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RESEARCH ARTICLE

A Retrospective Study in Clinical Presentation and Imaging Patterns in Progressive Supranuclear Palsy

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Abstract

First described in 1964 by Steele, Richardson, and Olszewski, PSP is the second most common form of atypical parkinsonism but it is still a relatively rare disease, with prevalence estimates ranging from 1.39 to 6.4 per 100,000. **Methodology:** 18 patients, diagnosed as probable Progressive supranuclear palsy based on MDS criteria, were studied. Age of onset, symptomatology, disease progression, signs of cognitive dysfunction, occulomotor dysfunction, procerus sign, rocket sign, applause sign, rigidity and other extra pyramidal signs were analysed. Patients were subjected to neuroimaging to look for radiological features. **Results:** Common age of onset was in 5th-6th decade, but as late as 9th decade was noted. Most patients developed recurrent falls after one year of disease onset. Earliest was within 6 months of disease onset. 60% patients experienced dysarthria, usually at 3rd year of the disease. In our study only 3 had dysphagia, happening at 3rd year of the disease. 22% had frontal lobe involvement in form of disinhibition and dysexecution. All patients except 2 had vertical gaze palsy. 52% patients had procerus sign.3 patients had rocket sign and applause sign. Only 11 patients underwent neuro imaging, all 11 patients showed midbrain to pons ratio less than 0.5 and mid brain to pons area ratio less than 0.15. 2 patients in whom MRPI was measured showed a value more than 13.5. **Discussion:** The MDS criteria 2017 identified four functional domains oculomotor dysfunction, postural instability, akinesia, and cognitive dysfunction. The most disabling symptom of PSP usually relates to balance impairment. Occulo motor abnormalities include, vertical gaze palsy, impairment of saccades, optokinetic nystagmus, and the presence of square wave jerks, blepharospasm and involuntary eye closure. Pseudobulbar symptoms in PSP patients are characterized by dysarthria, dysphagia and pseudobulbar affect MRI of patients with PSP include generalized and brain-stem, particularly midbrain atrophy.

Keywords: Atypical Parkinsons, Magnetic Resonance Parkinsonism Index, Midbrain to Pons Area Ratio, Procerus Sign, Progressive Supranuclear Palsy (PSP), Recurrent Falls, Vertical Gaze Palsy

1. Introduction

First described in 1964 by Steele, Richardson, and Olszewski as a progressive illness, PSP is the second most common form of atypical parkinsonism but it is still a relatively rare disease, with prevalence estimates ranging from 1.39 to 6.4 per 100,000. The MDS criteria 2017 identified four functional domains oculomotor dysfunction, postural instability, akinesia, and cognitive dysfunction.

2. Aim and Objectives

To study various clinical, radiological features and disease progression in progressive supranuclear palsy.

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3. Review of Literature

The 1996 NINDS-SPSP criteria prioritized gaze palsy and unexplained early falls as core features, achieving high specificity but missing many early or variant cases. In response, the 2017 Movement Disorder Society (MDS) criteria introduced a probabilistic, domain-based framework that considers oculomotor dysfunction, postural instability, akinesia, and cognitive/linguistic deficits, improving early recognition and identifying variant phenotypes[1]. Variant PSP clinical presentations, including initial predominance of Ocular Motor Dysfunction (PSP-OM), Postural Instability (PSP-PI)[2], Parkinsonism resembling idiopathic Parkinson's disease(PSP-P), frontal lobe cognitive or behavioral presentations (PSP-F)[3], including behavioral variant Fronto-Temporal Dementia (bvFTD), Progressive Gait Freezing (PSP-PGF), Corticobasal Syndrome (PSP-CBS)[4], primary lateral sclerosis (PSP-PLS)[5],Cerebellar Ataxia (PSP-C)[6], and Speech/Language Disorders (PSP-SL), including nonfluent/agrammatic Primary Progressive Aphasia (nfaPPA) and progressive Apraxia of Speech (AOS).

Pathologically, PSP is now firmly recognized as a primary tauopathy[7]. The defining feature is the accumulation of 4-repeat tau isoforms in neurons and glia, forming neurofibrillary tangles, tufted astrocytes, and coiled bodies. Early neuropathological studies highlighted the predilection of tau deposition in the brainstem, basal ganglia, cerebellar dentate nucleus, and frontal cortex, explaining the characteristic motor, oculomotor, and behavioral symptoms. More recent molecular work has emphasised how tau misfolding, propagation, and seeding contribute to the disease's progressive nature, drawing parallels to prion-like mechanisms seen in other neurodegenerative disorders.

MRI studies described midbrain atrophy with the classic hummingbird and morning glory signs. Quantitative biomarkers such as the MR Parkinsonism Index (MRPI) further improved diagnostic differentiation. Diffusion tensor imaging and functional connectivity studies demonstrated disruptions in frontal-subcortical pathways, while PET imaging highlighted frontal hypometabolism and emerging tau PET ligand applications, though current ligands lack ideal specificity for 4R tau.

Therapeutic literature reflects the challenge of modifying a tau-based neurodegenerative process. Dopaminergic therapy has shown limited benefit. Multiple clinical trials targeting tau pathology—including monoclonal antibodies like gosuranemab and tilavonemab—have not produced meaningful clinical improvement, though they have advanced biomarker development and trial methodology. Current therapeutic directions include antisense oligonucleotides and microtubule-stabilizing approaches.

4. Material and Methods

A retrospective case series from Institute of neurology, madras medial college included 18 patients, diagnosed as probable progressive supranuclear palsy based on MDS criteria. Age of onset, symptomatology, disease progression, signs of cognitive dysfunction, occulomotor dysfunction, procerus sign, rocket sign, applause sign, rigidity and other extra pyramidal signs were analysed. Patients were subjected to neuro imaging to look for radiological features.

5. Results (Including Observations)

Common age of onset was in 50-70 years of age, mean age-58.7 (Table 1) but as late as 9th decade was noted. More males when compared to females M:F= 11:7.83%(n=15) (Chart 1) developed recurrent falls after one year (Chart 2) of disease onset. Mean = 12 months Earliest was within 6 months of disease onset. 50% (n=9) patients experienced dysarthria, mean latency of onset- 33 months, median latency-36 months. In our study 27% (n=5) had dysphagia, mean latency of onset- 39 months, median latency-36 months (Chart 3) 16% (n=3) patients had frontal lobe involvement in form of disinhibition and dysexecution (Table 1).

16% (n=3) patients had rocket sign and 11%(n=2) applause sign. 89% (n=16) had vertical gaze palsy. 89% (n=16) patients had procerus sign (Table 1). Only

Table 1. Showing patient's age, various symptom onset. clinical signs and radiological index

SNO	Age/ sex	Brady-kinesia dura-tion	First Fall	Gaz-epalsy	Dysar-thria onset	Dys-phagia onset	Frontal	Rocket sign	Ap-plause sign	Pro-cerus sign	MPAR	MRPI
1	52/F	1.5 y	1.5 y	Vertical	-	-	5	+	+	+	0.13	15.56
2	51/M	4 y	4y	Vertical	3 y	3 y	17	-	-	+	0.12	16.32
3	51/F	3 y	1 y	Vertical	3 y	3 y	18	-	-	+	0.14	14.11
4	60/F	3 y	1 y	Vertical	2 y	3 y	12	+	-	+	0.11	17.12
5	81/M	6 m	-	Vertical	-	-	17	-	-	+	-	-
6	63/M	2 y	9 m	V>H	-	-	16	-	-	+	0.12	16.47
7	55/M	3 y	1 y	V>H	1.5 y	3 y	18	-	-	+	0.13	15.22
8	57/M	1 y	1 y	Vertical	-	-	17	-	-	+	0.12	16.42
9	56/M	8 m	8 m	Slow saccade	-	-	17	-	-	-	-	-
10	61/M	1 y 3 m	1 y	Vertical	1 y	-	15	-	-	+	-	-
11	62/M	3 m	1m	Vertical	-	-	17	-	-	+	-	-
12	55/M	2 y	1 y	Vertical	1 y 3 m	-	16	-	-	+	0.14	-
13	56/F	1y	1 y	Vertical	-	-	18	-	-	-	-	-
14	65/M	5y	1.5 y	V>H	4 y 6 m	4y 6 m	11	+	+	+	0.13	15.6
15	62/M	1.5 y	1 y	Vertical	1 y	-	18	-	-	+	0.12	16.21
16	60/F	1y 2 m	11 m	Vertical	1 y	-	18	-	-	+	0.12	16.36
17	51/F	1 y	11 m	Vertical	-	-	18	-	-	+	-	-
18	58/F	10 m	10 m	Slow saccades	-	-	18	-	-	+	-	-

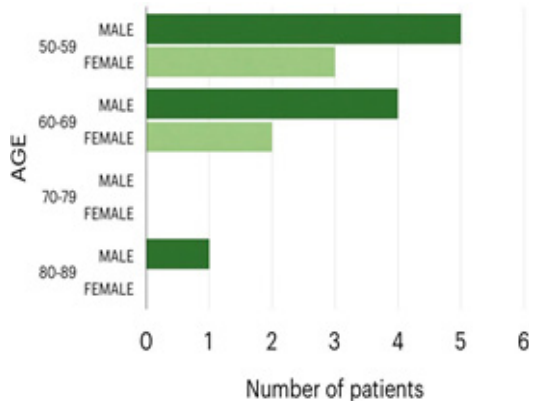

Chart 1. Showing age at occurrence of first symptom.

