings that closely matched the histology diagnosis were used to make the PSP diagnosis. This case demonstrates the value of MRI in the diagnosis of PSP in locations with limited resources where histological diagnosis is challenging.

## 2 | CASE REPORT

A 55-year-old carpenter developed a progressive worsening generalized body stiffness, slowing of movement, urine incontinence, memory loss, and postural instability resulting in occasional falls, often backwards, over 4 years. The symptoms were associated with incomprehensible handwriting and tripping while walking due to the inability to look up and down. There was no associated tremor, involuntary sustained position of a limb or neck, jerking movement of limbs, visual hallucinations, dysphagia, or motor weakness. Further interviewing revealed that the symptoms progressively worsened about a year before presenting to our facility. His past medical history was notable for deep vein thrombosis to the left femoral vein treated with rivaroxaban 15 mg once daily and iron deficiency anemia resulting from chronic lower gastrointestinal bleeding from external hemorrhoid.

On examination, his vital signs were notable for a blood pressure of 123/78 mmHg in the supine position, 125/79 mmHg in the erect position and 119/72 mmHg in a sitting position, a pulse of 79/min, respiratory rate of 16/min, oxygen saturation of 98% in room air and body temperature of 37.6°C. His face looked startled, and he had difficulty reopening his eyelids after closure. His posture was characterized by the extension of his neck (retrocollis) and torso. He was fully conscious; the mini-mental status examination (MMSE) yielded a score of 20 out of 30; the domains missed on the MSSE were calculation, recall, attention, and language. On the frontal assessment battery, he scored 13 out of 18. The most affected domains were mental flexibility, conflicting instruction, and inhibitory control. Glabella, snout, palm omental reflex, and "applause sign" were all present. However, no abnormality was found on the cranial nerves, motor system (apart from rigidity) and sensory system examinations. Cerebellar signs were also absent.

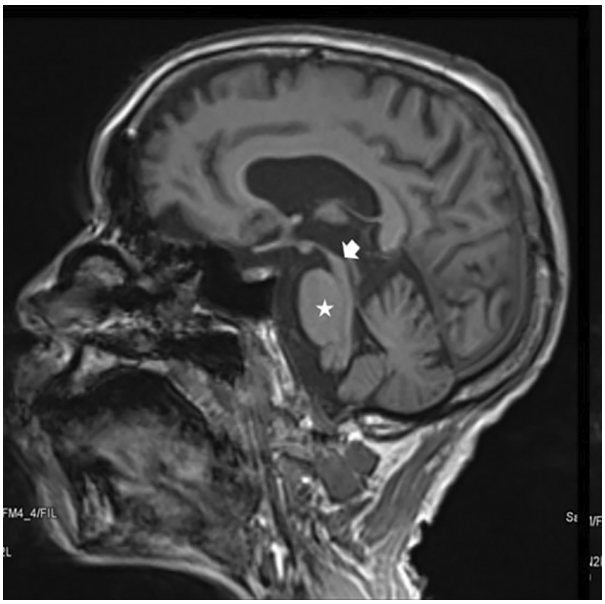

**FIGURE 1** Midsagittal MRI of the brain demonstrates prominent midbrain atrophy (arrowhead) without pontine atrophy (Asterix), forming the silhouette of the "penguin" or "hummingbird" sign.

The thyroid stimulating hormone level (2.3 mLU/L) and Syphilis serology tests were also within normal limits. The brain MRI revealed brainstem atrophy, specifically involving the midbrain, with a radiologic "hummingbird sign" or "penguin silhouette" sign, which is attributed to prominent midbrain atrophy with a comparatively preserved pons and looks like a hummingbird or penguin in silhouette (Figure 1), the pontine area was 0.43 $cm^2$, the mid-brain area was 5.18 $cm^2$, while the mid-brain to pons ratio was 0.083 (Figure 2). The diagnosis of PSP was based on the clinical presentation, and a failure of symptom improvement after a trial with carbidopa/levodopa titrated to a dosage of 150 mg/1.5 g within weeks and maintained physical therapy and amantadine 129 mg once a day.

Measurement of the mid-brain and pons and their values; midbrain (0.43 $cm^2$); pons (5.18 $cm^2$); pons/midbrain = 0.083.

