Alzheimer's Disease

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Abstract

- Dementia is a group of progressive neurodegenerative brain disorders associated with signs and symptoms spanning cognitive, sensory, and psychological function. and more or less gradual erosion of mental and later physical function.[1] The risk of dementia-related mortality significantly increases with gradual loss of one's ability to perform daily activities in addition to diminished anatomical protection of one's airway.
- Neurodegenerative disorders can only be diagnosed at autopsy. Brains are fixed in formalin and sent to a neuropathologist for further examination. The most common gross abnormalities are cortical atrophy, hippocampal atrophy, and enlarged ventricles. Dependent upon the differential diagnosis, as formulated from the patient's clinical presentation and gross brain appearance, the neuropathologist will take sections of interest for microscopic analysis. Typically, a variety of special stains are required to visualize neuronal pathologies. The most common anatomical regions of interest are the cerebral cortex, hippocampus, basal ganglia, midbrain, and cerebellum. The neuropathologist produces a report describing his/her gross and microscopic findings in addition to a broad interpretation of the findings. A forensic pathologist further interprets the neuropathological findings within the context of his/her postmortem findings and scene investigation.

Introduction

- There are multiple forms of dementia including Creutzfeldt-Jakob disease, Lewy body dementia, Frontotemporal dementia, Huntington's disease, mixed dementia, normal pressure hydrocephalus, posterior cortical atrophy, Parkinson's disease, vascular, Korsakoff syndrome, and Alzheimer's disease.
- Alzheimer's Disease (AD) is the most common form of dementia; roughly 5.8 million people in the United States are recorded as having AD.[2] The symptoms will usually start to show around age 60 years, but the risk of developing AD increases with age.[2] The number of people with AD is projected to increase to 13.8 million by mid-century.[2] It is number 6 in the top 10 leading causes of death in the United States.[2]
- Those with AD pass away from the complications due to the disease and not the disease itself. When a case arrives, a medical history is also presented. Neurodegenerative disorders can only be diagnosed at autopsy. At UND Forensics the brains are sent to a neuropathologist for further examination.
- AD is commonly characterized by the accumulation of two different proteins, beta amyloid (Aβ) forming plaques and tau forming neurofibrillary tangles. Aβ accumulates extracellularly (i.e., in the neuropil), while tau protein accumulates inside neurons.[3]

Results

Figure 1.

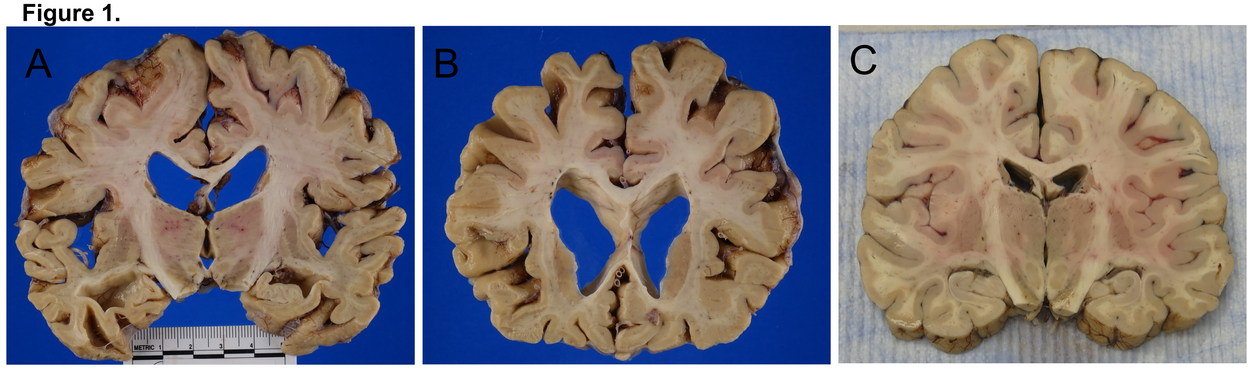

Figure 1: A. Cortical atrophy of the parietotemporal section of the brain also showing ventricle enlargement. **B.** Cortical atrophy of the frontotemporal section of the brain also showing ventricle enlargement. **C.** Parietotemporal section of the brain that is grossly unremarkable for comparison.

Figure 2.

