Background Information:
A 66-year-old Caucasian woman presented with a history of depression, anxiety, and dementia for about 2 years. She demonstrated multiple cognitive difficulties including memory deficit, and she later became more confused, agitated, and at times, delusional. She was employed at a bank, but lost her ability to do simple mathematics. For the last year of her life, she was unable to care for herself and her activities of daily living were impaired. Her walking became unsteady and she started to have frequent falls and gait dysfunction. She frequently experienced right-sided headaches and her behavior progressively changed with psychotic symptoms.

The patient was admitted to the hospital after being found on her house floor due to a fall. She continued to have episodes of severe agitation requiring sedation, neurologic and psychiatric evaluations. Laboratory tests were unremarkable. An MRI revealed no evidence of acute stroke but showed severe volume loss and mild chronic ischemic white matter disease. An EEG demonstrated right temporal slowing, suggesting a structural abnormality, but without any seizure activity. Cranial nerve exam revealed significant ataxia, with left-sided drift at the corner of the mouth. She had increased tone in all limbs with accentuated right upper extremity. There was moderate to pronounced bilateral thinning of the cortical mantle but with preservation of cortical white matter demarcation throughout the cerebral ribbons in all lobes. There was no evidence of lobar predilection. The hemispheres were abnormal. The cerebral cortex exhibited moderate gliosis without disruption of the cortical white matter junction. There was no evidence of lobar predilection. There was absence of hippocampal sclerosis. The cerebral cortex exhibited moderate gliosis without disruption of the cortical white matter junction.

Methods:
The brain had diffuse cortical atrophy without lobe predilection. The hemispheres were symmetrical without externally discernable evidence of cerebellar infarcts, parenchymal hemorrhage, trauma, brain abscess, swelling, midline shift, or subfalcine herniation. Basal view of the brain was unremarkable, and the brainstem and cerebellum show no gross abnormality. Serial coronal sections of the cerebrum revealed diminution in bulk of white matter and diffuse thinning of the cortical mantle but with preservation of cortical white matter demarcation throughout the cortical ribbons in all lobes. There was moderate to pronounced bilateral thinning of the cortical mantle but with preservation of cortical white matter demarcation throughout the cerebral ribbons in all lobes.

Microscopic evaluation revealed extensive neurodegenerative changes in the cerebral cortex involving the frontal, lateral temporal, parietal and occipital areas and in the cortical white matter junction. There were no evidence of lobar predilection, infarct, or microvascular intercortical lesions. No Lewy bodies were present, substantiated by negative alpha-synuclein immunohistochemical stain. Both sections of the substantia nigra exhibited, for the most part, preservation of neuronomin bearing neurons, even the right side, which grossly showed pallor when compared to the left. The cerebral cortex exhibited moderate gliosis without disruption of the cortical white matter junction. There were no evidence of lobar predilection. The hemispheres were abnormal. The cerebral cortex exhibited moderate gliosis without disruption of the cortical white matter junction.

Microscopic evaluation revealed extensive neurodegenerative changes in the cerebral cortex involving the frontal, lateral temporal, parietal and occipital areas and in the cortical white matter junction. These changes were characterized by profusion of phosphorylated tau positive neurofibrillary tangles, pretangle neurones, neurofil thread dystrophies in the context of neuritic plaques, and dense and diffuse accumulation of Aβ deposits. Multiple sections of the hippocampus and the basal ganglia also revealed the same extensive neurodegenerative changes.

Neuropathologic Changes of Alzheimer Disease: A Case Study
Mark Vincent C. Olorvida MHS, PA Student, Mentors: Christos D. Katsetos, M.D., Ph.D., Ahmed Abdulrahman, M.D., Drexel University College of Medicine, Philadelphia, PA

Figure 1. Gross photos. A. normal, showing dilatation of lateral ventricles (arrows) with rounding of lateral ventricular angles and diminution in bulk of white matter. B, C and D. Right lateral view (E). Axial sections of the midbrain revealed pallor of the right substantia nigra compared to the left (arrow). E. Axial sections of the brainstem and cerebellum were unremarkable, with no grossly overt abnormalities.

