

Tackling dementia in patients with Parkinson's disease

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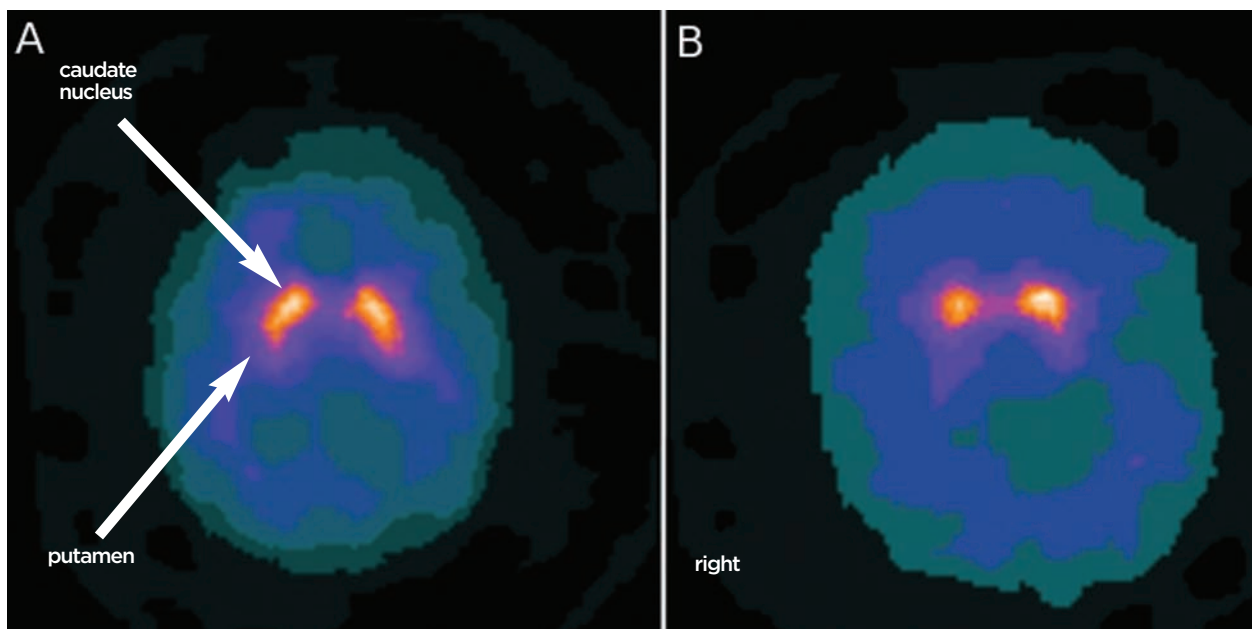
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FIGURE 1

A A normal ^{123}I -ioflupane SPECT image (DaTSCAN).
B DaTSCAN showing reduction in tracer uptake in the putamen and, to a lesser extent, the caudate nucleus, most marked on the right side. These findings would strongly support a clinical diagnosis of dementia with Lewy bodies



What are the differential diagnoses?

How can an accurate diagnosis be made?

What are the treatment options?



ALMOST 200 YEARS AGO, JAMES PARKINSON DESCRIBED A CONDITION WITH 'INVOLUNTARY

tremulous motion, lessened voluntary powers,' but with 'uninjured senses and intellect' that would later be named Parkinson's disease by Charcot. Since then, it has emerged that cognitive impairment is present in a large proportion of patients with Parkinson's disease.

Cognitive symptoms in patients with Parkinson's disease are associated with more rapid deterioration and eventually, a two-fold increase in mortality.¹ Patients with cognitive impairment place a greater burden on their care givers and many such patients are admitted to nursing homes.

Lewy bodies are eosinophilic neuronal inclusion bodies that contain α -synuclein and, when accompanied by the clinical triad of tremor, rigidity and bradykinesia, histopathologically define idiopathic Parkinson's disease.

Dementia with cortical Lewy bodies (DLB) is associated with deficits of acetylcholine and dopamine. These neurotransmitters have been found to be deficient in Alzheimer's and Parkinson's disease, respectively.

Dementia more than a year after the onset of motor features associated with Parkinson's disease is defined as Parkinson's disease with dementia (PDD). If it develops within one year of the motor features, the term dementia with Lewy bodies (DLB) is used.²

There continues to be some controversy about whether DLB and PDD are the same condition, however, since clinical and pathological features are similar, it is generally accepted that both represent a continuum of the same disorder, and they will be treated as one for the purpose of this review.

