MOVEMENT DISORDERS AND DEMENTIA

FOCUS ON DEMENTIA WITH LEWY BODIES

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DEMENTIA

- de·men·tia
- dəˈmen(t)SH(ē)ə/
- noun
- noun: dementia
- a chronic or persistent disorder of the mental processes caused by brain disease or injury and marked by memory disorders, personality changes, and impaired reasoning.
- synonyms: mental illness, madness, insanity, derangement, lunacy
- "her failing memory is not necessarily a symptom of dementia"
DEMENTIA

LATIN

demens

dement-

out of one's mind

late 18th century

Mentions

1800 1850 1900 1950 2010
PROGRESSIVE NATURE OF DEMENTIAS
2015 ALZHEIMER’S DISEASE FACTS AND FIGURES

1 in 3 seniors dies with Alzheimer’s or another dementia.

6

Alzheimer’s disease is the 6th leading cause of death in the United States.

Almost two-thirds of Americans with Alzheimer’s disease are women.

Every 67 seconds, someone in the United States develops the disease.

Only 45% of people with Alzheimer’s disease or their caregivers report being told of their diagnosis.

More than 90% of people with the four most common types of cancer have been told of their diagnosis.

By 2050, these costs could rise as high as $1.1 trillion.

In 2015, Alzheimer’s and other dementias will cost the nation $226 billion.
DEMENTIA – BUPA DATA

People living with dementia around the world

- Americas: 29.9m (2050)
  - A: 15.8m (2030), 9.4m (2015)
  - C: 15.8m (2050)
  - D: 4.6m (2015)

- Africa: 18.6m (2050)
  - I: 7.0m (2030)

- Europe: 67.2m (2050)
  - B: 18.6m (2050)
  - E: 10.5m (2015)

- Asia: 131.5m (2050)
  - J: 38.5m (2030)
  - K: 22.9m (2015)

- World: 131.5m (2050)
  - L: 74.7m (2030)
  - M: 46.8m (2015)
MOVEMENT DISORDERS AND DEMENTIA

- Parkinson’s disease
- Dementia with Lewy Bodies
- Atypical Parkinsonism
- Lewy body variant of Alzheimer’s disease
- Vascular dementia
- Tau disorders – Mixed pathology
- Huntington’s disease
- Prion disorders
- Other rare causes
DEMENTIA WITH LEWY BODIES

• Second most common type of Degenerative dementia following Alzheimer’s.

• 4.2 percent of all dementias in the community and 7.5 percent of all those under care at a facility.

• Significant concern for overlap with Parkinson’s disease and other related conditions.

• Important to distinguish this disorder from other categories by expert neurological evaluation.
prevalence of 1175 to 13,800 per 100000, in patients over 65. More common in the Midwest and the Northeast

- PD Dementia: 2.5 per 100000 person-years
- DLB: 3.5 per 100000 person-years
- Combined DLB plus PDD: 5.9 per 100000 person-years

Ref: Incidence of Dementia with Lewy Bodies and Parkinson's Disease Dementia
Rodolfo Savica, Brandon R. Grossardt, et al
IMPORTANT REMINDER

- Alzheimer’s disease
- Vascular Brain injury
- Lewy body disease
DEMENTIA WITH LEWY BODIES

• CLINICAL FEATURES
  • Dementia which interferes with normal social and occupational function. *(central feature).*
  • Impairments of attention, executive and visuospatial function *(central feature).*

• CORE FEATURES
  • Fluctuating cognition with pronounced variation in attention and alertness
  • Visual hallucinations – Detailed and recurrent.
  • Parkinsonism on exam
DEMENTIA WITH LEWY BODIES

- SUGGESTIVE FEATURES
- REM sleep behavior disorder
- Severe sensitivity to neuroleptic agents
- Low uptake on DaT scan or PET
- Criteria must be met for diagnosis
- PROBABLE DLB: One core plus one other core or suggestive feature
- POSSIBLE DLB: One core and no suggestive features, or one or more suggestive features.
DEMENTIA WITH LEWY BODIES

