



Specimen: RA04-122  
Service:  
Autopsy: 8/19/2004 11:40  
Accessioned: 8/19/2004  
Reported:

Patient: Li  
Expired: 8/5/2004 00:00  
Medical Record #: Account #:  
DOB/Age/Sex: 8/22/1937 (Age: 66) M  
Location/Client: / Rhode Island Hospital  
Part Type: A: Autopsy Neuro Only Body  
Restrictions: Brain Only

Submitting Phys:

## Autopsy Report

### Final Diagnosis

The attending pathologist whose signature appears on this report has reviewed the case materials and has reviewed/edited the report in rendering the final diagnosis.

### Final Neuropathology Diagnosis

CEREBRAL AUTOSOMAL DOMINANT ARTERIOPATHY WITH SUBCORTICAL INFARCTS AND LEUKOENCEPHALOPATHY (CADASIL)  
CEREBRAL ATHEROSCLEROSIS, NON-OCCLUSIVE, MILD

lat/11/12/2004

\*\*\*Electronically Signed Out\*\*\*

### Case Discussion

### Gross and Microscopic Descriptions:

### Procedures/Addenda

### Autopsy - Neuro

Ordered: 8/19/2004 Reported: 11/16/2004

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CEREBRAL ATHEROSCLEROSIS, NON-OCCLUSIVE, MILD

The 1040-gram brain is submitted for neuropathological examination after formalin fixation. The leptomeninges are mildly opaque and fibrotic overlying the parasagittal convexities and show no evidence of subarachnoid hemorrhage or purulent exudate. The

LI  
MR#:

brain is symmetric. There is no grossly obvious cerebral edema and no evidence of subfalcine, transtentorial, or cerebellar tonsillar herniation. The blood vessels of the circle of Willis have a normal anatomic distribution. Mild, patchy, non-occlusive atherosclerosis is noted throughout. The cranial nerves are without abnormalities. The brainstem and cerebellum are externally unremarkable.

The cerebellum and brainstem are separated from the cerebrum at the midbrain. Coronal sections through the cerebral hemispheres reveal moderate lateral ventricular dilatation with expansion of the frontal, temporal and occipital horns. Almost all of the white matter shows an irregular, "pitted" appearance. Focal areas, most notably in the deep white matter regions adjacent to the ventricles, but also, subjacent to the cortical gray matter, show "collapse" of the white matter. The white matter in these aforementioned "collapsed" regions is extremely soft with gray discoloration. Additionally, there are multiple lacunes in the subcortical white matter, ranging from less than 0.1 cm to 1.0 cm in greatest linear dimension. The lacunes are distributed in both the deep white matter as well as directly subjacent to the cortical gray matter. The majority of the cortex is unaffected; however, the cortical gray matter immediately adjacent to these "collapsed" white matter areas is markedly thinned (< 0.1 cm in thickness), soft and discolored. The deep gray matter structures are affected as well. The putamen and thalamus are most severely affected and show the same pitted appearance as noted in much of the white matter, as well as multiple lacunes. The cerebellum is sectioned parasagittally and the brainstem is sectioned transversely. The cerebellar hemispheres and vermis have intact folia throughout and are externally unremarkable. The midbrain, pons, and medulla are externally unremarkable. The cerebral aqueduct is patent and not dilated, and the fourth ventricle is normal in size and configuration.

te, M.D.

## Neuropathology

### Gross Neuropathology Examination

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### Microscopic Neuropathology Examination

Slide 1. Left prefrontal cortex: The neurons of the gray matter are preserved. The white matter shows diffuse myelin pallor with extensive rarefaction of myelin fibers, prominent astrocytosis and foci of cavitory necrosis with relative preservation of the subcortical U-fibers. Some areas of cavitation are noted to superficially extend into the cortical gray matter. The penetrating arteries and arterioles of the white matter show concentric thickening of the vessel walls. Many vessels show deposition of finely granular, eosinophilic material surrounding swollen myocytes within the media, and adventitial fibrosis, while other vessels show concentric, hyalinized thickening of their media and adventitial fibrosis without the aforementioned deposition of granular material. There is marked widening of the perivascular spaces and focal perivascular rarefaction. The meninges are thickened and many of the blood vessels show changes similar to those noted in the white matter. A Bielschowsky silver stain fails to demonstrate neurofibrillary tangles and plaques.

Slide 2. Left middle frontal gyrus: Mild, diffuse hypoxic-ischemic changes are evident in the cortical gray matter characterized by pericellular vacuolation and mild interstitial edema. There is evidence of diffuse white matter pallor, extensive rarefaction of myelin fibers, prominent astrocytosis and cavitory necrosis with relative sparing of the subcortical U-fibers. The penetrating arteries and arterioles of the white matter show concentric thickening of the vessel walls. Many vessels show deposition of finely granular, eosinophilic material surrounding swollen myocytes within the media, and adventitial fibrosis, while other vessels show concentric, hyalinized thickening of their media and adventitial fibrosis without the aforementioned deposition of granular material. There is

marked widening of the perivascular spaces and focal perivascular rarefaction. The meninges are thickened and many of the blood vessels show changes similar to those noted in the white matter.

