Identifying Dementia with Lewy Bodies

Albert Simon DHSc, MEd., PA-C
Professor and Chair
Department of Physician Assistant Sciences

Much of the information in the presentation was taken or modified from UptoDate and emedicine

Outline

- Part 1 Overview of dementia
- Part 2 Focus on Lewy Body Dementia

Objectives

- 1. Define dementia
- 2. Outline the pathogenesis of Dementia with Lewy Bodies (DLB)
- 3. List the clinical manifestations and differentiate common types of dementia
- 4. Outline the approach to treatment of DLB
- 5. Identify effective screening strategies to identify dementia

Overview of Dementia

What is Dementia?

- Dementia is a disorder that is characterized by a decline in cognition involving one or more cognitive domains (learning and memory, language, executive function, complex attention, perceptual-motor, social cognition). The deficits must represent a decline from previous level of function and be severe enough to interfere with daily function and independence.

Oh No DSM-5!

Now called

- Major Neurocognitive Disorder
- Also Category of Minor Neurocognitive Disorder

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). American Psychiatric Association, Arlington 2013

Major NCD

- Significant Cognitive Decline
- Interfere with independence
- Not due to delirium
- Not due to other mental disorder

Neurocognitive Disorders of the DSM-5
http://sgec.stanford.edu/content/dam/sm/sgec/documents/resources/dementia_and_caregiving/1_DiagnosisRosenDSM5NCD_AR4.pdf

Mild Neurocognitive Disorder

- Moderate Cognitive Decline
- NOT Interfere with independence
- Not due to delirium
- Not due to other mental disorder

Neurocognitive Disorders of the DSM-5
http://sgec.stanford.edu/content/dam/sm/sgec/documents/resources/dementia_and_caregiving/1_DiagnosisRosenDSM5NCD_AR4.pdf

Delirium

- Rapid Onset in hours to days
- Linked to Medical Condition
- Substance Intoxication/Withdrawal, Medications, other causes
- May resolve completely

Neurocognitive Disorders of the DSM-5
http://sgec.stanford.edu/content/dam/sm/sgec/documents/resources/dementia_and_caregiving/1_DiagnosisRosenDSM5NCD_AR4.pdf

Difference between DSM 4 and DSM 5

- The DSM-5 definition differs substantively from prior versions
  - cognitive domains have been renamed and expanded to include social cognition and complex attention
  - memory dysfunction has been deemphasized, now all six cognitive domains given equal weight in the criteria for diagnosis.
- This change reflects that other forms of dementia may not have met criteria for dementia given that in these forms memory function may have been largely preserved

Siberski, J. Dementia and DSM-5, Changes, Cost and Confusion Aging Well Vol 5 No.6 p. 12 2017

Difference from Mild Cognitive Impairment

- Mild cognitive impairment (MCI) is defined by the presence of memory difficulty and objective memory impairment but preserved ability to function in daily life.
- Patients with MCI are at increased risk of dementia.
- This term somewhat subsumed under Minor Neurocognitive Disorder

Siberski, J. Dementia and DSM-5, Changes, Cost and Confusion Aging Well Vol 5 No.6 p. 12 2017

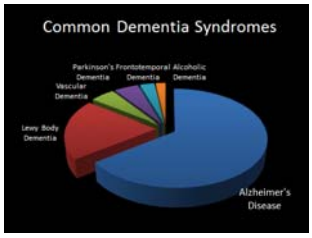
Burden of Dementia

- Overall aging of population
- Over 5 million Americans with Dementia as of 2012
- We must prepare for dealing with increasing numbers
- New pharmacologic agents may offer hope in the future

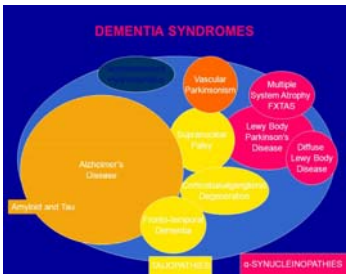
Alzheimer's Association. 2012 Alzheimer's disease facts and figures

Major Dementia Syndromes

- Alzheimer disease (AD) (60-80%)
- Dementia with Lewy bodies (DLB) (7-30%)
- Frontotemporal dementia (FTD)
- Vascular (multi-infarct) dementia (VaD)
- Parkinson disease with dementia



The Coming Alzheimer's Epidemic, the Cholinergic Hypothesis, and Nerve Growth Factor Gene Therapy https://neuroamer.com/2014/10/07/the-coming-alzheimers-epidemic-and-the-cholinergic-hypothesis/



The Dementias William S. Woodfin, M.D. Neurology Specialists of Dallas Clinical Assoc. Prof. of Neurology UT Southwestern Medical School.

