76. Alzheimer's Disease

Etiology/Pathophysiology

- A common, relentlessly progressive form of dementia usually seen in advanced years, characterized by personality change, language dysfunction, and memory failure
- Comprises at least 50% of all cases of dementia
- Characterized by atrophy of the cerebral cortex, particularly the temporal lobes
- Neuronal loss primarily affects cholinergic neurons; associated with 50–90% reduction in choline acetyltransferase activity
- Primarily affects elderly patients; however, there is a familial form that affects younger patients
- Prevalence <1% under age 65; 30–40% of age 85 and older
- Genetic mutations have been implicated, such as apoE e4 polymorphism of the apolipoprotein gene on chromosome 19
- Histology shows neurofibrillary tangles (filaments with tau protein), neuritic plaques (core of extracellular amyloid), and granular-vacuolar degeneration

Differential Dx

- Normal cognitive aging
- Pseudodementia of depression
- Other dementing diseases (e.g., multi-infarct dementia, Pick's or Parkinson's disease, progressive supranuclear palsy, diffuse Lewy body disease, NPH)
- Metabolic and endocrine disorders (e.g., vitamin B_{12} deficiency, Wernicke's encephalopathy)
- Medication effects
- Infections (e.g., HIV, CJD, neurosyphilis, cryptococcal meningitis)

Presentation/Signs & Symptoms

- Normal consciousness is preserved
- Insidious onset of slowly progressive memory loss
- Later impairment of intellect, language, and abstract thought
- Aphasia, agnosia, and apraxia
- Loss of executive function
- Delusions and hallucinations in 20–40%
- Depression in 25%
- Extrapyramidal symptoms (rigidity, bradykinesia, or postural instability) in 60%
- Seizures in 10–20%
- Myoclonus in 10%

Diagnostic Evaluation

- History and neurologic examination including serial mental status exams and neuropsychological tests
- Definitive diagnosis can only be proven by autopsy: Neurofibrillary tangles and neuritic plaques are seen on microscopic examination
- No laboratory tests or imaging is diagnostic
- Useful tests include head CT scan or MRI (atrophy), EEG (generalized slowing), metabolic profile, thyroid function testing, vitamin B_{12} level, RPR
- Genetic testing for the apo-ε allele may identify familial cases
- CSF analysis may be indicated to exclude infectious etiologies of dementia

Treatment/Management

- There is no cure—treatment is palliative
- Eliminate all unnecessary medications, especially those with known CNS and anticholinergic effects
- Anticholinesterase inhibitors may initially slow progression of the disease (e.g., donepezil, galantamine, rivastigmine)
- NMDA receptor antagonists (memantine) is now being used
- In select cases, SSRIs and neuroleptics (e.g., seroquel, risperdal) may be tried
- Home health support and counseling for caregiver

Prognosis/Complications

- Progressive clinical course with occasional plateaus
- Duration 4–8 y, rarely as long as 20 y (mean time from diagnosis to death is 8 y)
- Eventual terminal state with mutism, incontinence, and limb contractures
- Death most often occurs due to pneumonia