

Parkinsonism: A Clinical Approach.

Kuljeet Singh Anand, Ankur Wadhwa

Department of Neurology,

Dr. RML Hospital & PGIMER, New Delhi, India

Abstract :A constellation of six cardinal features helps in diagnosing parkinsonism. A detailed history and meticulous clinical examination with reference to extrapyramidal system, autonomic functions and neuro ophthalmologic signs might be helpful in differentiating Parkinson's disease from atypical causes of parkinsonism. The vivid phenotypic spectrum of atypical parkinsonism makes the early differential diagnosis challenging and puts a lot of burden on investigations and neuro imaging. These may play a supportive role, but their sensitivity and specificity are low and a good clinical examination is imperative to reduce its cost. This review briefly discusses these issues and might prove helpful in diagnosing various parkinsonian disorders at an early stage decreasing the cost of investigations and help in prognosticating the care givers about these syndromes.

INTRODUCTION

In 1817, James Parkinson first described the syndrome that included tremulousness occurring at rest, muscular weakness, a stooped posture and festination of gait, with preservation of sensation and cognition. He published his findings based on his observations of six patients, only one of whom he actually examined and followed for a certain period of time. Later in the same century, Charcot recognized that rest tremor was not an absolute part of this syndrome, and suggested instead it be referred to as 'Parkinson's disease' (PD) in honor of its first descriptor.¹

The term *parkinsonism* denotes a constellation of the following six cardinal features: (1) tremor at rest, (2) bradykinesia, (3) rigidity, (4) loss of postural reflexes, (5) flexed posture, and (6) freezing (motor blocks). These features form the basis for clinically defining whether a particular case is that of definite, probable, or possible parkinsonism (TABLE 1).²The acronym TRAP has been used traditionally to describe the four major characteristics of parkinsonism accounting for.

Table 1 : Parkinsonism diagnostic criteria

1. Tremor-at-rest
2. Bradykinesia
3. Rigidity
4. Loss of postural reflexes
5. Flexed posture
6. Freezing (motor blocks)

Definite: At least two of these features must be present, one of them being 1 or 2.

Probable: Feature 1 or 2 alone is present.

Possible: At least two of features 3 to 6 must be present

This review briefly discusses the cardinal features of Parkinsonism, characteristics of Parkinson's disease (PD) and its differentiation from other parkinsonian disorders.

CORE FEATURES

Tremor: The classical tremor in Parkinson's disease is a supination, pronation (pill-rolling) tremor which starts in one hand and spreads to the other. It is typically described as a 4-6 Hz rest tremor and

should be differentiated from the postural tremor of essential tremor (5-8 Hz), enhanced physiological tremor (8-12 Hz) and the cerebellar outflow tremor (2-5 Hz). The classical PD tremor often involves the legs, jaws, chin or lips and unlike essential tremor almost never involves the head/neck or voice. Also about a quarter of PD patient almost never develop a characteristic rest tremor throughout their illness.³Stress, anxiety, synkinesis of the opposite limb or walking may aggravate the rest tremor whereas it tends to disappear in action (contrasting feature essential tremor) and sleep. Many patients of PD may present initially with a postural tremor, however a delay of several seconds after assuming an outstretched horizontal position may differentiate it from ET. This tremor has been referred to as emergent tremor.⁴

Rest tremor in PD is a complex phenomenon, and its pathophysiology is not well understood. Functional neuroimaging studies and electrode recordings during brain surgery point to the contribution of several different brain structures.

The cerebellum is likely to play a modulating role⁵ potentially explaining similar involvement of this structure in patients with ET. Deep brain stimulation of the thalamus may suppress PD tremor, possibly by inhibiting thalamocortical loops.⁶

Rigidity: Denotes an increase in muscle tone to passive movement, that affects both agonist and antagonist muscles and is uniformly present throughout the range of motion at a given joint. It involves both flexures and extensors and does not vary with the speed of movement. It should be differentiated from spasticity which predominantly involves the antigravity muscles, is not uniformly present throughout the range of movement, varies with the speed of movement and Geganhaltan in which resistance is intermittent and increases with degree of force used by the examiner. Another important point worth mentioning is that electromyography (EMG) is electrically silent in spasticity whereas findings in parkinsonian rigidity are similar to those of voluntary muscle contractions.⁷ The phenomenon of activated rigidity (FROMENT SIGN) brings out rigidity in the limb being tested with the performance of voluntary movements in the opposite limb (e.g. opening/closing of fist or abduction and adduction of shoulder). This, like the milder forms of rigidity, is better appreciated by placing one hand over the muscles being tested (e.g., placing the left thumb over the biceps and the remaining fingers over the triceps while flexing and extending the elbow with the right hand). Prominent axial rigidity involving the nuchal muscles with much less hypertonia in appendicular muscles

Correspondence: Dr. Kuljeet Singh Anand, Department of Neurology, Dr.RML Hospital & PGIMER, New Delhi, India
e-mail: kuljeet_anand@rediffmail.com

suggests possibility of Progressive supranuclear palsy (PSP), whereas marked degree of unilateral rigidity or paratonia points towards diagnosis of Cortico basal syndrome (CBS).

Bradykinesia: One of the clinical hallmark of PD which may be apparent to the clinician even before formal examination in bradykinesia. It usually manifests initially as slowness in performing daily activities, such that the patient starts taking a longer time for completing jobs which earlier would be completed in a short time span and slow reaction times. Masked expressionless facies (Hypomimia), decreased blink rate, difficulty in getting up from a chair may all be readily apparent to the clinician. Formal testing for bradykinesia however involves asking the patient to perform rapid alternating movements of the hand (finger taps, hand grips and pronation-supination of hands) and heel taps. PD patients usually show a successive decrement in amplitude of finger taps, motor blocks or freezing and dysrhythmia.

Another manifestation of bradykinesia is Micrographia in which there is decrementing amplitude of letters/ alphabets on continued writing.⁸ The pathophysiology of bradykinesia is not well understood, but it is thought to result from failure of basal ganglia output to reinforce the cortical mechanisms that prepare and execute the commands to move.¹ The premovement EEG potential (Bereitschaft potential) is reduced in PD, probably reflecting inadequate basal ganglia activation of the supplementary motor area.⁹

POSTURAL INSTABILITY

The 'Pull test' has been traditionally used for testing postural instability in parkinsonism. It involves quickly pulling the patient backwards by the shoulders. An abnormal response is characterized by the patient taking two or more steps backwards. Postural instability however does not develop until late in PD and an early instability should suggest the clinician to think for alternative diagnosis like PSP.¹⁰ The average period from onset of symptoms to the first fall in progressive supranuclear palsy (PSP) is 16.8 months, as compared to 108 months in PD, 42 months in MSA, 54 months in dementia with Lewy bodies, and 40.8 months in vascular parkinsonism. Many patients with postural instability, particularly when associated with flexed truncal posture (camptocormia), have festination, manifested by faster and faster walking as if chasing their center of gravity to prevent falling.

Several factors like poor postural stability, slowness, a narrow base, and inability to reposition the feet often cause parkinsonian patients to fall back while arising from a chair. PSP patients may "rocket" out of the chair inappropriately quickly, failing to recognize their postural instability, whereas PD patients may make several slow attempts, push their arms by the sides of the chair, or may need support of an assistant to get up from chair. Gait disturbances in typical parkinsonism include lack of arm swing, shortened and later shuffling stride, freezing in the course of walking (especially at a door frame or when approaching an obstruction or a chair), and in more severe cases, propulsion and spontaneous falls. In PD, the base of the gait is usually narrow, and tandem gait is performed well. When the gait is wide-based, a superimposed ataxia is a consideration, as is seen in MSA-C, although some of the spinocerebellar ataxias may present with parkinsonism and ataxia. Toe walking (*cock-walk*) is seen in some parkinsonian disorders (e.g., due to manganese poisoning), and a peculiar loping gait may indicate the rare patient with akinesia in the absence of rigidity, which may be one phenotype of PSP. The so-called magnetic foot, or *marche à petits pas*, (also seen in Binswanger

disease, and normal pressure hydrocephalus) more commonly results in a lower-body parkinsonism, typically associated with cerebrovascular disorders such as lacunar strokes. A striking discrepancy of involvement between the lower body and the upper limbs, with normal or even excessive arm swing, is an important clue to the diagnosis of vascular parkinsonism.

NEURO-OPHTHALMOLOGIC FINDINGS

PD patient may be disturbed due to any of the following ocular or visual complaints¹¹: decreased blink rate, ocular surface irritation, altered tear film, visual hallucinations, blepharospasm, decreased blink rate and decreased convergence.

Whereas vertical saccade amplitude may be markedly diminished in PSP and latency may be prolonged in CBD, these movements are typically normal in PD.¹² A finding that may help distinguish these disorders. Increased frequency of square-wave jerks (SWJ) is abnormal, though the exact pathophysiology is unknown. This finding may be present in PD patients, but it is more likely to occur in patients with PSP. It is important to assess not only horizontal and vertical gaze (typically impaired in PSP) but also optokinetic nystagmus to note whether vertical saccadic eye movements (particularly as the optokinetic tape moves in upward direction) are impaired, as in PSP. Patients with PSP typically have trouble making eye contact because of disturbed visual refixation. As a result of persistence of visual fixation when PSP patients turn, their head turn lags behind their body turn.

Table 2: "Red flags" for an incorrect diagnosis of PD

-
- Absence of symptom asymmetry early in disease course
 - Frequent falls, in early stages
 - Rapidly progressive parkinsonism (e.g., Hoehn and Yahr stage 3 in less than 3 years)
 - Prominent eye movement abnormalities (e.g., supranuclear vertical gaze palsy)
 - Pyramidal or cerebellar dysfunction
 - Cortical sensory disturbances (agraphesthesia, astereognosis)
 - Apraxia & alien limb
 - Dementia or psychosis early in disease course
 - Prominent autonomic dysfunction in early stages
 - Levodopa unresponsiveness
-

Features suggesting atypical parkinsonism

Certain clues and red flags for an incorrect diagnosis of PD (table 2) are described below and may be helpful in differentiating PD from atypical parkinsonian disorders.

- Dementia early in the course of the disease points against the diagnosis of PD
- Obvious pyramidal tract dysfunction suggests diagnoses other than PD like corticobasal syndrome, vascular parkinsonism or multi system atrophy
- In PD or MSA, the less affected limb may show mirror movements as the patient attempts to perform rapid repetitive or alternating movements with the most affected limb¹³. On the other hand, in CBS, the most affected limb may mirror movements performed in the less affected limb.
- Prominent abnormalities on sensory examination, apart from increase in vibration threshold that occurs with age is unlikely to be present in PD patients. Cortical sensory disturbances like astereognosis suggest diagnosis of corticobasal syndrome.
- Fluctuations in cognition, early hallucinations and sensitivity to

- neuroleptics agents favour dementia with Lewy body (DLB).
- Some patients with parkinsonism and frontal lobe involvement exhibit signs of perseveration such as the *applause sign*, manifested by persistence of clapping after being instructed to clap consecutively three times as quickly as possible. Although initially thought to be characteristic of PSP, it is also present in some patients with other parkinsonian disorders¹⁴
- Prominent asymmetry beyond three years from symptom onset along with cortical myoclonus and dystonia are suggestive of

- cortical basal syndrome
- Early autonomic dysfunction, abnormal postures (PISA syndrome, anterocollis) and emotional lability help in diagnosis multi system atrophy over PD
- An exaggerated grasp response indicates disturbance of the frontal lobes and the possibility of a concomitant dementing process.

The following table (table 3) summarizes differentiating features of PD from three common parkinsonian syndromes.