General Risk Factors for Dementia

- Age
- Genetic Factors
- Mild Cognitive Impairment
- Hemorrhagic or Ischemic stroke
- Cardiometabolic factors (BP, DM, BMI, Cholesterol, Smoking, A.fib)
- Sedentary Life Style

Uptodate, Evaluation of cognitive impairment and dementia

Approach to the Patient with Suspected Dementia

- Concentrate on History and Physical Examination
- Selected laboratory and imaging workup on a case by case basis

History and Physical Examination

- History
  - Often c/o memory loss reported by spouse or significant other
  - Focus Hx on acquired, progressive cognitive impartment and behavioral change
  - Drug hx (especially analgesics, anticholinergics, psychotropic medications, and sedative-hypnotics)
  - Usually need longer than initial appointment (interview family members)

Uptodate, Evaluation of cognitive impairment and dementia

History and Physical Exam

- Physical exam
  - Look for evidence of undiagnosed medical problems (e.g. Vit B 12 def etc)
    - focal neurologic deficits to suggest stroke
    - Bradykinesia, cogwheel rigidity, tremor or other evidence of Parkinson disease
  - Complete neurologic exam and cognitive testing
    - Mini mental status exam
    - Mini-cog

http://emedicine.medscape.com/article/1135041-clinical#b3

Laboratory and Imaging Studies

- American Academy of Neurology recommends screening of hypothyroidism and Vitamin B 12 deficiency
- No evidence to support "routine" laboratory tests (e.g. CBC, CMP)
- Routine genetic testing not recommended
- AAN recommends neuroimaging with either a non-contrast head CT or MRI but those in family or general IM practice may relay on their knowledge of the patient in lieu of ordering neuroimaging initially
- Some recommend ordering neuroimaging when it may place family members at ease

Knopman DS, DeKosky ST, Cummings JL, et al. Practice parameter: diagnosis of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2001; 56:1143.

Focus on Lewy Body Dementia

The Basics of Lewy Body Dementia

DLB is a disease associated with abnormal deposits of a protein called alpha-synuclein in the brain.

These deposits, called Lewy bodies, affect chemicals in the brain whose changes, in turn, can lead to problems with thinking, movement, behavior, and mood. LBD is one of the most common causes of degenerative dementia, after Alzheimer's disease

https://www.nia.nih.gov/alzheimers/publication/lewy-body-dementia/basics-lewy-body-dementia

The Basics of Lewy Body Dementia

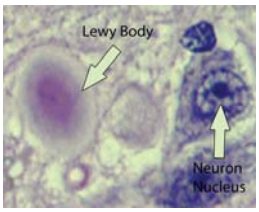
- In addition to dementia, distinctive clinical features include: visual hallucinations, parkinsonism, cognitive fluctuations, dysautonomia, sleep disorders, and neuroleptic sensitivity

http://www.nia.nih.gov/alzheimers/publication/lewy-body-dementia/basics-lewy-body-dementia

Frederic Heinrich Lewy (1885-1950)

- Describe “neuronal inclusion bodies” associated with Parkinson Disease
- His findings were first published in *Handbook of Neurology* in 1912
- C. Tretiakoff who was the first to ascribe the name "Corps de Lewy" or "Lewy bodies" to the inclusions in 1919

What are Lewy Bodies?

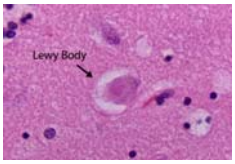


- Lewy bodies are cytoplasmic eosinophilic masses made up of alpha synuclein and other proteins
- Alpha-synuclein is a normal synaptic protein that may play a role in vesicle production.
- An aggregated and insoluble form of alpha-synuclein is a major component of Lewy bodies. The mechanism underlying the accumulation of alpha-synuclein is not well understood

Uptodate.Epidemiology, pathology, and pathogenesis of dementia with Lewy bodies

Pathogenesis

- In the healthy brain, alpha-synuclein plays a number of important roles in neurons, especially at synapses, where cells communicate with each other.
- In LBD, alpha-synuclein forms into clumps inside neurons
- This process causes neurons to work less effectively and, eventually, to die. The activities of brain chemicals important to brain function are also affected.
- The result is widespread damage to certain parts of the brain and a decline in abilities affected by those brain regions.



NIH, Lewy Body Dementia: Information for Patients, Families, and Professionals

LBD Effects Different Areas of the Brain

- the cerebral cortex, (information processing, perception, thought, and language)
- the limbic cortex, (emotions and behavior)
- the hippocampus, (memories)
- the midbrain, including the substantia nigra, (movement)
- the brain stem, (sleep and maintaining alertness)
- brain regions important in recognizing smells (olfactory pathways)

NIH, Lewy Body Dementia: Information for Patients, Families, and Professionals

Is this one disease?