## 3 | DISCUSSION

According to Schrag et al., PSP is the most frequent degenerative atypical Parkinsonian condition with a prevalence of 6.4/100,000.[16] The incidence is estimated to rise with age from 1.7 cases/100,000 in the 50–59 age group to 14.7 cases/100,000 in the 80–99 age group.[17,18] The average age

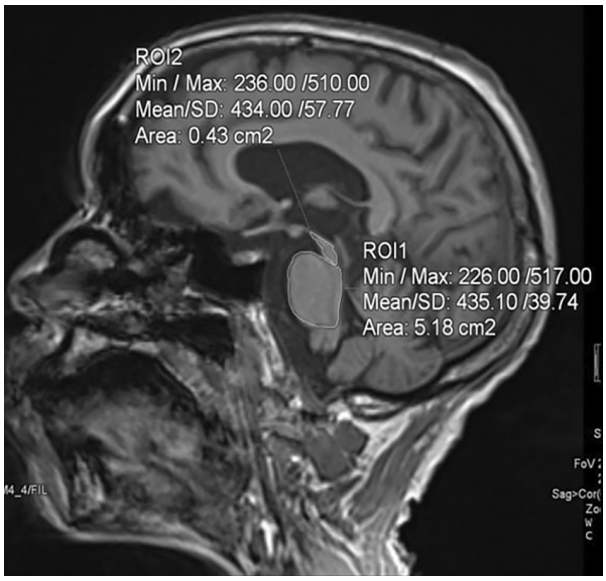


**FIGURE 2** Brain magnetic resonance imaging of the patient showing. Measurement of the mid-brain and pons and their values; midbrain (0.43cm2); pons (5.18cm2); pons/midbrain = 0.083.

of diagnosis is around 65 years with no racial or gender preference.

Because of its increasing clinical complexity, PSP is frequently misdiagnosed as Parkinson's disease (PD), multiple system atrophy (MSA), or dementia with Lewy body (DLB)[19] owing to their similarities in the anatomic pattern of abnormalities in the basal ganglia and brain stem.[20] The clinician's ability to diagnose PSP is further complicated by the fact that it may be associated with a number of neuropathological conditions, including Alzheimer's disease.[8]

Most PSP patients have gait abnormalities, unsteadiness (a tendency to fall backwards) and Levo-dopamine unresponsive parkinsonism. The gait has a peculiar staggering quality with huge irregular steps forward that distinguish it from the broad-based gait of cerebellar ataxia. Some patients report early complaints of vertical gaze palsy, pseudobulbar palsy, cognitive impairment, and a decrease in blink rate to fewer than 4/min resulting in a surprised facial look. Eye-opening can be due to either active involuntary contraction of the orbicularis oculi (blepharospasm) or the inability to deliberately open the eyes (apraxia of eyelid opening).[2,20] With the exception of pseudobulbar palsy, the index case displayed the typical PSP symptoms, and a clinical diagnosis was concluded by employing the NINDS-SPSP clinical criteria with a sensitivity of 45.5% and a specificity of 90.5%.[21] At first, Parkinson's disease was assumed to be the cause of his rigidity, bradykinesia, and postural instability. The unfavorable response to levodopa; however, pointed to a different diagnosis.[22]

Other Parkinson plus syndromes including cortical-basal degeneration (CBD), multiple system atrophy, and dementia with Lewy bodies were also taken into consideration owing to the index case's bradykinesia, postural instability, and autonomic dysfunctions such as incontinence of urine.[23] However, the likelihood of CBD was downgraded given the absence of limb dystonia, myoclonus, cortical sensory impairments, and an alien limb.[24] Likewise, the exclusion of dementia with Lewy bodies was supported by the absence of key symptoms such as visual hallucinations, changes in cognitive function, resting tremors, and limb rigidity.[25] Additionally, multiple system atrophy was ruled out by the absence of cerebellar symptoms and down-gaze supranuclear palsy.[26] The absence of symptoms for upper and lower motor neuron lesions also ruled out amyotrophic lateral sclerosis despite a history of supportive clinical manifestations including urine incontinence, postural instability, bradykinesia, and supranuclear gaze palsy.[27]