Methods:
The brain had diffuse cortical atrophy without lobe predilection. The hemispheres were symmetrical without externally discernable evidence of cerebellar infarcts, parenchymal hemorrhage, trauma, brain abscess, swelling, midline shift, or subfalcine herniation. Basal view of the brain was unremarkable, and the brainstem and cerebellum show no gross abnormality. Serial coronal sections of the cerebrum revealed diminution in bulk of white matter and diffuse thinning of the cortical mantle but with preservation of cortical white matter demarcation throughout the cerebral ribbons in all lobes.

Microscopic evaluation revealed extensive neurodegenerative changes in the cerebral cortex involving the frontal, lateral temporal, parietal and occipital areas and in the cortical white matter junction. These changes were characterized by profusion of phosphorylated tau positive neurofibrillary tangles, pretangle neurones, neurofil thread dystrophies in the context of neuritic plaques, and dense and diffuse accumulation of Aβ deposits. Multiple sections of the hippocampus and the basal ganglia also revealed the same extensive neurodegenerative changes.

Neuropathologic Changes of Alzheimer Disease: A Case Study
Mark Vincent C. Olorvida MHS, PA Student, Mentors: Christos D. Katsetos, M.D., Ph.D., Ahmed Abdulrahman, M.D., Drexel University College of Medicine, Philadelphia, PA

Figure 1. Gross photos. A. normal, showing dilatation of lateral ventricles (arrows) with rounding of lateral ventricular angles and diminution in bulk of white matter. B, C and D. Right lateral view (E). Axial sections of the midbrain revealed pallor of the right substantia nigra compared to the left (arrow). E. Axial sections of the brainstem and cerebellum were unremarkable, with no grossly overt abnormalities.

Results:
Final gross impression included prominent diffuse cortical atrophy suggestive of a neurodegenerative process. There was no evidence of stroke, brain abscess, infection, tumor, demyelinating disease or traumatic brain injury. There was absence of hippocampal sclerosis. No developmental brain abnormalities or abnormalities of neuronal cortical migration were identified.

Microscopic evaluation confirmed severe neurodegenerative changes affecting the neocortex, mesolimbic region, and basal ganglia, consistent with hyper amyloid Alzheimer disease (AD). There was no evidence of frontotemporal dementia, diffuse Lewy body disease, vascular dementia or other neurodegenerative processes associated with dementia. The final neuropathologic diagnosis was Alzheimer disease, high, with an ABC score of A3, B3, and C3.

Conclusion:
The three main components related to assessment of AD neuropathologic changes are collecting and grading surges: A for Amyloid, B for Braak and C for CERAD, refers to neuritic plaques. Each component is assessed and assigned with 1 of 4 scores (0, 1, 2, 3); the scores are combined for a given disease, which is considered a part of the neuropathologic change. These levels are correlated with clinicopathologic changes as well as the presence/absence and extent of other contributing disease.

AD can exist in ‘pure form’, but it commonly coexists with pathologic changes of other diseases that can contribute to cognitive impairment. Therefore, it is important to assess non-AD brain lesions and to document the type and extent of comorbidity in brains of individuals with AD neuropathologic change because they can potentially contribute to the patient’s cognitive impairment or dementia.

Microscopic examination of the brain with AD will show variable degrees of cortical atrophy, resulting in a widening of the brain sulci that is most pronounced in the frontal, temporal, and parietal lobes. With significant atrophy there is a prominent ventricular enlargement (hydrocephalus ex vacuo) secondary to loss of brain parenchyma. Microscopically, neurofibrillary tangles are a major component of AD neuropathologic changes. These are bundles of paired helical filaments primarily composed of abnormally phosphorylated tau protein that displace or encircle the nucleus. The tangles can be visualized with a variety of histochemical stains or with immunohistochemistry directed against tau or phosphory-tau epitopes. Senile plaques, the other major component of AD neuropathologic changes, are focal collections of neuritic tangles, and dense and diffuse accumulation of Aβ. These plaques can be visualized by histochemical and immunohistochemistry directed against β-amyloid epitope. Other features of AD neuropathologic changes include granulovacuolar degeneration, Lewy bodies, Hirano bodies, and cerebral amyloid angiopathy, but these are less straightforward to assess. Moreover, the timing of any of these pathologic changes relative to functional changes is difficult to assess with certainty in autopsy samples. It is important to recognize that the recommended use of the recommended brain, parenchymal AD deposits, and neuritic plaques as the defining histopathologic lesions of AD neuropathologic change does not preclude the possibility that other processes or lesions that may be critical contributors to the pathophysiology of AD.

References: