

Parkinsonian Features

When Are They Parkinson Disease?

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Parkinsonian syndromes can be classified into 2 major groups: Parkinson disease (PD) and atypical parkinsonian disorders. Common characteristics include akinesia, expressed as slowness and paucity of movement (eg, decreased arm swing or facial expression) and difficulty in initiating movement, and are associated with rigidity with or without resting tremor. Parkinsonian syndromes frequently occur in the elderly, their prevalence increasing markedly with age (14.9% at the age of 65 to 74 years; 52.4% at the age of 85 years or older).¹ The most common parkinsonian syndrome, PD affects approximately one half million Americans. The incidence of PD is about 10 times that of atypical parkinsonian disorders.^{2,3}

Diagnosis of PD was thought to be straightforward, but 3 recent large clinicopathologic studies showed that specialists misdiagnosed 25% to 40% of patients followed up in practice or assessed after reading detailed clinical vignettes.⁴⁻⁶ Misdiagnosis by nonspecialists is likely to be even higher. Early and accurate diagnosis is important because prognosis and treatment of patients with PD is markedly different from those for patients with atypical parkinsonian disorders. The survival of patients with early PD approximates that of the US population,⁷ particularly when they are treated appropriately.⁸ Patients with any of the atypical parkinsonian disorders have shorter survival (usually <10 years)⁹ and exhibit more frequent complications.

Several clinical features help differentiate patients with early PD from those with atypical parkinsonian disorders. For instance, the presence of early autonomic dysfunction and of pyramidal or cerebellar signs helps to distinguish multiple system atrophy (MSA) from PD, while early hallucinations, unrelated to treatment, and dementia support the diagnosis of dementia with Lewy bodies. To make an early and accurate diagnosis of these disorders, the

clinician should evaluate the patient's medication and bladder history; blood pressure; mental functions (including apraxia); eye movements; akinesia, rigidity, tremor, and writing (micrographia); and gait, posture, and postural stability.

Although PD is chiefly a sporadic disorder, approximately 10% is familial. Familial PD usually has an earlier onset, more rapid progression, and other unusual features.

Clinical History

Patients with PD usually present after the age of 50 years with motor complaints, such as tremor at rest, micrographia, slowness or poverty of movements, or stiffness. Typically, the onset is insidious and progression is slow, initially affecting 1 limb and then spreading to the others. Asymmetric involvement usually persists. Tremor, usually at rest, increases in periods of anxiety and disappears during sleep or motor actions. Postural tremor, which usually occurs while the patient maintains a posture such as extension of the upper extremities, should be differentiated from essential tremor, which is slowly progressive and not associated with akinesia or rigidity. Decreased associated movements or slowness when walking may occur relatively early in the disease, whereas short or shuffling steps, instability, and falls occur later. Reduced speech volume and monotony may occur relatively early, but sialorrhea secondary to dysphagia develops later. Faintness, impotence, and urinary disturbances (eg, urgent micturition, incontinence) usually occur late in PD. Depression may antedate or coincide with motor symptoms. However, dementia is not an early feature in PD. Patients with PD may experience drug-induced hallucinations but not hallucinations unrelated to medications or periods of unexplained confusion.

Before concluding that a patient has PD, the clinician should carefully review the patient's therapeutic history. Drug-induced parkinsonism is frequently secondary to dopamine receptor blockers used primarily as antipsychotics and antiemetics and less commonly with calcium channel blockers (eg, flunarizine) or cardiac antiarrhythmic agents (eg, amiodarone).

Neurologic Examination

The results of the Mini-Mental State Examination are usually normal in early PD. The "parietal signs" of visual and sensory hemineglect can be assessed by the simultaneous application of the same stimulus, such as touch, to both sides of the body (eg, the forearms). Patients with PD distinguish simultaneous stimuli, but those with sensory hemineglect fail consistently to recognize the stimulus on 1 side. Akinesia may be assessed by the patient's tapping the index finger and thumb and by foot tapping, and rigidity, by flexing and extending the neck and each extremity. Tremor should be assessed with the patient at rest, while performing an activity, and while maintaining a posture. Balance should be assessed with the "pull test" (the patient should be able to maintain balance while being pulled backward). Findings on the pull test are abnormal (the patient is unable to recover unaided) only in later stages of PD. Evaluation of eye movements, particularly the speed of vertical and horizontal saccades, (quick eye movement between 2 stimuli) helps exclude other parkinsonian disorders. Elderly patients with parkinsonism may have age-related limited upward gaze and convergence, but their saccades remain normal. To exclude orthostatic hypotension, blood pressure should be measured with the patient recumbent and then standing. A systolic drop of at least 30 mm Hg or a diastolic drop of at least 15 mm Hg within 3 minutes of standing suggests orthostatic hypotension, not usually seen in early PD.

Diagnostic Criteria

Several clinical criteria for the diagnosis of PD have been proposed.^{10,11} Akinesia and rigidity are almost universal in PD, and a tremor ultimately develops in about 75% of patients. Nevertheless, classical tremor is highly suggestive of PD or drug-induced parkinsonism, since it rarely occurs in atypical parkinsonian disorders. The presence of postural instability occurs late in PD; when seen early, it suggests an alternative diagnosis. Virtually all PD patients have a good or excellent response to levodopa preparations given in appropriate doses for an adequate period (eg, 800-1000 mg/d for ≥ 1 month).

