Early diagnosis of Parkinson’s disease

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Core features

Summary
Early diagnosis of Parkinson’s disease is often difficult. The insidious onset of the disease, its slow progression and the lack of laboratory tests to confirm the diagnosis contribute to this difficulty. Nevertheless, early diagnosis can be greatly facilitated by the systematic application of diagnostic clinical criteria and the selective use of radiological and laboratory tests.

Keywords: Parkinson’s disease, diagnosis

Parkinson-plus syndromes

- progressive supranuclear palsy
- Shy Drager syndrome
- multi-system atrophy

Parkinson’s disease

Sequence of appearance of features
Early:

- resting tremor of one hand
- rigidity and/or bradykinesia

Late:

- mid-line features
- disturbance of gait, speech, phonation and righting reactions

When to investigate a patient with an extrapyramidal syndrome

- onset before the age of 40 years
- onset with bilateral signs
- symmetrical disease
- severe, early autonomic failure
- presence of pyramidal tract or eye signs
- poor initial response to adequate doses of levodopa
- family history of a movement disorder
- rapidly progressive disease

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The early diagnosis of Parkinson’s disease is often difficult. In a recent study¹ Parkinson’s disease was confirmed at *post mortem* examination in only 76 out of 100 patients who had been previously diagnosed by a neurologist or a geriatrician with special interest in movement disorders. The core features of Parkinson’s disease are tremor, rigidity, bradykinesia, gait disturbances and postural instability. In the absence of atypical features (see below), a history of encephalitis or treatment with neuroleptic drugs, a confident diagnosis of Parkinson’s disease can be made if two or more of these features are present. It is arguable whether the use of more stringent diagnostic criteria such as those adopted by the UK Parkinson’s Disease Society Brain Bank² confers any additional advantage in clinical practice. Although such criteria improve the diagnostic accuracy by distinguishing Parkinson’s disease from the rarer Parkinson-plus syndromes (see box), they often exclude genuine cases of Parkinson’s disease¹ and, in so doing, deny these patients effective treatment. The sequence in which the cardinal features of Parkinson’s disease occur is often helpful in distinguishing it from other extrapyramidal disorders (see box).

Symptoms and signs

Most of the other commonly described symptoms and signs of Parkinson’s disease are due to one or more of the core features described above. For example, infrequent blinking, hypomimia (facial immobility), and the ‘reptilian stare’ result from a combination of muscular rigidity and bradykinesia (see figure). Another group of frequently reported symptoms are excessive fatigue, fleeting muscular pain (often described by patients as rheumatism), intermittent paraesthesiae, and burning skin sensations.

Investigation

The features summarised in the box suggest an extrapyramidal disorder other than Parkinson’s disease. Radiological and laboratory investigations are often helpful in these circumstances. Parkinson’s disease is a slowly progressive disorder predominantly of middle and old age. In a large community survey³ the mean age at disease onset was 65.3 years and the incidence and prevalence increased progressively with advancing age. For example, in this study the disease prevalence in those 40 to 44 years old was 12.5 per 100 000 of the population compared to an overall prevalence of 164.2. Clearly patients presenting with extrapyramidal features before the age of 40 require a careful evaluation to exclude metabolic and other basal ganglia disorders.

Atypical features

Although erectile impotence, excessive sweating, a feeling of incomplete bladder emptying, constipation and orthostatic hypotension are common symptoms in Parkinson’s disease,⁴ these are usually mild and tend to occur late in the disease. Severe early autonomic failure in patients with extrapyramidal signs suggests the diagnosis of Shy Drager syndrome. Similarly, the presence of an extensor plantar response in these patients is an indication of coincidental cerebrovascular disease or a widespread neurodegenerative disorder such as multi-system atrophy or progressive supranuclear palsy. In these circumstances neuroradiological investigations are useful in distinguishing Parkinson’s disease from other parkinsonian syndromes and magnetic resonance imaging (MRI) is particularly helpful. Stern *et al*⁶ have found that a combination of putamenal hypointensity and brainstem atrophy on MRI is a consistent finding in Parkinson-plus syndromes and, when taken with other clinical features, virtually excludes Parkinson’s disease.

Figure Facial hypomimia in a parkinsonian patient

Apomorphine test

- sc apomorphine (50 µg /kg)
- measure motor function 90 min later
- 95% cases Parkinson's disease improve
- 25% cases Parkinson-plus syndromes improve

Focal and segmental dystonias are rare but well-recognised features of untreated Parkinson's disease.⁶ However, in a young patient dystonia is more likely to be a manifestation of levodopa-responsive dystonia or Wilson's disease. A detailed family history, ophthalmic examination for Kayser–Flecher rings and copper studies are mandatory in these patients.

Idiopathic parkinsonism is almost invariably a unilateral disease in its early stages and even when the disease is advanced it is nearly always asymmetrical. A presentation with bilateral or symmetrical extrapyramidal tract signs should raise the suspicion of a parkinson-plus syndrome. Occasionally, patients with normal pressure hydrocephalus present in this way and these patients may even partially respond to levodopa drugs.⁷

Response to levodopa

A significant response to levodopa and dopamine agonists is an essential diagnostic criterion of Parkinson's disease. An initial sustained symptomatic improvement of 70% or more with the introduction of these drugs is considered confirmatory evidence of Parkinson's disease. It is noteworthy that this response is not affected by disease severity or the patient's age,⁸ nor is it influenced by the disease duration when therapy is commenced.⁹ Interestingly, the slowness and poverty of movements and muscle stiffness that occur in old age do not improve with levodopa therapy.¹⁰

The response of patients with Parkinson's disease to levodopa therapy can usually be predicted by the apomorphine test (see box).^{11–13} Interestingly, severe drowsiness during the test occurs in all patients with Parkinson-plus syndromes but not in parkinsonian patients and this has been suggested as a feature which distinguishes Parkinson-plus syndromes from Parkinson's disease.¹² The apomorphine test may give false negative results in a minority of patients with Parkinson's disease. In one study¹³ this occurred in two out of 35 patients with early Parkinson's disease. Thus, while a positive apomorphine test supports the diagnosis of Parkinson's disease, it is not diagnostic of the condition and the result of the test must be interpreted in conjunction with other clinical findings.

Conclusions

Parkinson's disease is essentially a clinical diagnosis. In some cases investigation with MRI may be helpful in the differential diagnosis of Parkinson's disease from Parkinson-plus syndromes and is indicated in patients presenting with symmetrical or bilateral disease and those with early severe autonomic failure or rapid disease progression. A trial of levodopa therapy or the apomorphine test are also invaluable in these situations. When cerebrovascular disease or normal pressure hydrocephalus is suspected a computed tomographic brain scan is the investigation of choice. Finally, the diagnosis of Wilson's disease should be excluded in young patients with extrapyramidal tract signs, especially if there is a family history or other unusual signs.

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