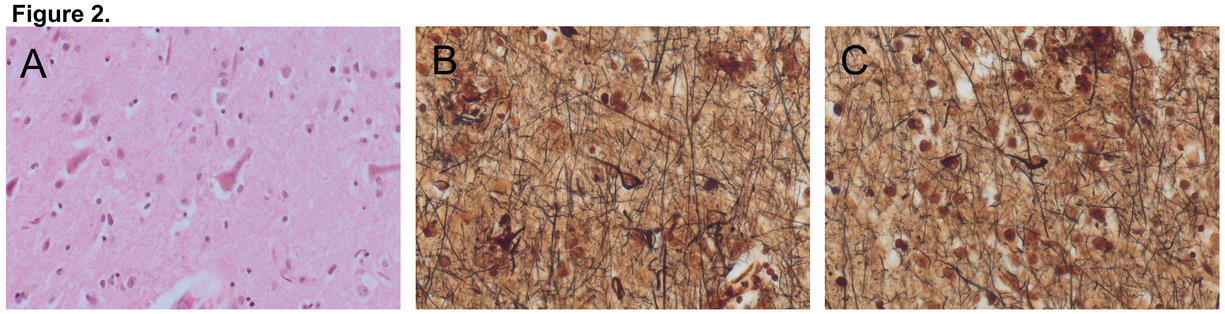

Figure 2: A. On routine stain (H&E), neurofibrillary tangles appear as basophilic cytoplasmic structures. **B. and C.** A Bielschowsky silver stain aids in identification of neurofibrillary tangles. The tangles are composed of hyperphosphorylated tau protein.

Figure 3.

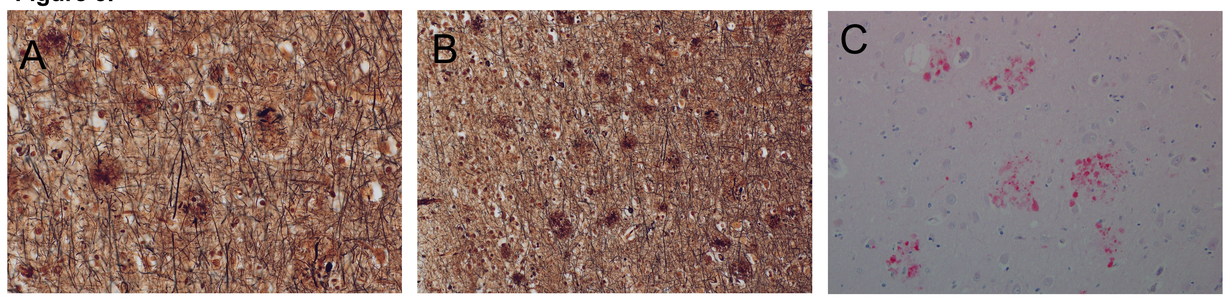

Figure 3: A. and B. A Bielschowsky silver stain aids in identification of Alzheimer's plaques. The plaques are composed of central deposits of beta amyloid (Aβ) surrounded by dystrophic neuritic processes, which collectively form a spherical mass. **C.** A Congo red stain highlights the amyloid deposits at the center of the plaques.

References

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Methods

- The scalp is reflected over the face to expose the skull. The skull cap is removed using a bone saw. The dura mater can be pulled down and the brain removed by cutting the optic nerves, olfactory nerves, and blood vessels. The tentorium cerebelli is cut to expose the cerebellum and the spinal cord is detached. Photographs are taken of the brain still in the cranial cavity and after being removed. Then the brain is fixed in 10% formalin and sent to the neuropathologist.
- The neuropathologist sections the brain coronally and examines it for any gross abnormalities. Photographs are taken for each cut section. Then more sections are taken for microscopic analysis. A standard list for all neurodegenerative diseases includes:
  - Middle frontal gyrus
  - Anterior cingulate gyrus
  - Basal ganglia
  - Amygdala
  - Anterior hippocampus
  - Mid-hippocampus
  - Superior and middle temporal gyri
  - Thalamus
  - White matter at triple watershed
  - Occipital (calcarine) cortex
  - Cerebellar cortex and dentate nucleus
  - Midbrain
  - Pons
  - Medulla
  - Anterior thalamus at mammillary bodies
  - Dorsolateral prefrontal cortex
  - Nucleus accumbens
  - Superior frontal gyrus
  - Choroid plexus
- Most important areas for diagnosis of AD are the cortex, hippocampus, basal ganglia, midbrain, and cerebellum.
- Once tissues are fixed to a slide, they are then stained using H&E and Bielschowsky. Congo red stain can also be used for identifying amyloid deposits.

Discussion

- Those with AD often present with muscle atrophy, weight loss, possible bone atrophy, and a dysfunctional epiglottis.
- There has been many clinical trials and research looking at Aβ in order to overcome AD. Many of the drugs have not been deemed safe or effective due to the heterogeneity of etiology and pathobiology in AD.[4]
- In sporadic AD, accumulating Aβ leading to plaques can start about 20 years prior to the onset of AD and not show any symptoms. It is believed this is due to impaired waste clearance instead of overproduction of the peptide. [4]
- Biomarkers are being analyzed in an attempt to predict the onset of AD. Early detection allows healthcare professionals to treat them more effectively with disease-modifying therapeutics.
- Although, clearance of Aβ plaques did not show improved symptoms for those with AD.
- Future research that interests me would be looking into Aβ and the role it plays in AD to develop potential treatment methods.