Other Dementias

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[Diffuse Lewy Body Disease 1](#_Toc5998185)

[Pathogenesis, Pathophysiology, Pathology 1](#_Toc5998186)

[Clinical Features 2](#_Toc5998187)

[Management 3](#_Toc5998188)

[Vascular Dementia 3](#_Toc5998189)

[Causes and Types 3](#_Toc5998190)

[Pathology 3](#_Toc5998191)

[Clinical Features 4](#_Toc5998192)

[Diagnosis 5](#_Toc5998193)

[Treatment 6](#_Toc5998194)

Diffuse Lewy Body Disease

Pathogenesis, Pathophysiology, Pathology

Lewy bodies - intracytoplasmic, single or multiple, eosinophilic, round-elongated inclusions that have **dense core** surrounded by **pale halo**.

* composed of **fine 7-8 nm straight filaments** (densely packed in core but loose at rim); immunocytochemically - neurofilament antigens, α-synuclein, ubiquitin.

Dementing disorders associated with Lewy bodies can be categorized into three groups:

1. Parkinson disease without cortical Lewy bodies or AD changes (Lewy bodies only in substantia nigra)
2. Parkinson disease with ***cortical Lewy bodies*** (**diffuse Lewy bodies disease, DLBD**)
3. Alzheimer disease with ***cortical Lewy bodies*** (**Lewy body variant of AD, LBV** – 15-30% of all AD cases).

**Lewy body-related pathology** is the second most common dementia histopathology behind AD!

i.e. Lewy bodies are found in 15-25% degenerative dementias.

* Lewy bodies, if ***present in cortex***, are invariably also ***present in brain stem***:
  1. **Lewy bodies in brain stem** (easily seen on *hematoxylin-eosin* sections) - reside in substantia nigra, locus caeruleus, and raphe nuclei.
  2. **cortical Lewy bodies** often lack surrounding halo and are more difficult to visualize (unless *immunostains for ubiquitin* are used); maximal numbers in cingulate gyrus, insular cortex, parahippocampal gyrus.

Lewy bodies:

|  |  |
| --- | --- |
| H & E stain | immunoperoxidase stain for ubiquitin |
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[Source of picture: “WebPath - The Internet Pathology Laboratory for Medical Education” (by Edward C. Klatt, MD) >>](http://library.med.utah.edu/WebPath/webpath.html" \t "_blank)

* brain is normal ÷ slightly atrophic.
* neurotransmitter deficits mostly involve **cholinergic** and **dopaminergic** systems;

**nucleus basalis atrophy** and cholinergic deficiency (LBV > DLBD) are more severe than in AD!

N.B. relationships among DLBD, AD, and Parkinson disease are debated because there is evidence to support all points of view.

Clinical Features

* mean age of DLBD onset is 57 years.
* male to female ratio 1.7:1.
* death ensues after 10-15 years.

**mixed (cortical-subcortical) dementia**

moderate÷severe **dementia** + mild÷moderate **parkinsonism**.

* literature is divided on whether parkinsonian or cognitive symptoms present first.
* **dementia**:
* multifactorial nature (presence and frequency of ***cortical Lewy bodies*** may be contributor);
* prominent visual hallucinations, paranoid delusions, illusions, and behavioral dyscontrol are characteristic clinical features;
* frequent fluctuations of behavior, cognitive ability, and level of alertness (episodic confusion and lucid intervals suggesting delirium).
* absence of severe aphasia, agnosia, apraxia.
* **parkinsonism** reflects ***basal ganglia*** & ***nigral degeneration***; subcortical degenerative changes → psychomotor slowing; i.e. bradykinesia > resting tremor.
* repeated unexplained falls occur early!

Management

Whether treatment is necessary at all, and if so, what symptoms warrant treatment?

***Treatment of dementia*** (may exacerbate parkinsonian syndrome!!!) – as in AD:

* *acetylcholinesterase inhibitors* serve as 1st-line therapy for neuropsychiatric as well as cognitive symptoms.
* patients are very sensitive to *neuroleptic* medications (exaggerated adverse responses to standard doses) - use most selective neuroleptics (risperidone, clozapine).

