DEMENTIA

HIHIM 409

Definition

- Acquired generalized and often progressive impairment of cognitive function that affects the content, but not the level, of consciousness.

DSM-IV Criteria for Dementia:

1. The gradual onset and continuing decline of cognitive function from a previously higher level, resulting in impairment in social or occupational function

2. Impairment of recent memory (the inability to learn new information), and at least one of the following:
   a) Language (word-finding difficulties)
   b) Disturbances of praxis (inability to execute skilled motor activities in the absence of weakness)

3. The cognitive deficits are not due to other psychiatric disease, neurologic diseases, or systemic diseases, and the deficits do not exclusively occur in the setting of delirium

Mild Cognitive Impairment

- MMSE 24-28
- Problem with recollection
- Does not meet dementia criteria

Differential Diagnosis:

1. Alzheimer Disease (pure ~40%, + mixed~70%)
2. Vascular Disease, MID (5-20%)
3. Drugs, Depression, Delirium
4. Ethanol
5. Medical / Metabolic Systems
6. Endocrine (thyroid, diabetes)
7. Neurologic, Nutritional (other primary degenerations, etc.)
8. Tumor, Toxin, Trauma
9. Infection, Idiopathic,
10. Amnesia, Autoimmune,
Treatable causes

- ~15% of causes
- NPH
- IC mass lesion (tumor, SDH)
- B12 def.
- Hypothyroidism
- Syphilis
- Depression

Evaluation

- Good history and physical
  - Time course, associated symptoms, PMH, Drugs
  - Family Hx and good mental status examination
- CBC, chem. 18 (with electrolytes and LFTs), TFTs, B12, RPR/VDRL, ESR, ANA, RF
  - Young pts: Wilson's work-up, porphyria work-up, 24-hour urine for heavy metals, HIV, PPD, ACE level, vitamin E
- CT &/or MRI
- EEG
- EKG

Evaluation (cont.)

- Urinalysis
- LP (with cytology, AFB and fungal stains, ACE level, MS profile, etc.)
- Neuropsychological testing if trouble with diagnosis
- Arteriogram/Brain biopsy as indicated

Dementia Vs acute confusional state

<table>
<thead>
<tr>
<th></th>
<th>Acute Confusional State</th>
<th>Dementia</th>
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</thead>
<tbody>
<tr>
<td>Level of consciousness</td>
<td>Impaired</td>
<td>Not impaired, except occasionally late in course</td>
</tr>
<tr>
<td>Course</td>
<td>Acute to subacute, fluctuating</td>
<td>Chronic, usually progressive</td>
</tr>
<tr>
<td>Autonomic instability</td>
<td>Often present</td>
<td>Absent</td>
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<tr>
<td>Progress</td>
<td>Usually reversible</td>
<td>Usually irreversible</td>
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Alzheimer’s Disease (AD)
Alzheimer's Disease (AD)

Epidemiology
- Most common degenerative disease of the brain
- 10% of people over age 65 years have AD
- 20% of persons ≥ 80 years
- 30% of ≥ 90 years old
- Male = Female

Histopathology:
- Macroscopic:
  - Atrophy, mostly temporoparietal and frontal
- Microscopic:
  - Loss of neurons and synapses
  - Neurofibrillary tangles (NFTs)
  - Amyloid plaques (Neurotic plaques)
  - Granulovascular degeneration
- Chemistry:
  - Loss of neurotransmitters, especially acetylcholine (ACh)

Clinical Care Options for HIV, 1997; National Institute on Aging, 1997; American Cancer Society, 1998; American Heart Association, 1997; Post Trauma Treatment Associates, 1996.

Brain Cross-Sections

Normal

Alzheimer's
AD: a progressive CNS disorder with a characteristic pathology

Brain atrophy
Senile plaques
Neurofibrillary tangles

Katzman, 1986; Cummings and Khachaturian, 1996

Numerous tangles in hippocampus

Amyloid plaque

Tangles
Plaques

Hippocampus

Amygdala

PLASMA OF ABDOMINAL HOMOSIS IN THE DOME OF A Klucherianum to the
blee a black fibrillic mass in this crumpled image. The plaque is surrounded by a
blee of abnormal proteinaceous amyloid and degenerating spongy cells that
are fluid and fluid.
Risk factors for AD: Down’s syndrome

Strong risk factors for AD*

- Age
- Down’s syndrome
- Family history
- Certain genes associated with increased risk but do not cause AD e.g. ApoE4