PSP is characterized by neuronal loss, globose neurofibrillary tangles, tau-positive inclusions in tufted astrocytes, and gliosis mainly in the basal ganglia, cerebellum, brainstem, and cerebral cortex to a lesser extent.[3,4,7] On MRI, this destruction of the midbrain and pontine structures causes recognizable changes in brainstem including atrophy, dilatation of the cerebral aqueduct, thinning of the midbrain tegmentum, and dilatation of the fourth ventricle.[28] Since neuropathology is the gold standard for PSP diagnosis,[6] subsequent research has exploited distinctive MRI characteristics to refine the clinical diagnosis.[29]

Additional findings have suggested that decreased midbrain diameter on normal MRI may help distinguish PSP from Parkinson's disease, cortical-basal degeneration, multiple system atrophy, and DLB.[30] Indeed, the hummingbird sign observed on MRI for the index case is highly suggestive and can be used to distinguish between PSP and other Parkinsons' plus syndromes.

A study compared the size of the midbrain tegmentum and pons in 21 patients with PSP, 23 patients with Parkinson disease, 25 patients with MSA, and 31 matched in age-healthy control participants using MRIs. The average midbrain area of PSP patients (56.0 $mm^2$) was significantly reduced than that of PD patients (103.0 $mm^2$), MSA patients (97.2 $mm^2$), and the age-matched control group (117.7 $mm^2$). The measures of the midbrain area suggested no overlap between PSP patients, PD patients, or healthy control participants. The ratio of the midbrain to the pons area in individuals with PSP (0.124) was substantially lower than in those with PD (0.208), MSA-P (0.266), and healthy control participants (0.237).[10] These findings led to the hypothesis that a midbrain area less than 70 $mm^2$ strongly supports a diagnosis of PSP (sensitivity of 100%, specificity of 91.3%). In contrast, a ratio of less than 0.15 between the midbrain tegmentum area and pons area excludes

the diagnosis of PD and MSA (sensitivity of 100%, specificity of 100% for PSP). Likewise, the "penguin silhouette" sign commonly seen in all PSP patients on the mid-sagittal MRI was suggested as a new imaging sign for PSP.[31] In the index case, the pons-midbrain ratio was significantly reduced, there was mid-brain atrophy, and the "penguin silhouette" sign was clearly apparent.

The clinical diagnosis of PSP falls into three categories by the National Institute of Neurological Disorders and Stroke (NINDS)-SPSP criteria: probable, possible, and confirmed requiring histopathology.[6] A higher overall tau load significantly correlated with significant volume loss in the subthalamic nucleus, midbrain, substantia nigra, and red nucleus, along with glial lesions, according to Carlos et al.'s study of the relationship between antemortem MRI findings in PSP patients and postmortem histological findings.[11]

Given the clinical variability of PSP presentation and its relationship with other neuropathological disorders such as Parkinson disease, the clinical diagnosis of PSP in the reference case was challenging. A clinical-radiological diagnosis of PSP was made with the help of unique PSP MRI features that coincide with a neuropathological diagnosis.

PSP often has an aggressive and relentless disease progression[32] with a severe impact on the quality of life; most patients become care-dependent 3–4 years after their initial manifestation, with a median survival of 6–9 years following diagnosis.[33] The patient's prognosis largely depends on early presenting symptoms except for early dysphasia.[33] The index case presented with early manifestations of falls, cognitive symptoms, and supranuclear gaze palsy, underscoring an unfavorable prognosis with shorter survival.[34]

## 4 | CONCLUSION

Given the high rate of clinical PSP misdiagnosis, a distinctive neuroradiologic feature may aid in PSP diagnosis. This PSP case served as an example of how a brain MRI aid in diagnosing PSP.

### AUTHOR CONTRIBUTIONS

**Baraka Alphonce:** Writing–original draft; writing–review and editing. **Francisca Komanya:** Writing – review and editing. **Mbelwa Bitesigilwe:** Writing – review and editing. **John R Meda:** Supervision; writing – review and editing. **Azan Nyundo:** Supervision; writing – review and editing.

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### CONFLICT OF INTEREST STATEMENT

The author declares there is no conflict of interest.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

### CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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