What Is Lewy Body Dementia Lewy Body Dementia Association

Is this one disease?

- DLB may represent several diseases with the shared common finding of cortical Lewy bodies, or is it a single disease with a spectrum of additional pathological features?
- Risk factors for DLB appear to overlap with many of the known risk factors for both Alzheimer disease and Parkinson disease.
- Amyloid plaques which are usually associated with AD are common in DLB but they are usually less severe than in AD
- Neurofibrillary tangles, a hallmark lesion for AD, are usually few or absent in DLB but tangles can occur with Lewy bodies in the same cell
- Relationship between LBD and PDD

Uptodate, Clinical features and diagnosis of dementia with Lewy bodies

LBD vs PDD

- *Using the "one-year rule"*
  - *dementia with Lewy bodies,* in which cognitive (thinking) symptoms appear within a year of movement problems
  - *Parkinson's disease dementia,* in which cognitive symptoms develop more than a year after the onset of movement problems
- Largely arbitrary since disease progression is variable.
- If dementia occurs in a patient with a clear history of Parkinson disease that has existed for more than a year likely PDD vs LBD
- Other clinical and laboratory features may help to distinguish but still some grey areas between these conditions

Uptodate, Clinical features and diagnosis of dementia with Lewy bodies

Genetic Factors

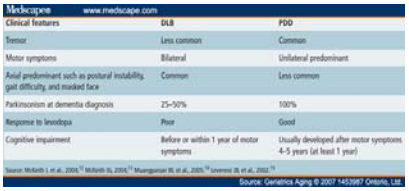
- Studies of monozygotic twins shows that DLB is generally discordant pointing us to conclude that environmental or other factors play an important role in the pathogenesis of DLB

Clinical Manifestations

- Cognitive impairment
- Visual hallucinations
- Parkinsonism like symptoms (more bilateral than Parkinson disease)
- REM sleep behavior disorder (hand gestures, violent thrashing)
- Neuroleptic sensitivity (Can be severe to antipsychotics)
- Repeated falls (may be related to orthostasis)
- Autonomic dysfunction (urinary incontinence, constipation etc)
- Systematized delusions(ie caregiver is an imposter)
- Depression

http://emedicine.medscape.com/article/1135041-overview

Clinical Manifestations



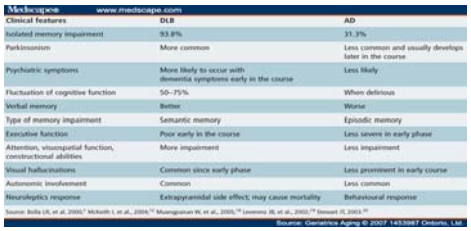
Medscape www.medscape.com

Clinical features	DLB	PDD
Tremor	Less common	Common
Motor symptoms	Bilateral	Unilateral predominant
Axial predominant such as postural instability, gait difficulty, and masked face	Common	Less common
Parkinsonism at dementia diagnosis	25–50%	100%
Response to levodopa	Poor	Good
Cognitive impairment	Before or within 1 year of motor symptoms	Usually developed after motor symptoms 4-5 years (at least 1 year)

Source: McKeith I, et al., 2004;[1] McKeith IG, 2004;[2] Muangpaisan W, et al., 2005;[3] Levenmo JB, et al., 2002.[4]

Source: Geriatrics Aging © 2007 1453987 Ontario, Ltd

Clinical Manifestations



Medscape www.medscape.com

Clinical features	DLB	AD
Isolated memory impairment	93.8%	31.3%
Parkinsonism	More common	Less common and usually develops later in the course
Psychiatric symptoms	More likely to occur with dementia symptoms early in the course	Less likely
Fluctuation of cognitive function	50–75%	When delirious
Verbal memory	Better	Worse
Type of memory impairment	Semantic memory	Episodic memory
Executive function	Poor early in the course	Less severe in early phase
Attention, visuospatial function, constructional abilities	More impairment	Less impairment
Visual hallucinations	Common since early phase	Less prominent in early course
Autonomic involvement	Common	Less common
Neuroleptics response	Extrapyramidal side effect; may cause mortality	Behavioural response

Source: Bolla LR, et al. 2000;[7] McKeith I, et al., 2004;[1] Muangpaisan W, et al., 2005;[3] Levenmo JB, et al., 2002;[4] Stewart JT, 2003.[8]

Source: Geriatrics Aging © 2007 1453987 Ontario, Ltd

Diagnosis of DLB

- First establish dementia (refer to earlier section)
- Radiologic criteria (MRI and CT) most helpful earlier in the disease
- Largely based on history and physical findings along with screening tools.
- Consider referral to neurologist experienced in diagnosis of LBD

