Chinese expert consensus statement for diagnosis and treatment of dementia with Lewy bodies 2020

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Dementia with Lewy bodies (DLB) is the second most common type of neurodegenerative dementia, and prone to misdiagnosis and missed diagnosis in the clinic. Based on the evidence about DLB, we proposed the following recommendations on the diagnosis and management of DLB.

Epidemiology

The prevalence of DLB was 1.05% in individuals aged ≥60 years in north rural China, and the prevalence of DLB was 10.10% in the population with dementia.[1] The sex ratio (male percent/female percent) was 1.34 (51.70%/48.30%). Another research showed that patients with DLB comprised 5.60% of all dementia cases in Chinese memory clinics.[2]

Pathology and genetic characteristics

Lewy bodies (LBs) are the characteristic pathology of DLB. Two types of LBs have been identified: the brainstem (classical) type and the cortical type. A number of studies have now confirmed that ApoE4 is a genetic risk factor for DLB. Presence of *glucocerebrosidase* and *a-synuclein* mutations were also found to strongly increase the risk of developing DLB.[3]

Clinical features

Dementia, required for the diagnosis of DLB, is defined as a clinical syndrome characterized by progressive decline in performance in one or more cognitive domains, which interferes in social or occupational functioning. The impairment of attention, executive, and visuospatial function usually occurs early.

Core clinical features

Cognitive fluctuation

Cognitive fluctuation is the most classical feature of DLB affecting approximately 70% to 90% of DLB patients. The typical clinical presentation is delirium-like with frequent interruptions in awareness, which are often associated with transient episodes of confusion and communicative difficulties. The duration of these episodes may range from minutes to hours to days, and patients will dramatically recover after that.

Visual hallucination

Recurrent and vivid visual hallucinations frequently occur in 50% to 80% of DLB patients. The hallucinations typically occur at night and have been described as colorful animals or dwarves walking around in the house. These visual impairments can be accompanied by auditory and olfactory illusions.

Parkinsonism

Spontaneous Parkinsonian features, such as bradykinesia and rigidity, not due to aging, arthritis, antidopaminergic medications, or stroke, occur in about 85% to 89% of DLB patients. Rest tremor is much less frequent in DLB than Parkinson disease dementia.

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Rapid eye movement (REM) sleep behavior disorder

REM sleep behavior disorder (RBD) presents in up to 80% of DLB patients. It is a parasomnia manifested by recurrent dream enactment behaviors associated with an absence of normal REM sleep atonia.[4]

Supportive clinical features

Psychiatric symptoms

Psychiatric symptoms include behaviors and mood disturbance like depression, anxiety, apathy, delusions, agitation, and paranoia, some of which increase with the progression of dementia. Paranoid delusions and thief delusions are not specifically associated with DLB.[5] Capgras syndrome, a form of misidentification delusion that is characterized by the fixed false belief that a familiar person has been replaced by an imposter, sometimes occurs in patients with DLB.[6] Severe antipsychotic sensitivity is recommended as supportive features in the diagnosis of DLB.

Autonomic dysfunctions

Autonomic dysfunctions, such as orthostatic hypotension (OH), constipation, urinary incontinence, drooling, excessive sweating, and erectile dysfunction, occur in 30% to 50% of DLB patients and are commonly present in DLB as early as 5 years prior to diagnosis. The recurrent falls and transient episodes of unconsciousness are also related to OH.

Hypersomnia

Sleep disturbance, including insomnia and hypersomnia, was common in DLB. The Lewy pathology was related to the excessive daytime sleepiness in neocortical regions.

Hyposmia

Hyposmia can develop several years prior to the onset of cognitive symptoms in DLB than Alzheimer's Disease (AD).[7] Hypotheses are available to support the view that the process of α-Syn deposition may occur earlier in the olfactory bulb than that in the neocortex.

Biomarkers

Indicate biomarkers

(1) DLB has reduced dopamine transporter (DAT) uptake in basal ganglia demonstrated by single-photon emission computed tomography (SPECT) or positron emission tomography (PET) imaging. DAT-PET and DAT-SPECT are recommended for the differentiation of DLB from AD (Ia, A).
(2) Postganglionic sympathetic nerve is affected by Lewy-related pathology in DLB; thus, there is reduced uptake on ^{123}I-meta-iodobenzylguanidine (MIBG) myocardial scintigraphy. Combination of DAT SPECT and MIBG myocardial scintigraphy enabled more accurate differentiation between DLB and AD by 96% and 90%.[8]

MIBG scintigraphy is recommended for the differentiation of DLB from non-DLB dementia (Ia, A).
(3) Polysonography (PSG) is a reliable method used to detect the REM sleep without atonia, which is a necessary diagnostic criterion of RBD. PSG is recommended to confirm RBD in DLB (Ib, A).

Supportive biomarkers

DLB is associated with a relative preservation of temporal lobe structures. The low uptake on SPECT/PET perfusion/metabolism scan, reduced occipital activity, and the posterior cingulate island sign on fluorodeoxyglucose (FDG)-PET imaging were supportive biomarkers of DLB. Prominent posterior slow-wave electroencephalogram (EEG) activity with periodic fluctuations in the pre-alpha/theta range may discriminate DLB from AD at the earliest stages of dementia.