EPIDEMIOLOGY

PDD together with DLB account for around a fifth of all cases of dementia in older people reaching autopsy,³ thus making it the second most common

degenerative dementia in the elderly, after Alzheimer's disease. The reported prevalence varies greatly between studies and the true figure is difficult to assess. A systematic review found the average prevalence to be around 40%.⁴

Longitudinal studies suggest that most patients with Parkinson's disease would eventually develop dementia if they were to survive for long enough. The annual risk of dementia in Parkinson's patients is around 1.7 times that of age-matched controls.^{5,6} The risk of developing dementia is dependent solely on the age of the patient, and not on the duration of the disease.⁷

DIAGNOSIS

Although patients with Parkinson's disease may suffer from all types of dementia, the diagnosis of PDD in the presence of long-standing and pronounced motor features rarely poses a diagnostic dilemma. Conversely, the diagnosis of DLB may be more difficult.

SYMPOSIUM CARE OF THE ELDERLY

DEMENTIA IN PARKINSON'S DISEASE

Table 1

Consensus criteria for the clinical diagnosis of probable dementia with Lewy bodies

Central feature	<ul style="list-style-type: none"> ● progressive cognitive decline (deficits in attention, frontal-subcortical skills and visuospatial ability especially prominent)
Core features (at least two of the following):	<ul style="list-style-type: none"> ● fluctuating cognition ● recurrent visual hallucinations ● parkinsonism
Supporting features	<ul style="list-style-type: none"> ● repeated falls ● syncope ● transient loss of consciousness ● neuroleptic sensitivity ● systematised delusions ● other hallucinations
Diagnosis less likely in the presence of:	<ul style="list-style-type: none"> ● vascular disease (focal neurology or evidence on CT/MRI) ● evidence of any physical illness that could account for the clinical picture

Adapted from McKeith IG, Dickson DW, Lowe J et al. Diagnosis and management of dementia with Lewy bodies: third report of the DLB Consortium. *Neurology* 2005;65 (12): 1863–72

Unlike patients with Alzheimer's disease who tend to present with memory problems, patients with DLB typically have rather non-specific problems with frontal and executive function, often fluctuating during the course of the week or even during the day. Patients can show poor attention and disinhibition, and have difficulty multitasking, often struggling with common tasks at home and in the workplace.⁸ During early stages of the disease, there can be very little change in the mini-mental state examination (MMSE), as executive function is underrepresented in this test.

'The risk of developing dementia is dependent solely on the age of the patient, and not on the duration of the disease'

No single pathognomonic clinical sign can be used to make the diagnosis of DLB, so the clinician relies on the revised consensus clinical criteria which have a specificity of 80% and sensitivity of 60–80% (see table 1, above).²

These criteria require the presence

of at least two of the following three syndromes:

- Persistent visual hallucinations
- Fluctuating defects in cognitive and functional ability (over a period of hours or days)
- Parkinsonism

The diagnosis can be supported further by the presence of other clinical features, such as repeated falls, non-visual hallucinations, systematised delusions and neuroleptic sensitivity that can be seen with both typical and atypical neuroleptics.² During REM sleep, patients with behaviour disturbance experience vivid dreams associated with simple or complex motor behaviour. This occasionally precedes the development of Parkinson's disease and DLB.

Visual hallucinations are present in approximately two-thirds of patients with DLB and, at presentation, are the most specific factor in differentiating the condition from Alzheimer's disease.^{9,10} Patients commonly describe images of children or small animals, which disappear when attention is focused directly on them. The visuospatial defects observed tend to be more pronounced than expected for the overall level of cognitive function, again suggesting a marked deficit in visual processing in DLB. It is therefore not surprising that the development of visual hallucinations has been associated with a higher risk of dementia in patients with Parkinson's disease.¹¹

No investigation can reliably differentiate PDD and DLB from Alzheimer's disease and this is complicated further when the two

coexist in the same patient. Structural imaging, such as MRI, may sometimes reveal a degree of atrophy of the medial temporal lobes and can be used to support the diagnosis of dementia. Novel imaging methods, such as ¹²³I-ioflupane SPECT imaging (DaTSCAN) are now available to image basal ganglia pathology directly by labelling the presynaptic dopamine transporter site (see figure 1, p15).¹² Although very useful in the differential diagnosis, they are often only accessible through specialist memory clinics.

MANAGEMENT

Clinicians dealing with patients with DLB or PDD are faced with a mixture of cognitive, psychiatric and motor symptoms. The involvement of a multidisciplinary team is key. As treatment of one complaint may lead to the deterioration of another, patients and their carers need to be engaged in active dialogue to identify the factors most important to them. An early referral to a specialist clinic may not only help to confirm the diagnosis, but also to co-ordinate the group of professionals working with the patient.