Slide 3. Left parietal cortex: Moderate, diffuse hypoxic-ischemic changes are evident in both the gray and white matter characterized by pericellular vacuolation, interstitial edema and rare neurons exhibiting signs of acute neuronal injury. There is evidence of mild gliosis in the cortical gray matter. The white matter and vasculature show changes similar to those noted above; however, there is progression in the severity of these changes, rostrally to caudally. Additionally, focal blood vessels in the gray matter show changes similar to those seen in the white matter.

Slide 4. Left occipital cortex: Moderate, diffuse hypoxic-ischemic changes are evident in both the gray and white matter characterized by pericellular vacuolation, interstitial edema and rare neurons exhibiting signs of acute neuronal injury. There is evidence of mild gliosis in the cortical gray matter. The white matter and vasculature show changes similar to those noted above; however, there is progression in the severity of these changes, rostrally to caudally. An acute, focal, embolic, wedge-shaped infarct is noted in the cortical gray matter. A Congo red stain for amyloid is negative.

Slide 5: Left hippocampus: Mild to moderate hypoxic-ischemic changes are evident in the hippocampus and associated gray matter structures characterized by pericellular vacuolation and interstitial edema. There is focal neuronal loss in the CA1 region of the hippocampus as well as rare neurons, most notably in the CA1 region and subiculum, exhibiting signs of acute neuronal injury. The aforementioned white matter changes are present in this section; however, the degree of pallor, rarefaction of myelin fibers and astrocytosis is to a considerably lesser degree. There are, however, focal areas within the white matter, which are severely affected and show cavitory necrosis. Many of the small and medium sized vessels, primarily in the white matter and immediately adjacent gray matter, show pronounced, concentric thickening of their walls characterized by a zone of subintimal basophilia, smudgy eosinophilic material within their outer media and adventitial fibrosis. The myocytes, however, do not appear to be swollen. Focal vessels also have widened perivascular spaces as well as hemosiderin-containing macrophages associated with them. Additionally, one vessel is noted to have abundant reactive astrocytes associated with it. A Bielschowsky silver stain demonstrates rare neuritic plaques in the entorhinal cortex.

Slides 6 & 7. Caudate/putamen/globus pallidus: Moderate hypoxic-ischemic changes are evident in the striatum characterized by pericellular vacuolation and interstitial edema. There is evidence of diffuse white matter pallor, extensive rarefaction of myelin fibers, prominent astrocytosis as well as multiple foci of cavitory necrosis. The anterior limb of the internal capsule, external and extreme capsule are all involved. Foci of cavitory necrosis are noted to extend into the adjacent gray matter structures. The white matter vessels show the aforementioned changes. The vessels of the caudate and putamen are extensively involved and show varying degrees of affliction. Focal vessels show the characteristic, aforementioned, concentric thickening of their walls, while other vessels appear to be almost completely devoid of their smooth muscle layer and collapsed. There is marked widening of the perivascular spaces and focal vessels are associated with hemosiderin-containing macrophages.

Slide 8. Amygdala: Mild hypoxic-ischemic changes are evident characterized by pericellular vacuolation and interstitial edema. There is evidence of diffuse white matter pallor, extensive rarefaction of myelin fibers, prominent astrocytosis as well as multiple foci of cavitory necrosis. A focal collection of macrophages within an area of rarefaction, surrounded by reactive astrocytes and consistent with a subacute infarct is noted in the white matter. The white matter vessels show the aforementioned changes. The vessels are extensively involved and show varying degrees of affliction. Focal vessels show the characteristic, aforementioned, concentric thickening of their walls, while other vessels appear to be almost completely devoid of their smooth muscle layer and collapsed. There is marked widening of the perivascular spaces and focal vessels are associated with hemosiderin-containing macrophages. A Bielschowsky silver stain fails to demonstrate neurofibrillary tangles and plaques.

Slide 9. Thalamus: The thalamic nuclei and associated white matter structures show the aforementioned changes noted in the amygdala. Multiple subacute infarcts are noted in the thalamic gray matter.

Slide 10. Midbrain: A representative section of the midbrain shows the same white matter and vascular changes already described above. Of particular note, there is extensive Wallerian degeneration noted within the cerebral peduncles. The periaqueductal gray matter shows gliosis. There is evidence of moderate, diffuse hypoxic-ischemic changes characterized by pericellular vacuolation, interstitial edema and rare neurons exhibiting signs of acute neuronal injury. There is mild neuronal loss and gliosis within the substantia nigra. No inclusions are seen.

Slides 11 & 12. Pons: The pons is severely affected and shows the white matter and vascular changes already described above. Subacute infarcts are seen as well as other, older cavitory lesions. Of particular interest, the pontine crossing fibers are extensively and severely involved. There is marked gliosis noted within both the gray and white matter. Moderate, hypoxic-ischemic changes are also noted characterized by perineuronal vacuolation, interstitial edema and scattered neurons exhibiting signs of acute neuronal injury. There is mild neuronal loss and gliosis noted within the locus ceruleus. No inclusions are seen. The meningeal blood vessels are markedly thickened and sclerotic and show the aforementioned vascular changes previously described.

Slide 13. Medulla: There is evidence of moderate hypoxic-ischemic changes noted in the medulla. Scattered neurons exhibiting signs of acute neuronal injury are seen. There is extensive Wallerian degeneration of the pyramids.

Slide 14. Cerebellar vermis: There are multiple foci of Purkinje cell dropout and many of the remaining Purkinje cells show signs of acute ischemic injury. There is mild to moderate cell loss within the granular cell layer. The white matter shows mild gliosis.