Diagnosis

The flowchart for diagnosis of DLB uses the updated fourth consensus report of the DLB consortium as shown in Figure 1.

Treatment

Nonpharmacologic interventions

Nonpharmacologic interventions include physical therapy, occupational therapy, exercise, social interaction, cognitive therapy, mindfulness, behavioral therapy, bright light therapy, environment modification, music therapy, and other alternative therapies.

Pharmacological interventions

Cognitive symptoms

Reduced choline acetyltransferase activity is a feature of DLB. Donepezil and rivastigmine are both first-line treatments for the improvement of cognitive function in DLB (Ia, A). Memantine (IIa, B) and galantamine (IIIb, B) are second choice for the treatment of cognitive function in patients with DLB.

Neuropsychiatric symptoms

Donepezil and rivastigmine are both recommended to relieve behavior and psychological symptoms of dementia (BPSD) like apathy, depression, delusion, and hallucinations resulting from DLB (Ia, A). Memantine has been proven to significantly improve the behavioral and psychotic symptoms in DLB (Ia, A). Antipsychotic drugs are not recommended as first-line treatments for BPSD of DLB due to their high prevalence of side effects. Quetiapine is IIIb level evidence and B level recommendation, while olanzapine and risperidone are recommended as C level and clozapine is recommended as D level. selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SSNI) should be prescribed by specialists and are categorized under D level recommendation.
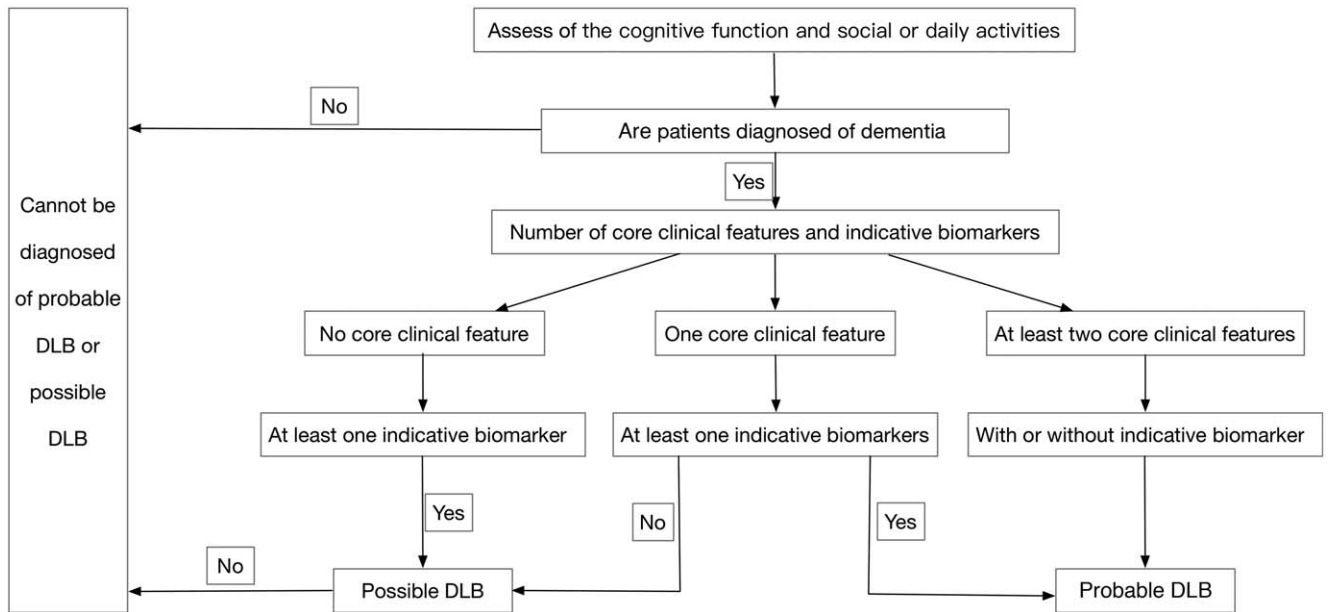
Figure 1: The flowchart for diagnosis of DLB. DLB: Dementia with Lewy bodies.

Motor symptoms

Levodopa using for motor symptoms in DLB has IIb level evidence and is recommended as B level recommendation. Although zonisamide researches showed IIIb level evidence and we recommend it as B level for the side effect seems slight.

RBD and sleep disturbances

Clonazepam can benefit RBD symptoms in DLB with IIIa level evidence B level recommendation. Non-benzodiazepines are D level recommendation for the negative effects while DLB patients with sundowning symptom can use ramelteon as IIIb level evidence and B level recommendation.

Autonomic dysfunctions

The autonomic symptoms in patients with DLB have been associated with more rapid disease progression and shorter survival. However, to date, no evidence-based treatment has been established for their treatment. Midodrine, droxidopa, and fludrocortisone can be used to DLB with sever OH with V-level evidence and D level recommendation.

Prognosis

Patients with DLB frequently have a poor prognosis as a result of severe complications, with a disease course of 5 to 10 years. DLB patients with non-amnestic cognitive impairments (eg, deficits in attention, visuospatial, and executive function) lived slightly longer (a median of 9 months longer) than DLB patients with amnestic cognitive impairments.

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