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Recognizing dementia with Lewy bodies in older people

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Aging
HEALTH

It is not unreasonable to ask if it is, in fact, important to recognize dementia with Lewy bodies (DLB) in older people. What follows in this editorial is a justification for the affirmative response. First of all, it should be clear that diagnosing the presence of dementia is important. The patient, while insight is still present, needs to know that dementing illnesses are progressive, and that plans must be made for the future. The family too, must be made aware that the patient can no longer be relied upon in the same ways as before. Demented people pose risks in medical, financial and social realms. But why should it matter whether the diagnosis of an incurable dementing illness is accurate or not? It is plausible to argue that once it is determined that the dementia is not the result of a treatable disorder then one can reasonably conclude that the die has been cast and nothing much will alter the outcome. Is a name so important? What is wrong with calling everything Alzheimer's disease (AD)?

In days gone by, neurologists were often mocked with the description of their approach to patients of 'diagnose then adios'. In those times naming a disease may have been more fulfilling as an intellectual exercise than as an aid for patients, but this is no longer true.

For one thing it turns out that it is extremely important to patients and families to simply know the name of the condition they are suffering from and battling against [1]. Having a name to call the family catastrophe is no small matter. The name not only provides a link to the internet and other sources of information as well as support associations, but also provides a focus for channeling the family's energy and thought processes. It helps to know one's enemy. We often symbolize an illness as a battle, and to do battle requires having an enemy. Patients and their families appreciate this.

There are also practical reasons for making the diagnosis of DLB. Although it is frequently mistaken for AD, even by experts, it often looks different as it progresses.

What is DLB? It was first recognized by Okazaki *et al.* in 1961 as a pathological oddity in a patient thought to have been suffering from AD [2]. The oddity was that the Lewy bodies, pathological hallmarks of Parkinson's disease (PD), previously thought to be confined to pigmented nuclei in the brainstem, were found in the cortex, a locus never previously known to be affected. It then remained a very rare observation until a surprising report in the 1980s claimed that a dementing disorder with Lewy bodies in the cortex was actually the second most common cause for dementia in England, more prevalent than vascular dementia [3]. This stunning report was not initially accepted, but with the improved staining techniques that had developed since the 1961 report, it became clear in short order that DLB was either the second or third most common dementing disorder in the western world, vascular dementia being approximately equally prevalent. DLB affects people aged between 53 and 83 years [3], with a mean age of death of 78 years, in contrast to a mean age of death of 85 years for AD patients [4].

If a patient exhibits the cardinal features of the disorder, they are highly likely to have the disease, making the criteria quite specific, but they are also quite insensitive, meaning that many people with DLB diagnosed at autopsy had only some, but not all, of these clinical abnormalities. The major distinguishing features between DLB and AD are parkinsonism and fluctuating levels of cognitive dysfunction. DLB is, both pathologically and clinically, a variant of PD [3]. Although not widely known, two large studies, one prospective and one retrospective, have demonstrated that by the time of death 80% of people with idiopathic PD are demented [5]. One hypothesis regarding the difference between PD and DLB is that the former begins in the brainstem and works its way up while the latter starts in the cortex and works its way down [6]. Either way, Parkinsonism is a major clinical feature so that, by consensus criteria, DLB is considered the diagnosis if dementia

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precedes the onset of Parkinsonism or develops within the first 12 months of it [3]. Fluctuations of levels of confusion are the second major hallmark, a phenomenon that is not usually present in AD. DLB patients are also much more likely to have visual hallucinations than AD patients and have a much greater sensitivity to the motor side effects of antipsychotic drugs [7], so often given for the behavioral problems that are associated with dementing diseases. This is a crucial point since many demented patients are treated with antipsychotic drugs, despite there being a ‘black box’ warning concerning their use [8,9], and their extrapyramidal side effects are often not appreciated by prescribing doctors. Another interesting phenomenon that is common in DLB but rare in AD is rapid eye movement sleep behavior disorder. There are other clinical aspects of DLB that distinguish it from AD. In general, the profile on neuropsychological testing is different. AD patients have cortical abnormalities, that is, problems involving language or praxis, usually both. They have difficulty naming things, understanding complex sentences, writing grammatically correct sentences, or performing tasks such as copying figures, or performing gestures such as saluting or mimicking brushing the teeth, that they are fully capable of doing, but simply cannot marshal the correct ‘motor program’ to perform the activity. DLB patients have a profile that is the same as those with PD dementia. In AD, patients fail to lay down a memory trace when they are asked to remember something. Thus, once the memory is lost, it can never be retrieved. In DLB, the memory trace is generally registered, but the patient has difficulty accessing it, so that with appropriate prompts, memories can often be resurrected. DLB patients manifest ‘executive dysfunction’ as their primary problem. They have fewer problems with language, for example, but have trouble ‘multitasking’, even early on. They have difficulty planning and, just as in PD, have difficulty doing two or more things at the same time. Unfortunately, the overlap in testing between the two syndromes is large enough that the neuropsychologist often cannot distinguish them. DLB patients also have more depression and autonomic dysfunction.