Genetics

<table>
<thead>
<tr>
<th>Gene</th>
<th>Chromosome</th>
<th>Protein</th>
<th>Mutation</th>
<th>Phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>APP</td>
<td>21p11.2</td>
<td>Amyloid precursor protein</td>
<td>Various missense mutations</td>
<td>Familial Alzheimer’s disease autosomal dominant</td>
</tr>
</tbody>
</table>
| PDI  | 1q42      | Presenilin 1 (PS1) | Various missense mutations | Familial Alzheimer’s disease autosomal dominant with early onset (55-65)
| PSEN1| 1q42      | Presenilin 2 (PS2) | Various missense mutations | Familial Alzheimer’s disease autosomal dominant with early onset (65-75)
| APOE | 19p13.2   | Apolipoprotein E | ApoE4 polymorphism | Increased susceptibility to Alzheimer’s disease |
| MAPT | 17p11.2   | Unknown | Tau (21 or chromosome 21 in Down’s syndrome) | Down’s syndrome (early onset Alzheimer’s disease) |

Natural History of Alzheimer’s Disease

Clinical features of AD

- Gradual decline of intellectual function
- Poor short-term memory
- Visuospatial disorientation
- Language/speech problems — aphasia, anomia, and later echolalia, mutism
- Apraxia — dressing, idiomotor
- Personality changes: indifference, apathy
- Psychiatric: Hallucination, delusions, behavioural disturbances
- Limb rigidity, flexion posture
- Urinary and faecal incontinence
MRI: profound atrophy

Dementia with Lewy bodies

Vascular dementia

Treatment
- No cure
- Anticholinesterases
  - Tacrine, Donepezil, Rivastigmine
- Alpha tocopherol (vitamin E)
- Selegiline
- Psychotropic drugs: agitation, delusions
- Antidepressants
- Nursing home

Dementia with Lewy bodies
- Up to 20% of dementias
- Dementia (as previously defined)
- Lewy bodies diffusely through cortex
- Markedly fluctuating cognitive impairment
- Visual and/or auditory hallucinations
- Paranoid delusions
- Falls
- Extrapyramidal features: rigidity & bradykinesia
- Neuroleptic sensitivity: extrapyramidal S/Es

Vascular dementia
- Also called multi-infarct dementia (MID)
- About 15-20%
- Decline can be linear or step-wise
**Vascular dementia**

- Step-wise decline
  - uneven steps, varying plateau

**VaD -vs- AD**

- Earlier onset than AD and M > F
- Sudden onset, stepwise deterioration
- h/o high bp, strokes
- Evidence associated arteriosclerosis, eg coronary artery disease
- Focal neurological symptoms and signs
- Focal pathology on brain imaging

**Fronto-temporal dementia**

**Pick’s disease**

- Macroscopic and brain scan - atrophy only in frontal and temporal areas (until late in disease)
- Diagnosis easily missed initially
- Histopathology:
  - Pick cells
  - Pick inclusion bodies
- No amyloid plaques nor NFT
- No Rx
Fronto-temporal dementia  
Pick’s disease (cont.)
- Onset 40-60 y.o. (20-80 y. range)
- Preservation of memory until late
- Early symptoms: behavioural or psychiatric
  - Apathy, irritability
  - Loss of concern
  - Impaired judgement and insight
  - Language affected

Cretzfeldt-Jakob disease
- Transmissible: cornea transplants, intracerebral recording electrode implants, growth hormone
- Rapidly progressive dementia
- Focal involvement of the cerebral cortex, basal ganglia, cerebellum, brainstem, and spinal cord
- Etiologic agent: proteinaceous infectious particle (prion)
  - PrP^C
    - Cellular isoform
    - Mutation leads to accumulation of PrP^Sc
  - PrP^Sc

Cretzfeldt-Jakob disease (cont.)
- Dementia
- Psychiatric symptoms
- Myoclonus
- Extrapyramidal signs
- Cranial nerve palsies
- New Variant: bovine spongiform encephalopathy
  - Earlier onset (mean age, about 30 years)
  - More prolonged course (median duration over 1 year)
  - Prominent early psychiatric abnormalities, including depression and personality changes.
Creutzfeldt-Jakob disease (cont.)
- Investigation:
  - EEG: periodic sharp waves and spikes
  - Detection of PrP<sup>Sc</sup> in brain tissue
- Prognosis:
  - Invariably fatal
  - Death w/in 1 yr

NORMAL-PRESSURE HYDROCEPHALUS
- Sometimes called communicating (lateral, 3<sup>rd</sup>, 4<sup>th</sup> ventricles remain in communication) or nonobstructive hydrocephalus
- Triad
  - Dementia
  - Gait apraxia
  - Incontinence
- Idiopathic or secondary (meningitis, SAH)
- Memory defects, but rarely aphasia and agnosia

NORMAL-PRESSURE HYDROCEPHALUS (cont.)
- Weeks-months
- Gait apraxia early, with weight bearing
- Pyramidal signs
- Urinary incontinence
- Lp: normal or low opening pressure
  - Remove 30-50 cc; prognostication
- CT scan or MRI: enlarged lateral ventricles without increased prominence of cortical sulci
- Cisternography: delayed clearance
- Rx: CSF shunting; VA, VP, LP

THE END