***Treatment of parkinsonian syndrome*** (with levodopa) may exacerbate neuropsychiatric disorder.

Nonpharmacological aspects of caregiving are similar to AD.

Vascular Dementia

* 2nd most common dementia of elderly in USA (but No.1 in Asia!)

Causes and Types

- brain injury from cerebrovascular disease:

* 1. **multiple cortical infarcts** (multiple ischemic lesions in cerebral cortex\* cumulatively result in loss of enough neurons\*\* to produce dementia) - ***multi-infarct dementia***

\*not necessarily in eloquent locations

\*\*usually destroying at least 100 ml of brain volume

N.B. many use "multi-infarct dementia" interchangeably with “vascular dementia”.

* 1. occlusive disease of small penetrating cerebral arterioles [microangiopathy] → **multiple bilateral lacunar infarcts** (small infarctions in deep hemispheric white matter**)** resulting in *état lacunaire* (***Binswanger disease, s. subcortical arteriosclerotic encephalopathy***)
  2. strategically placed **single infarct** (may cause specific cognitive deficit, aphasia, amnesia, but rarely causes dementia)
  3. cerebral **hypoperfusion** (chronic, reversible) - most experts reject such mechanism.
  4. ***amyloid angiopathy*** (not associated with dementia, but predisposes older persons to hemorrhagic lobar stroke).

Pathology

Multiple remote cystic infarcts in various locations over several years:



[Source of picture: “WebPath - The Internet Pathology Laboratory for Medical Education” (by Edward C. Klatt, MD) >>](http://library.med.utah.edu/WebPath/webpath.html" \t "_blank)

Clinical Features

Clinical features vary, but few generalizations are applicable (when compared with Alzheimer's disease):

1. **men** > women
2. often have **risk factors** (hypertension, diabetes, hyperlipidemia, cigarette smoking).
3. history of **transient ischemic attacks**
4. ***earlier age*** of onset (< 75 yrs)
5. onset may be ***abrupt***
6. **stepwise deterioration!!!** (episodes of sudden neurologic deterioration)
7. **focal neurologic signs** (limb rigidity, spasticity, hyperreflexia, extensor plantar responses, gait disturbance)
8. **pseudobulbar palsy** (emotional lability, dysarthria, dysphagia).
9. ***memory disturbance is of retrieval type*** - able to register information but difficulty spontaneously recalling it - categorical clues or multiple choices help.
10. ***shorter*** survival (after mental status changes onset).

Clinical subtypes:

**Cortical syndrome** (***multi-infarct dementia***) - abrupt onset of cognitive failure, focal sensorimotor signs, severe aphasia (when present).

**Subcortical syndrome** (***Binswanger disease***):

|  |  |
| --- | --- |
| 1. dementia of subtle onset and slow progression (vs. multi-infarct dementia) 2. bilateral pyramidal signs (lateralizing motor signs are uncommon). 3. gait imbalance (with *marche a petit pas*) 4. "frontal" abulic behavior, mildly impaired memory. 5. pseudobulbar signs, urinary incontinence. 6. associated (but not always) with severe hypertension and systemic vascular disease. | multiple areas of abnormal high signal intensity in periventricular white matter, corona radiata and lentiform nuclei (arrows). D:\Viktoro\Neuroscience\S. Symptoms, Signs, Syndromes\S10-15. Dementia, Delirium\00. Pictures\Binswanger's disease (MRI).jpg |

Diagnosis

- brain imaging (provides supporting, but not diagnostic, evidence):

* 1. focal infarctions in **strategic cortical locations**.
  2. ***Binswanger disease*** - ischemic periventricular **white matter** changes, sparing cortex and basal nuclei.

Treatment

- by **stroke prevention strategies**:

1. antihypertensives
2. cigarette cessation
3. blood cholesterol reduction
4. anticoagulants / antiplatelet therapy (aspirin, clopidogrel, ticlopidine).

Bibliography see p. S11

[Viktor’s Notes℠ for the Neurosurgery Resident](http://www.neurosurgeryresident.net/)

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