The involvement of carers is also important, and the diagnosis needs to be explained to them. Social workers and care support workers can work with patients and their carers to assess requirements, arrange appropriate financial support such as the disability living allowance, attendance allowance and carer's allowance or respite care. An effort must be made to structure the home environment to make it safe and help patient mobility. Well lit rooms and the use of glasses and hearing aids, where required, can help to reduce the number of hallucinations.

Although not included in the NICE guidelines on the treatment of dementia, cholinesterase inhibitors used in Alzheimer's disease do have a role in DLB and PDD. Two large randomised controlled trials showed moderate improvements in cognitive function in patients treated with rivastigmine.^{13,14} The greatest impact, however, seemed to be on the psychotic features of the disease, with patients experiencing an improvement in their hallucinations and delusions. It has been suggested that the patients who suffer from visual hallucinations are most likely to benefit from rivastigmine.¹⁴

To date, no studies have compared the effect of cholinesterase inhibitors versus neuroleptic drugs on the

key points

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Dementia with cortical Lewy bodies (DLB) is associated with deficits of acetylcholine and dopamine. These neurotransmitters have been found to be deficient in Alzheimer's and Parkinson's disease, respectively. Dementia more than one year after the onset of motor features associated with Parkinson's disease is defined as Parkinson's disease with dementia (PDD). If it develops within one year of the motor features, the term dementia with Lewy bodies (DLB) is used. Since clinical and pathological features are similar, it is generally accepted that both represent a continuum of the same disorder.

PDD together with DLB account for around one fifth of all cases of dementia in the elderly reaching autopsy, thus making it the second most common degenerative dementia in older people, after Alzheimer's disease. Longitudinal studies suggest that most patients with Parkinson's disease would eventually develop dementia if they were to survive for long enough.

The diagnosis of PDD in the presence of long-standing pronounced motor features rarely poses a diagnostic dilemma but the diagnosis of DLB may be more difficult. Patients with DLB typically have rather non-specific problems with frontal and executive function, often fluctuating during the course of the week or even during the day. During early stages of the disease, there can be very little change in the MMSE. Diagnosis of DLB relies on the revised consensus clinical criteria which require the presence of at least two of the following three syndromes: persistent visual hallucinations, fluctuating defects in cognitive and functional ability, and parkinsonism.

Visual hallucinations are present in approximately two thirds of patients with DLB and, at presentation, are the most specific factor in differentiating it from Alzheimer's disease. Visual hallucinations have been associated with a higher risk of developing dementia in patients with Parkinson's disease. No investigation can reliably differentiate PDD and DLB from Alzheimer's disease.

Clinicians dealing with patients with DLB or PDD are faced with a mixture of cognitive, psychiatric and motor symptoms. The involvement of a multidisciplinary team is key. An early referral to a specialist clinic may not only help to confirm the diagnosis, but also to co-ordinate the group of professionals working with the patient. Well lit rooms and the use of glasses and hearing aids, where required, can help to reduce the number of hallucinations.

Cholinesterase inhibitors used in Alzheimer's disease have a role in DLB and PDD. Trials show moderate improvements in cognitive function in patients treated with rivastigmine. The greatest impact, however, seems to be on the psychotic features of the disease. Patients with DLB are less likely to have a good motor response from L-dopa than patients with Parkinson's disease or PDD.

psychiatric features of DLB or PDD. However, as a large number of patients can experience the life-threatening neuroleptic sensitivity syndrome, characterised by sedation, rigidity, postural instability and confusion, cholinesterase inhibitors are often used first line.

In severe cases, low-dose clozapine has been shown to be most efficacious without leading to worsening of parkinsonian signs.¹⁵

Although, overall, patients with DLB are less likely to have a good motor response from L-dopa therapy than patients with Parkinson's disease or PDD,¹⁶ patients with severe parkinsonism seem to gain a similar benefit, independent of the aetiology.¹⁷ While dopamine replacement therapy can ease some of the severe motor features associated with PDD and DLB, it can lead to worsening of hallucinations and the development of psychotic features.

In one study, only 22% of patients on L-dopa therapy showed an improvement in motor rating scales, without developing psychiatric complications.¹⁸ Therefore, it is often recommended that dopamine replacement therapy should be started at a low dose and titrated slowly and carefully according to the individual patient's need.

CONCLUSION

Primary care plays a significant role in the recognition of DLB and PDD. Early recognition and referral to a specialist memory clinic can help to educate the patient about their often worrying symptoms and initiate the relevant treatment. Through the involvement of the multidisciplinary team, appropriate care networks can be set up to provide support and education for both patients and carers.

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Useful information

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