Finally, people with DLB occasionally have episodes of unresponsiveness. These have not been well characterized and even authorities are not certain about the clinical spectrum of these spells or their pathophysiology. It is unknown what percentage of DLB patients have these spells. Patients have spells of appearing to be asleep with their

eyes open. They cannot be aroused, yet have no focal signs to suggest brainstem ischemia. They show no signs of seizure, such as stiffness, clonus, twitching or automatisms. Their importance in the clinical picture lies primarily in their recognition, so that after a few spells have been appropriately evaluated for seizure, cerebral ischemia, cardiac arrhythmia and hypotension, the family can be counseled to simply wait the spells out and not go to the emergency department. The spells also help with the diagnosis, since these are not part of the typical AD picture.

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Treatment for the dementia is with the same drugs that are used in AD. Although there is a larger acetylcholine deficit in DLB than in AD, the improvement from rivastigmine, the only drug approved in the USA for this purpose, is about the same as in AD [10]. In general, rivastigmine produces little effect, but in some cases it is clinically useful. It may make tremor worse but is generally well tolerated. Memantine, a glutamate antagonist has also been reported to be useful for the dementia, but not the motor dysfunction [11]. The parkinsonism that usually accompanies the dementia tends to be more symmetric, has less tremor and is less responsive to PD medications than idiopathic PD. This is partly owing to the earlier development of behavioral side effects of the drugs that limit the doses, but the actual motor benefits also seem to be less. One general rule to always follow in treating DLB patients for their motor function is that common experience has taught us that patients who do not respond to L-dopa will not respond to dopamine agonists, which are much more likely to induce or worsen hallucinations and delusions. Thus, if one is going to attempt to treat the movement disorder, L-dopa should be employed, starting at a low dose with slow increases. The upper limit of the dose is determined by the motor response and the drug side effects. Many authorities suggest a ceiling dose of 1 g of L-dopa/day, but there are no studies to support this and I generally do not go higher than 600–750 mg/day.

The behavioral problems that occur in DLB tend to be different than those in AD, but there can be a great overlap. Hallucinations are far

more common in DLB, but wandering, potentially harmful and inappropriate behaviors and aggression are far less common. The hallucinations and delusions may respond to antipsychotic drugs but none are approved for this purpose because studies have not reliably demonstrated significant benefit. In PD patients with psychotic symptoms, there is good evidence that clozapine, in very low doses may be very helpful and that quetiapine is well tolerated in terms of motor function, but may not work well for the psychosis. Both drugs are sedating and may exacerbate orthostatic hypotension. There is a lot of experience, only some of it published, that all the other antipsychotic drugs, including all the other atypicals, are frequently associated with motor worsening and should be avoided unless quetiapine and clozapine have failed, and then should be given at very low doses [12]. One of the cardinal features of DLB is increased sensitivity to the motor side effects of antipsychotic drugs. However, it should be noted that many AD patients, especially late in their course, also develop parkinsonism and may also be very sensitive to the extrapyramidal side effects of the antipsychotics.

The genetics of DLB are unknown, whereas there is much genetic data on AD, which seems to have a much higher inheritance pattern, an important fact that DLB families often like to hear, although further research may change opinion on this [13].

The Lewy Body Dementia Association is a great source of information for patients and doctors and has a very useful website.

Summary

Dementia with Lewy bodies is either the second or third most common cause of dementia in the western world. It is often mistaken early on for AD but has notable differences, particularly parkinsonism, extreme sensitivity to antipsychotic drugs, visual hallucinations, depression, rapid eye movement sleep behavior disorder and autonomic dysfunction. Distinguishing the various dementing illnesses may provide management benefits.

Future perspective

Although DLB is often considered to be a variant of AD, there are debates at neurological meetings as to whether PD with dementia and DLB are actually the same disorder. They are almost identical clinically and pathologically and thus it is more accurate to consider DLB a variant of PD. Thus, the future breakthroughs in AD research may be less applicable to DLB than the breakthroughs in PD.

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