Biomarkers of Alzheimer's Disease

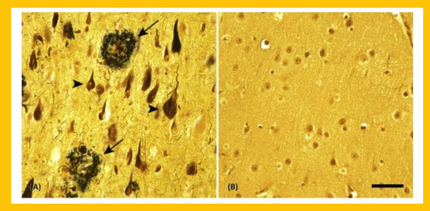
Monet Kumazawa
Masters of Pathologists' Assistant, College of Medicine, Drexel University, Philadelphia, PA, United States

DEFINING AD

- The most common type of dementia, originating as mild memory loss and resulting in progressive loss of ability to carry out daily activities.
- Grossly: enlarged ventricles, shrunken hippocampus
- Histologically: accumulation of insoluble fibrous material with extracellular amyloid and NFT (neurofibrillary tangles)
- Societally: a puzzling neurological degenerative disorder that we still have no clinical treatment for, nor an official metric for pre-clinical diagnosis

WHAT WE KNOW RIGHT NOW

- 1. Excess production, 2. Defective removal, or 3. Both
  → Accumulation of amyloid and NFT
  → CAA (cerebral amyloid angiopathy) and tauopathy
- Prion-like nature of cleavage as before seen, in:
  - Parkinson's Lewy bodies
  - ALS
  - FTLD



PATHA INVOLVEMENT

- Our goals: to determine AD before its clinical appearance, to provide guidance on preventative treatment
- Approaching neuroanatomy with our grossing skills
  → Collecting adequate specimens from patients
  → Allowing histology to reveal further information via silver stains, PAS counterstain, Alpha-synuclein stain
  → Testing, research expansion
- Along with tissue, potential use of fluids for cytology for genetic markers

"STAGING"

- A neurodegenerative disorder, not a cancer.
  → Thus, no T, nor N, nor M staging.
- Braak Staging
  - To assist with determination of pre-clinical staging
  - I and II with NFT in trans-entorhinal region of brain (medial of temporal lobe)
  - III and IV in limbic regions ex) hippocampus
  - V and VI with extensive neocortical involvement
- Thal Staging
  - Plaque formation and its location
  - 1) Neocortex 2) Hippocampus 3) Basal ganglia 4) Midbrain/medulla oblongata 5) Pons/cerebellum

ONGOING RESEARCH

- Pittsburgh B compound
  - An attempt to deter AD's definitive diagnosis occurring at autopsy
  - A radioligand: high amyloid affinity, entering BBB well enough to be visible on PET scans, rapid clearance from blood
  - Thus far, frontal retention of PIB is clinically significant
- Cleaving nature of amyloid and tau proteins, how to tackle polymorphic nature?
  - Increased difficulty of research, unable to test for infinite protein types
- Ca++ concentration monitoring, as formation of calcium-permeable membrane pores occurs
- An attempt to understand why AD is not observed in non-humans, despite our similar biological genotyping with other primates
- Prion-like nature of AB + tauopathy, and comparing AD to other neurodegenerative disorders
  - Tau involvement with stabilization of microtubules, and the turning point towards its aberrant nature
- Brain damage of NFL athletes, correlation with neurodegenerative disorders and recurrent concussions

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