Table 3: Differentiating features of PD from three common parkinsonian syndromes

	PD	MSA	PSP	CBD
Mean age at onset	6 th decade	5-6 decade	6-7 th decade	6-7 decade
Parkinsonism	asymmetric	symmetric	Symmetric with axial rigidity	asymmetric
Eye signs	Eye movements usually normal at initial stages	Nystagmus ,squarewave jerks (MSA-C)	Surpra nuclear gaze palsy (down>up),slow vertical saccades	Increased latency of saccades
Cognitive impairment	Usually late feature	Late feature,uncommon	Frontal subcortical, poor attention	Frontal Cortical/sub cortical
Tremor	Asymmetric , rest tremor	Often present, rarely pillrolling	Uncommon in classical PSP, may be seen in PSP-P	May be seen
Falls	Seen at later stages	Early in course	Earliest among these	Common early
Levodopa response	Good, may develop levodopa induced dyskinesia	Response partial, early stages	Occasional response, not usually prolonged	short-lived response
Bladder disturbance	Prominent at later stages	Urgency, frequency, incontinence, incomplete bladder emptying	Urgency, frequency, incontinence, incomplete bladder emptying	Urgency, frequency, incontinence, incomplete bladder emptying
Other features	RBD	RBS	Anxious look, applause sign	Myoclonus, apraxia, cortical sensory loss

REFERENCES

- Shahed J, Jankovic J. Motor symptoms in Parkinson's disease. *Handbook of Clinical Neurology*. 2007 ; 83: 329-342
- Fahn S, Jankovic J, Hallett M. *Principles and Practice of Movement Disorders*. Second edition Elsevier Saunders ;2011. Chapter 4, Parkinsonism: Clinical features and differential diagnosis; p.67.
- Hughes AJ, Daniel SE, Blankson S, Lees AJ. A clinicopathologic study of 100 cases of Parkinson's disease. *Archives of neurology*. 1993; 50:140-8
- Louis ED, Levy G, Mejia-Santana H et al. Risk of action tremor in relatives of tremor-dominant and postural instability gait disorder PD. *Neurology*. 2003; 61: 931-936.
- Deiber MP, Pollak P, Passingham R et al. Thalamic stimulation and suppression of parkinsonian tremor. Evidence of a cerebellar deactivation using positron emission tomography. *Brain* 1993; 116: 267-279
- Fukuda M, Barnes A, Simon ES et al. Thalamic stimulation for parkinsonian tremor: correlation between regional cerebral blood flow and physiological tremor characteristics. *Neuroimage*. 2004; 21: 608-615
- Hoefler PF, Putnam TJ. Action potentials of muscles in rigidity and tremor. *Arch Neurol Psychiatry*. 1940; 43: 704-725.
- Teulings H-L, Contreras-Vidal JL, Stelmach GE et al. Adaptation of handwriting size under distorted visual feedback in patients with Parkinson's disease and elderly and young controls. *J Neurol Neurosurg Psychiatry*. 2002; 72: 315-324.
- Dick JPR, Rothwell JC, Day BL, Cantello R, Buruma O, Gioux M, et al. The Bereitschaftspotential is abnormal in Parkinson's disease. *Brain* 1989;113:233-44
- Wenning GK, Ebersbach G, Vermy M et al. Progression of falls in postmortem-confirmed parkinsonian disorders. *Mov Disord*. 1999; 14: 947-950
- Biousse V, Skibell BC, Watts RL et al. Ophthalmologic features of Parkinson's disease. *Neurology*. 2004; 62: 177-180
- Vidailhet M, Rivaud S, Gouider-Khouja N et al. Eye movements in parkinsonian syndromes. *Ann Neurol*. 1994; 35:420-426
- Espay AJ, Li JY, Johnston L, Chen R, Lang AE. Mirror movements in parkinsonism: evaluation of a new clinical sign. *J Neurol Neurosurg Psychiatry*. 2005 Oct;76(10):1355-8
- Wu LJ, Situbrana O, Davidson A, Jankovic J. Applause sign in Parkinsonian disorders and Huntington's disease. *Mov Disord* 2008 Dec ;23(16):2307-11