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MR Parkinsonism Index in Progressive Supranuclear Palsy

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Abstract

Background: Progressive supranuclear palsy (PSP) is a neurodegenerative disease characterized by dystonic rigidity of the neck and axial muscles, frequent falls, supranuclear vertical gaze palsy and pseudo-bulbar palsy. There is neuronal loss in the tegmentum of the midbrain leading to its significant atrophy along with changes in substantia nigra, globus pallidus and red nucleus. *Case Report*: Here we are presenting specific MRI features of PSP in an elderly male with special note on humming bird sign and MR parkinsonism index which is very useful to correctly label the diagnosis of PSP in absence of pathological confirmation. *Conclusion*: Specific methods are needed for diagnosing PSP as the clinical differentiation of PSP from Parkinson disease (PD) and multiple-system atrophy of Parkinson type (MSA-P) may be difficult in early stages. Emphasis on utility of MRI brain in PSP has been proven especially when mid-sagittal sections are studied.

Keywords: Atrophy, Bulbar Palsy, Multiple System Atrophy, Parkinson Disease, Supranuclear Palsy.

Introduction

Progressive supranuclear palsy (PSP) is a sporadic neurodegenerative disorder characterized by hyper-phosphorylated tau protein and diverse clinical presentation in form of akinetic rigid parkinsonism, dizziness, unsteadiness, slowness, falls, and pseudobulbar dysarthria [1,2]. As this disease is often misdiagnosed with Parkinson's disease specific noninvasive diagnostic modality is the need of the hour of this era as pathological confirmation is not feasible and almost impractical in day to day clinic.

Clinically differentiating PSP from Parkinson disease (PD) and multiple system atrophy (MSA) is a daunting task especially in the initial stages of disease. The disease processes in PSP and MSA involve various brain areas like basal ganglia, cerebellum and brainstem [3]. Pathological confirmation of the diagnosis of PSP differentiating it with other mimickers is considered as mandatory and for classification purpose in NINDS criteria, but this is not always practical especially in developing world. It was concluded by Williams *et al*. that around half of patients with PSP pathology had a clinical syndrome of PSP, rest half had Parkinson's disease syndrome [4].

MRI brain with special sections has become the modality of choice for diagnosing atypical parkinsonism and differentiating it from subtypes like MSA-P, early PD. MR imaging and pathologic findings indicate that in PSP, midbrain and the superior cerebellar peduncles (SCPs) are atrophic, whereas in MSA, middle cerebellar peduncles (MCPs) and the pons are mainly involved [5]. PD does not involve any of these structures. Thus, the purpose of this case presentation is to highlight the importance of MR imaging measurements of brain structures (MCP, SCP, midbrain, and pons) for differentiating PSP from Parkinson variant of

MSA (MSA-P) and PD. We also tried to emphasize the different radiologic signs specific in diagnosing PSP which are helpful in clinical setting where pathological confirmation is not always possible.

Case Report

A 60 year old male, non-diabetic, hypertensive on treatment patient was admitted with history of frequent falls, slowly progressive difficulty in walking, difficulty in various aspects of activity of daily living (ADL) like bathing, eating, dressing clothes of three years duration. Subsequently he noticed difficulty in bending neck forward and stiffness of limbs. Relatives noted that he turns whole head to see any object and difficulty in getting down the stairs and reading newspaper indicating downgaze defect. There was memory impairment and delayed response to commands. There was no history of tremors or stoke like illness in past. Examination revealed generalized rigidity, truncal more than appendicular. Eye movements were restricted in all gazes. Oculocephalic maneuver and Bell's phenomenon were preserved. Nuchal dystonia was also noted. Glabellar tap was positive. His blink rate was 6-8/min. Cogwheel rigidity, tremors or autonomic features were not present in this patient. Postural reflexes were poor and speech was slurred, hypophonic and words were not clear.