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Diagnosis of Parkinson Disease (PD) Based on Clinicopathologic Studies

Features characterizing PD

Progressive onset and slow progression of asymmetric (unilateral) akinesia
Excellent and sustained levodopa response
Either classical pill-rolling rest tremor or rigidity

Features suggestive of an alternate diagnosis

Motor

Early instability and falls
Rapid disease progression
Absent, poor, or waning response to levodopa
Pyramidal signs
Cerebellar signs
Early dysarthria and/or dysphagia

Oculomotor

Supranuclear gaze palsy, slowing of saccades, difficulty initiating saccades

Cognitive and behavioral

Early dementia*
Visual hallucinations not treatment induced
Apraxia
Sensory or visual neglect, cortical disturbances

Autonomic

Early autonomic failure unrelated to treatment (orthostatic hypotension, impotence, or urinary disturbances)

*Dementia occurs in approximately 15% of PD patients but is not an early feature.

Based on clinicopathological studies,^{6,12} diagnosis of PD is highly probable when a patient presents with a slowly progressive akinesia with either the classical pill-rolling rest tremor or rigidity, excellent and sustained levodopa response, asymmetric parkinsonism at onset, and absence of unusual features (Table). Symptomatic improvement, once the patient has begun taking levodopa, is also strongly indicative of PD.

Other Studies

The diagnosis of PD remains primarily a clinical one. Neuroimaging, computed tomography, and magnetic resonance imaging of the brain may help to exclude other diagnoses, such as vascular disease and normal-pressure hydrocephalus. Similarly, laboratory testing is not usually needed except to rule out Wilson disease (eg, ceruloplasmin and copper levels) in patients younger than 50 years and hypothyroidism (eg, thyroid function tests).

Early diagnosis of PD and referral of the patient to a neurologist ensure appropriate disease management.

Features Suggestive of Atypical Parkinsonian Disorders

A patient probably does not have PD if the parkinsonian syndrome evolves rapidly (often achieving postural instability in 3 years), if the patient responds poorly or transiently to levodopa therapy, or if there are other non-PD-associated findings, such as supranuclear gaze palsy, early dementia or hallucinations unrelated to treatment, early autonomic failure, pyramidal or cerebellar signs, alien limb syndrome, (the patient feels a limb is not his or her own and it moves without the patient's volition), or severe ideomotor apraxia (the pa-

tient's inability to perform voluntary movements, notwithstanding preservation of motor and sensory functions) (Table).

The most common atypical parkinsonian neurodegenerative disorders are progressive supranuclear palsy (PSP), MSA, and dementia with Lewy bodies. The nosologic status of dementia with Lewy bodies, to which a number of different labels have been attached—diffuse Lewy body disease, senile dementia of the Lewy body type, Lewy body variant of Alzheimer disease—is unclear. Whether dementia with Lewy bodies is a distinct disorder or is part of the spectrum of a Lewy body disease that includes PD remains to be determined.⁴ At present, most neurologists consider PD and dementia with Lewy bodies as distinct nosologic entities.

Early hallucinations, unrelated to treatment, and dementia do not occur in early PD. Their presence suggests an alternative disorder, such as dementia with Lewy bodies or, less likely, an association of PD with Alzheimer disease.

Early postural instability is rarely a feature of PD. Falls as a presenting feature suggest PSP, but thereafter falls may occur with steadily increasing frequency in MSA. A corollary of early instability is rapid disease progression. "Malignant parkinsonism" is usually not PD. Absent, poor, or waning response to levodopa is exceedingly infrequent in PD. Unfortunately, the converse is not true for parkinsonian syndromes; at some stage, up to 30% of patients with MSA may initially show such a response, although usually losing it as the disease progresses.

Pyramidal signs (eg, Babinski) are not a feature of PD, but about one third to one half of patients with an atypical parkinsonian disorder develop pyramidal signs. Cerebellar signs (eg, wide-based gait, dysmetria) are not seen in PD, although it may be difficult to decide at later stages whether an unsteady gait results from postural instability due to advancing parkinsonism or to cerebellar ataxia.

Myoclonic jerks (muscle twitchings) of the fingers or limbs usually do not occur in uncomplicated PD. They do occur in about one third of patients with MSA and are even more frequent in corticobasal degeneration and dementia with Lewy bodies.

Marked slowing of vertical saccades commonly precedes the limitation of voluntary (to command) or pursuit (following stimuli) gaze that can lead to supranuclear gaze palsy.

Prominent early or severe difficulties with speech and swallowing do not suggest PD but occur in atypical parkinsonian disorders. Parkinson disease rarely causes early dysphagia, although it is present late in the disease.

Most PD patients gradually develop detrusor hyperreflexia, resulting in in-

creased urinary frequency and urgency, which are therefore poor discriminators among parkinsonian disorders. However, frank incontinence, especially with whole-bladder emptying, is much less common in PD than in MSA, especially early in the disease process. Urinary retention in PD should not occur unless it is caused by prostatic hypertrophy or anticholinergic drugs. In MSA either of these factors may more easily precipitate retention. Development of male impotence is virtually universal in MSA and is typically the first feature of the illness. It occurs late but with increasing frequency in PD, especially in older subjects. Severe postural faintness with recurrent syncope increases the suspicion of a diagnosis other than PD, particularly when it occurs early or in the absence of dopaminergic medication.

In summary, the early correct diagnosis of PD, followed by appropriate medical therapy, is important since it usually results in near-normal survival.^{7,8}

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