Description: Section of the brain, including cerebral cortex, hippocampus, brain stem and cerebellum.

A single blood vessel in the cortical parenchyma is practically effaced by severe mixed inflammatory infiltration composed by macrophages, neutrophils and occasional giant cells mixed with an eosinophilic proteinaceous material (amyloid) that obscures the wall and the vascular lumen. Additionally, throughout the cerebral cortex and hippocampus, there are multifocal relatively well defined round areas were the parenchyma has been replaced by a finely fibrillar pale eosinophilic material often with a darker, dense core (amyloid plaques). Amyloid plaques and vascular amyloid were confirmed by immunohistochemistry.

Morphologic diagnosis: Focal chronic severe granulomatous vasculitis with vascular amyloid and multifocal amyloid plaques.

Etiologic diagnosis: Cerebral Amyloid Angiopathy (CAA)

Typical Gross findings: No associated gross findings.

Discussion: The section of the brain submitted correspond to a Tg2576 mouse that produce mutant human beta amyloid (parenchymal plaques and cerebral blood vessels) and, among other transgenic mice, is used as an experimental model for Alzheimer’s Disease. Amyloid presence was confirmed by immunohistochemistry (see photomicrograph below) with a primary antibody that recognizes the amino terminal end of beta amyloid (Aβ, 1-16, 6E10 Monoclonal Antibody, Alexa Fluor® 488 Labeled, SIGNET) used to detect all forms of amyloid (Aβ 1-38,
Aβ1-40, Aβ1-42). Amyloid can also be identified by means of Congo-red or Thioflavin T histochemistry.

The Tg2576 mouse carries the Swedish mutation in APP, the K670M/ M671L. The overexpression of mutant human APP in the Tg2576 mouse is 5-fold, and the rate of amyloid deposition is moderate with amyloid deposits first detected at 6 months of age. CAA is sparse and is most commonly observed in mice 18 months of age and older.

CAA affects brain perfusion and there is now evidence that the neurovascular unit is affected in Alzheimer’s disease when CAA is present. Infiltrating inflammatory cells have been reported to be present in cases of severe CAA including T-cell infiltration and multinucleated giant-cell infiltration. CAA is also associated, in some cases, with the presence of hemorrhage.

References:

Please send your comments/questions to the whole LCPG list by hitting “reply to all”. A final document containing this material with answers and a brief discussion will be posted on the C. L. Davis website by the end of the current month (http://www.cldavis.org/lcpg_english.html).