Though the patient's initial presentation had Parkinson's features, but the presence of downward gaze difficulty, history of fall and poor response to levodopa/carbidopa indicated diagnosis of progressive supranuclear palsy (PSP). He was subjected for Magnetic Resonance Imaging (MRI) brain. All MRI examinations were done using 1.5 T units (superconducting magnet) and 3 mm thick sagittal images were obtained. The mid-sagittal images were taken at the level of the midbrain to pass through the center of inter-peduncular cistern and of aqueduct. Tegmentum of midbrain and pons were measured on the mid-sagittal MRI. It showed atrophy of superior cerebellar peduncle (SCP), midbrain tegmentum, with cisternal and ventricular dilatation and thinning of the quadrigeminal plate. There was classic humming bird sign **[Fig.1]**. The midbrain to pons ratio derived at mid-sagittal level, was significantly smaller (4.5/18 mm) than in control (18/28 mm) **[Fig.2]**. The width of superior cerebellar peduncle (SCP) was also atrophied (0.44 mm) as compared to that of middle cerebellar peduncle (MCP) which was 6 mm. The pons–midbrain area ratio (P/M) and MCP–SCP width ratio (MCP/SCP) were calculated, and MR Parkinsonism index was derived [(P/M)×(MCP/SCP)]. It was significantly larger (54.4 mm) in our patient than in control participant. Patient was continued on levodopa/carbidopa. Bradykinesia and rigidity improved with zolpidem. However, patient continued to decline with lesser improvement with medicines and physiotherapy.

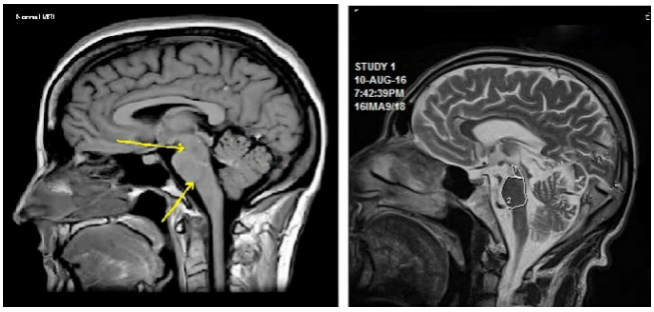

Fig.1: *MRI brain mid-sagittal section showing midbrain atrophy and relatively preserved pons in index patient (left) as compared to normal MRI (right).*

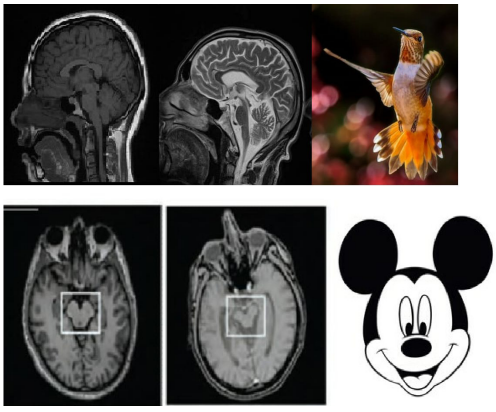

Fig.2: *Humming bird sign on mid-sagittal image (upper). Micky mouse sign on axial image (lower) is a result of atrophied tegmentum and dilated adjoining cisterns.*

