Neuropathology of Mixed Dementia

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1. Autopsy is the only way to determine the cause of dementia.

2. Common for dementia to have multiple pathologies ("mixed" dementia).

3. Autopsy plays a crucial role in diagnosis, teaching and research.
Causes of dementia

- primary neurodegenerative disease
  - Alzheimer’s disease
  - Lewy body disease
  - frontotemporal dementia

- cerebrovascular disease
- infection
- toxic/metabolic disorder
- tumor
- head trauma
Causes of Dementia

AD

LBD

VaD

other
Alzheimer’s Disease

- brain atrophy
- hippocampal atrophy
- senile plaques & neurofibrillary tangles
Lewy Body disease

Parkinson’s disease

- ↓ neurons in substantia nigra
- Lewy bodies

Dementia with Lewy bodies

- Lewy bodies in cerebral cortex
- α-synuclein

α-synuclein
Multiple infarct dementia
Causes of Dementia

- AD
- LBD
- VaD
- mixed dementia
AD and cerebrovascular disease

- both common conditions.
- several common risk factors.
- additive effect in causing dementia:
  - patients with autopsy proven AD and CVD have more severe dementia than those with pure AD.
  - patients with similar degree of dementia have fewer SP/NFT if CVD also present.
“Mixed” dementia

- coexistence of multiple pathologies.
- each pathology may be associated with dementia independently.
- each pathology judged to be of sufficient severity to contribute to dementia.
- pathologies have additive effect.
- usually AD with LB and/or CVD.
74 year old man with ↓ memory for 5 years.
visual hallucinations.
episode of right hand weakness (improved).

Pathological diagnosis = mixed dementia.
Pathological diagnosis of dementia

<table>
<thead>
<tr>
<th>Criteria 1</th>
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<tbody>
<tr>
<td>AD</td>
<td>75%</td>
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<tr>
<td>VaD</td>
<td>3%</td>
</tr>
<tr>
<td>LBD</td>
<td>9%</td>
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<tr>
<td>other</td>
<td>13%</td>
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<td>criteria 1</td>
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<td>other</td>
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<tr>
<td>mixed AD/VaD</td>
<td>20%</td>
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<td>mixed AD/LBD</td>
<td>19%</td>
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<td>mixed AD/other</td>
<td>5%</td>
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Mixed AD/VaD and mixed AD/LBD combined: 44%
Value of autopsy

- diagnosis
- teaching
- research

- family
- health care team
- students
- scientists