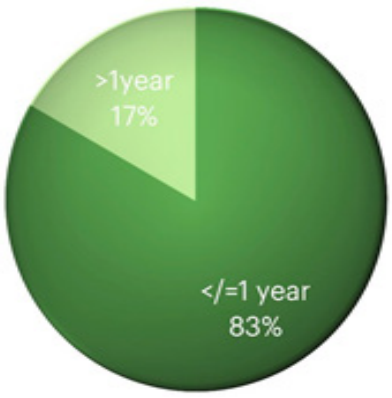

Chart 1. Showing year at occurrence of first fall.

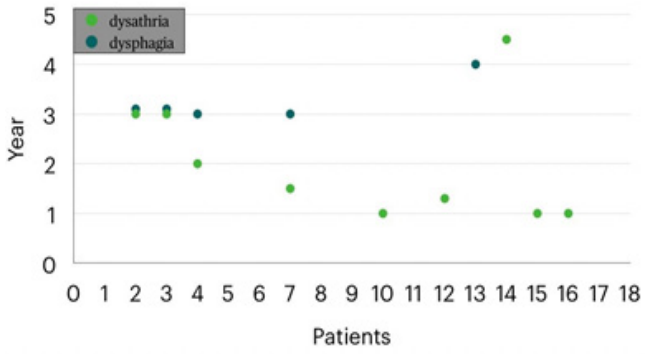

Chart 3. Showing year at onset of dysphagia and dysarthria.

11 patients underwent neuro imaging, all 11 patients showed mid brain to pons area ratio less than 0.15. MRPI value more than 13.5. A weak correlation, between age and MPAR with Correlation coefficient of 0.34 p value 0.24. Moderate correlation between age and MRPI with Correlation coefficient of 0.47 with p value 0.17. No significant correlation between dysphagia and MPAR P value (0.88)/ MRPI (0.37) (Table 1).

6. Discussion

PSP is a progressive illness characterised by vertical supranuclear ophthalmoplegia, axial rigidity, pseudobulbar palsy, and cognitive impairment, occurs more often in men, onset at a mean age of 63 years[1,8]. The earliest and most disabling symptom usually relates to gait and balance impairment, resulting in early recurrent falls associated with significant mortality. The average period from onset of symptoms to the first fall being 12 months[9]. In our study also fall occurred within in one year of disease onset in 83% of patients. supra nuclear ophthalmoparesis typically manifests by paralysis of downgaze, the most important distinguishing sign of PSP[10]. Other oculomotor abnormalities that are seen in patients with PSP include impairment of saccades[11], optokinetic nystagmus,and presence of square wave jerks[12]. Blepharospasm[13,14] and reduced bink rate[15]. In the late stages, the eyes may be fixed centrally and all oculocephalic and vestibular reflexes[16] are lost. The median latency to the development of dysphagia is 42 months in PSP[17] compared to 39 months in our case. As a result of chewing difficulties, inability to look down, and poor hand coordination, PSP patients are often described as "sloppy eaters". Loss of insight, particularly inability to accurately predict performance on future tasks (anticipatory awareness), though nonspecific is a common feature of PSP[18]. Another sign of frontal lobe dysfunction in PSP is the "applause sign" (which probably represents a perseveration of automatic behaviour)[19]. Median survival of 7.1 years[20]. Early dysphagia and early cognitive impairment are predictors of poor prognosis[21].

Imaging feature of patients with PSP include generalised and brainstem, particularly midbrain atrophy[22]. Particularly the ratio of the area of the midbrain to the area of the pons[23], was found to reliably distinguish PSP. other signs include hummingbird[24] penguin sign[25] and morning glory sign[26]. A Magnetic Resonance Parkinsonism Index (MRPI)[27] calculated by multiplying the pons area-midbrain area ratio (P/M) by Middle Cerebellar Peduncle (MCP) width-Superior Cerebellar Peduncle (SCP) width ratio greater than 13.55 is more predictive of evolving clinically unclassifiable parkinsonism into PSP. In our study, all 10 patients in whom, MRPI was calculated, had a value greater than 13.55.

7. Summary and Conclusion

Our study emphasises importance of recognising early symptoms and signs, and the supportive role of imaging. Despite no cure available at present, symptomatic management should aim to alleviate suffering of the affected.

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