Discussion

Neurodegenerative diseases with predominant features of parkinsonism including idiopathic Parkinson disease (PD), progressive supranuclear palsy (PSP), and multiple system atrophy (MSA) are challenging to differentiate clinically especially in the early course of the disease. In 1963, J Clifford Richardson described an "unusual syndrome" of postural instability, supranuclear gaze palsy, mild dementia, and progressive axial rigidity and bulbar palsy which was later named progressive supranuclear palsy (PSP) [6]. Macroscopic examination of the brain shows midbrain atrophy and substantia nigra depigmentation, along with mild frontal lobe atrophy while microscopic examination reveals neuronal loss, gliosis, neurofibrillary tangles, and neuropil threads in the brainstem and basal ganglia. An accurate method for diagnosing PSP is needed as the clinical differentiation of PSP from PD and multiple system atrophy of Parkinson type (MSA-P) is difficult when clinical symptomatology gives fewer clues and moreover there are no reliable diagnostic biomarkers. Studies with routine MR imaging, including volumetric MR imaging have proved to be useful in distinguishing PD from atypical parkinsonism when clinical signs are confusing. One study concluded the validity of NNIPPS MRI scale reliability to measure MRI abnormalities in PSP and MSA [7]. MRI studies on PSP have shown atrophy of the areas of midbrain and pons and dilatation of their surrounding cisterns, more clearly observed on mid-sagittal images than axial images, especially in the upper midbrain. Mid-sagittal images are more reliably reproducible than axial images and linear measurements [8]. Mid-sagittal images do not accurately evaluate atrophy of the colliculi thus assessment of tectal atrophy is difficult, even using the most recent MRI techniques. The reduction of the midbrain area, pontine area and midbrain pontine ratio significantly correlated with the duration and staging of the disease and manifestations of disease severity. The range of midbrain area, pontine area and midbrain pons ratio was lower in PSP as compared to PD [7]. MR imaging evidence indicates that the midbrain and the superior cerebellar peduncles (SCPs) are atrophic in PSP, whereas the middle cerebellar peduncles (MCPs) and the pons are mainly involved in MSA.

Although both the midbrain and the pons diminish in size in PSP patients, but midbrain atrophy appears to be more severe. Quattrone *et al*. reported that a midbrain area <70 mm^2 strongly suggests the diagnosis of PSP [9]. A ratio <0.15 of midbrain tegmentum to pons strongly suggest PSP and argues against the diagnosis of PD and the sensitivity and specificity on using this cut point of 0.15 are both 100%. MSA-P patients had a significantly smaller pons area than PSP patients, a finding which was also reported by Wszolek *et al*. and Slowinski *et al*. [10]. Subcortical and brainstem degenerations has been primarily implicated in the gaze palsy of PSP, motor impairment and ADL disturbances suggesting the role of brainstem area in predicting the clinical presentation and staging of patients with PSP. Similar observations were reported by other authors who also reported good correlation between brain stem atrophy and cognitive impairment and behavioral changes. Certain specific signs like penguin silhouette, humming bird and Mickey mouse signs have been described by various authors in PSP [11-13]. The humming bird sign (midbrain tegmental atrophy with preserved pons) was also appreciated in our case, a useful indicator of midbrain atrophy in PSP as described in previous studies. Imaging is also helpful to exclude hydrocephalus, extensive vascular disease, signs of normal pressure hydrocephalus and mass lesions if any. The pons–midbrain area ratio (P/M) and MCP–SCP width ratio (MCP/SCP) also gives a very important though less used index called MR Parkinsonism Index. One study proposed that the MR Parkinsonism index is a better measure to diagnose PSP. This index is higher in PSP thus allowing differentiation of patients with PSP from patients with PD, with MSA-P, and controls on an individual basis with

a sensitivity of 100%, a specificity of 100%, and a PPV of 100% [14]. In our patient, it was significantly larger (54.4 mm). The MR Parkinsonism index is strongly related to duration of the disease, making it a good indicator of the progression of PSP and thus helps to differentiate patients with probable PSP from patients with possible PSP. Hence, it correctly classifies patients with PSP in the early stages of the disease, prevents misclassification of the disease. This index can be calculated easily with use of routine MR imaging in non-research settings as well. Our findings indicate that the simple measurements of the midbrain and pons (or their ratio) on mid-sagittal MRI and MR Parkinsonism index would identify confirmed PSP in absence of pathological confirmation which is impractical in all patients.

However, the mainstay of diagnosis remains to be the NINDS criteria in which pathology has an important role but MRI brain can offer substantial benefits in diagnosing PSP and excluding other mimickers [15].

Conclusion

The goal of this case report is to highlight the usefulness of MRI brain in diagnosing PSP, especially in its early stages, and preventing its misdiagnosis as PD. The mid-sagittal MRI measurements of the midbrain area can differentiate PSP from PD, MSA-P and normal aging and these radiological measurements correlated well with the clinical aspects of the PSP syndrome.

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