• SUPPORTIVE FEATURES
• Falls, syncope
• Autonomic dysfunction
• Hallucinations
• Systematized delusions
• Depression
• Relative preservation of temporal lobe on CT or MRI
• Low uptake on SPECT or PET perfusion scan with reduced occipital activity
• Abnormal MIBG myocardial scintigraphy
• EEG slow waves with transient temporal sharp waves.
Donaghy and McKeith; The clinical characteristics of dementia with Lewy bodies and a consideration of prodromal diagnosis. Alzheimer's Research and Therapy 6(4):46 · July 2014
Braak STAGES FOR PARKINSONS

Braak stages 1 and 2
Autonomic and olfactory disturbances

Braak stages 3 and 4
Sleep and motor disturbances

Braak stages 5 and 6
Emotional and cognitive disturbances

Via olfactory bulb
Via vagus nerve
Premotor symptoms
Motor symptoms
Brainstem Lewy body
Cortical Lewy body
PATHOLOGY OF PD
LEWY BODIES
PLAQUES AND TANGLES IN ALZHEIMERS
VASCULAR BRAIN INJURY
SYNUCLEINO Pathy

• Disorder where we find problems with a protein called alpha synuclein
• Alpha synuclein is mis-folded and found in lewy bodies
• Synuclein is present diffusely in the Brain, smaller amounts in heart, muscles and other areas
• Of interest to us in Parkinson’s disease, MSA, DLB and other conditions.
SYNUCLEIN – THE DAMAGE

Synuclein: Abnormal folding

Misfolded proteins → Oligomers → Fibrils (β-pleated sheet) → Lewy bodies

Lewy neurites:
- Oxidative stress
- Disruption of axonal transport
- Protein sequestration
- Mitochondrial dysfunction
- Synaptic dysfunction
- Inhibition of ubiquitin/proteosome system

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Unraveling the Mystery of Alpha-Synuclein
A perspective by Dennis J. Selkoe, M.D.
DEMENTIA WITH LEWY BODIES

DIAGNOSIS

Evaluation by a neurologist

Assessment of clinical criteria

Laboratory studies: Include CBC, Chemistry TSH, B12, Folate, RPR, and HIV as needed.

MRI BRAIN

DaT scan

Neuropsychological testing by an expert neuropsychologist
PET SCAN IN PATIENT WITH PD

Normal

Parkinson

Pre
DaT scan in PD
TREATMENT

Balanced approach to care
Co-morbid factors:
General health is very important
Make sure we control infections – UTI
Electrolyte abnormalities
Dehydration
Depression
TREATMENT

Motor symptoms
Primary choice is levodopa
Other Parkinsons drugs cause hallucinations.

Sleep disorders
Clonazepam for anxiety and REM behavior disorder
Sleep study is important
TREATMENT

General issues
Constipation
Poor appetite
Address mobility and safety
Care giver also needs training, compassion and attention to respite.
Therapy at home or facility
TREATMENT

Medications used

1. Carbidopa levodopa
2. Clonazepam or other agents for sleep disorder
3. Cholinesterase inhibitors such as donepezil, galantamine, rivastigmine
4. Memantine has limited data and can cause fluctuations
Treatment

ANTIPSYCHOTICS
Quetiapine (seroquel)
Aripiprazole (abilify)
Clozapine (clozaril)

Limited data on Nuplazid (pimvanserin) in DLB as primary indication. Studied and approved for Parkinson’s disease hallucinations and delusions.
DEPRESSION AND DEMENTIA

Commonly seen in patients with DLB
Especially when they have insight into their disorder.

Treat aggressively with antidepressants.
Preference for Venlafaxine, paroxetine and Fluoxetine based on literature

Psychiatrist familiar with Parkinson’s disease is important for care.
CARE TEAM FOR DLB

Primary care MD
Neurologist
Psychiatrist
Caregiver
Therapists
Counselors
And community support for caregiver and patient
DLB resources

https://www.lbda.org

LEWY BODY DEMENTIA ASSOCIATION
FUTURE

Studies looking at biological markers of disease
Prodromal Lewy body disease (catch it early)
Further work into pathophysiology
Treatment options including work on leukemia drug is still preliminary.
Learn from yesterday, live for today, hope for tomorrow. The important thing is not to stop questioning.

*Albert Einstein*