Approach to the Patient with Parkinson Disease

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KEYWORDS

• Parkinson disease • Diagnosis • Treatment • Motor symptoms
• Nonmotor symptoms

KEY POINTS

- Progressive neurodegenerative disease is characterized pathologically by changes in the mesencephalic substantia nigra and physiologically by development of cardinal motor symptoms of resting tremor, bradykinesia, and rigidity, and eventually postural instability.
- All current treatment is based on symptom management, as no effective cure or disease modification is currently available.
- Appropriate diagnosis and periodic reassessment are critical to assure appropriate therapy and avoid mistreatment and delay in addressing other conditions with overlapping symptoms.
- Supporting the patient and caregiver holistically is important, as significant comorbid conditions related to the disease can impact quality of life and relationships; addressing psychological and support needs along with physical symptoms is critical to providing effective care.

First Described in 1817 by James Parkinson as a neurologic disorder primarily affecting musculoskeletal function and preserving senses and intellect, Parkinson disease (PD) is currently understood as a progressive neurodegenerative disease with motor, nonmotor, and behavioral findings. Significant advances in imaging technology have allowed the characterization of the underlying pathologic changes to the mesencephalic substantia nigra, and development of alpha-synuclein containing Lewy bodies in the remaining dopaminergic neurons. Although certain imaging techniques currently allow for detection in some patients as much as 20 years prior to the onset of motor symptoms, these advances have yet to produce a meaningful treatment to halt the progression of the disease or reverse its course. Current treatments are directed at optimizing symptomatic management.[1,2]

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The incidence of PD varies with age, commonly cited as approximately 1% by the sixth decade of life, and approaching 4% by the end of the eighth decade of life. Although the disease may occur as early as the teenage years, with disease occurring before the second decade of life labeled as juvenile-onset and between the second and fourth decades as young-onset, the average age at diagnosis is 70.5 years.[3] White, non-Hispanic persons living in the Midwest and northeastern United States are disproportionately represented in epidemiologic studies by review of claims data.[4]

CAUSATIVE AND PREDICTIVE FACTORS

Research into genetic factors and identification of environmental risk factors have yet to provide a definitive predictive model for PD. A positive family history is a risk factor for PD, with first-degree relatives of PD patients 2.3 times more likely to develop PD.[5] Genetic studies continue to identify numerous heritable forms of the disease, designated with PARK1, PARK2, and similar designations, with various autosomal-dominant, x-linked, and autosomal-recessive families. Despite these advances, most cases at this writing remain sporadic in nature.[6] Observational and case–control studies and meta-analysis of environmental risk factors support correlation with exposures to pesticides and herbicides, along with exposure to well water, living on a farm, and exposure to farm animals.[7,8] Protective exposures have also been studied, including smoking and coffee drinking.[9] Despite the noted risk reduction of smoking for PD, other health risks still preclude recommending smoking as a preventative measure.

DIAGNOSTIC GOLD STANDARD STILL ELUSIVE

Because no definitive laboratory and radiological test with gold standard level specificity for PD currently exists, history and physical examination remain the cornerstones of diagnosis. Classic cardinal motor symptoms of resting tremor, bradykinesia, and rigidity, and eventually postural instability, form the basis for the initial diagnosis of idiopathic PD (**Box 1**). Early disease can be easily misdiagnosed because of the relative vagueness of symptoms and mistaking early signs for normal aging processes.[10] Understanding the complex interaction of motor, cognitive, behavioral/neuropsychiatric, and autonomic dysfunction, as well as significant overlap with other neurodegenerative processes associated with tremor, makes a high index of suspicion and a broad differential diagnosis important in the clinical evaluation.

Most current practice guidelines for PD suggest referral to a physician with expertise in movement disorders should be considered for physicians who are unsure or lack experience in the initial diagnosis of PD. Because treatment may mask the clinical diagnostic features and further delay definitive diagnosis, consideration should be given to referral before initiation of treatment. Despite the lack of definitive outcome-based studies or cost-benefit analyses that demonstrate definite benefit of this approach, the significant psychological stress of the diagnosis of a chronic progressive neurologic disease with such profound impacts makes judgment in favor of early referral warranted, especially in cases where the diagnosis is unclear, in the younger patient, or rapid or unusual progression of symptoms. Periodic reassessment of the diagnosis should also be done for all patients to evaluate for possible misdiagnosis.[11] **Table 1** provides a partial list of diseases often misdiagnosed as PD.[1,12–14]

The natural course of idiopathic PD is a progressive decline in motor and cognitive function, with a contaminant rise in morbidity and mortality related to both. Changes in cognition are most closely related to patient age at diagnosis, and duration of disease and early or rapid progression of dementia may suggest an alternative diagnosis. One large review of mortality studies showed an average shortening of life expectancy