Uptodate, Clinical features and diagnosis of dementia with Lewy bodies

Clinical and radiologic features of dementia with Lewy bodies (DLB)

	Frequency in DLB (percent)*
Central feature (essential for the diagnosis)¶	
Progressive cognitive decline, dementia	100
Core features (two features essential for diagnosis of probable DLB, one for possible DLB)¶	
Fluctuating cognition	80-90
Recurrent well-formed, detailed visual hallucinations	50-75
Spontaneous features of parkinsonism	80-90
Suggestive features (one suggestive feature with one core feature may diagnose probable DLB, one or more suggestive features may diagnose possible DLB)¶	
REM sleep disorder	85
Severe neuroleptic sensitivity	30-50
Low dopamine transporter uptake in basal ganglia on SPECT or PET	
Supportive features (common features with undetermined diagnostic specificity)¶	
Repeated falls	35
Syncope or transient loss of consciousness	
Severe autonomic dysfunction	
Hallucinations in other modalities	20
Systematized delusions	50-75
Depression	30-40
Relative preservation of medial temporal lobe on MRI or CT	
Generalized low uptake on SPECT or PET perfusion imaging with reduced occipital activity	
Abnormal (low uptake) MIBG myocardial scintigraphy	
Prominent slow wave activity and temporal lobe transient sharp waves on EEG	
Conflicting features (features which make DLB less likely)¶	
Cerebrovascular disease evidenced by focal neurologic signs or neuroimaging	
Other physical illness or brain disorder which is consistent with some or all of clinical features	
First appearance of parkinsonism at late stage (severe) dementia	
Temporal sequence (feature which distinguishes DLB from Parkinson disease dementia)¶	
Dementia should occur before or concurrently with onset of parkinsonism	

* References for frequency provided in text.
¶ Consensus criteria of the third report of the DLB consortium. McKeith IG, Dickson DW, Lowe J, et al. Diagnosis and management of dementia with Lewy bodies: third report of the DLB Consortium. Neurology 2005; 65:1863.

UpToDate

Diagnosis

- Lewy Body Composite Risk Score (James E. Galvin, M.D., M.P.H)
- Study 256 patients using risk assessment tool to improve diagnosis
- Administration takes only about 3 minutes
- Used in conjunction with standard history and physical exam (neurologic exam)

IMPROVING THE CLINICAL DETECTION OF LEWY BODY DEMENTIA WITH THE LEWY BODY COMPOSITE RISK SCORE Alzheimers Dement (Amst). 2015 Sep 1;1(3):316-324

Lewy Body Dementia Risk Assessment

Table 1

Lewy body composite risk score

Please rate the following physical findings being present or absent for the past 6 mo and symptoms as being present or absent for at least 3 times over the past 6 mo.	
Does the patient...	Yes No
Have slowness in initiating and maintaining movement or have frequent hesitations or pauses during movement?	
Have rigidity (with or without cogwheeling) on passive range of motion in any of the 4 extremities?	
Have a loss of postural stability (balance) with or without frequent falls?	
Have a tremor at rest in any of the 4 extremities or head?	
Have excessive daytime sleepiness and/or seem drowsy and lethargic when awake?	
Have episodes of illogical thinking or incoherent, random thoughts?	
Have frequent staring spells or periods of blank looks?	
Have visual hallucinations (see things not really there)?	
Appear to act out his/her dreams (kick, punch, thrash, shout or scream)?	
Have orthostatic hypotension or other signs of autonomic insufficiency?	
Total score	

Copyright 2013 *The Lewy Body Composite Risk Score* James E. Galvin, MD, MPH

http://www.2ti.es/2015/10/test-lbcrs-de-galvin-diagnosticar-demencia-con-cuerpos-de-lewy/

THE LEWY BODY COMPOSITE RISK SCORE

	DBL vs AD	DBL vs Any Dementia
Sensitivity	94.2	97.9
Specificity	78.2	86.1

http://med.fau.edu/research/Lewy%20Body%20Composite%20Risk%20Score%20Form%20and%20Instructions.pdf

Treatment

- No treatment with disease modifying effects!
- General Tx
  - Behavior modifying therapy (Pet therapy, aromatherapy, Massage therapy)
  - Cholinesterase Inhibitors (ie Rivastigmine, Donepizil)
  - Avoid Neuroleptics if at all possible
  - REM sleep disorders (melatonin)
  - Parkinson Sx (tx similar to primary Parkinson disease)

Uptodate, Prognosis and treatment of dementia with Lewy bodies

Resource for patients and families

https://www.lbda.org

Lewy Body Dementia Association, Inc.

https://www.nia.nih.gov/alzheimers/publication/lewy-body-dementia/basics-lewy-body-dementia