Cerebral Amyloid Angiopathy
The Other Vasculopathy

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Cerebral Amyloid Angiopathy

1. Pathogenesis of CAA
2. Hemorrhage and white matter disease
3. *In vivo* detection
4. CAA-related inflammation
Growth of CAA Research

Title includes Amyloid (or Congophilic) Angiopathy
Pathogenesis of CAA
CAA-related Intracerebral Hemorrhage

Symptomatic lobar ICH

Microbleeds
Life Cycle of Aβ

1. Production of Aβ via cleavage of β-APP by β- and γ-secretases

2. Deposition of Aβ in tissue as plaques

3. Degradation of Aβ by proteases

4. Efflux of Aβ across blood brain barrier

5. Deposition of Aβ in vessels as CAA

6. Drainage of Aβ from the brain with interstitial fluid along basement membranes in the walls of capillaries and arteries
Prevalence of CAA in AD

ANY CAA pathology 80-100%
Moderate-severe CAA pathology 25%
Microbleeds 15-29%

Jellinger J Neural Transm 2002;109:813
Ellis Neurology 1996;46:1592
Cordonnier Neurology 2006;66:1356
Atri Neurodegen Dis 2005;2:305
Pettersen Stroke (abs) 2007;38:582
# Hemorrhages in CAA

<table>
<thead>
<tr>
<th></th>
<th>Front</th>
<th>Pariet</th>
<th>Temp</th>
<th>Occip</th>
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</thead>
<tbody>
<tr>
<td>Hems,% Total</td>
<td>24</td>
<td>19</td>
<td>31</td>
<td>26</td>
</tr>
<tr>
<td>(n=321)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cort Vol, %</td>
<td>41</td>
<td>19</td>
<td>22</td>
<td>18</td>
</tr>
</tbody>
</table>

p<0.0001

Rosand *Ann Neurol* 2005;58:459
Microbleeds in AD

Pettersen, Sathiyamoorthy, Gao, Szilagyi, Nadkarni, Black
*Stroke* (abs) 2007;38:582
Iowa-type Hereditary CAA

Grabowski Ann Neurol 2001;49:697
CAA and White Matter Disease

p<0.02

Gurol Neurology 2006;66:23
# CAA and Dementia

**MRC Cognitive Function and Aging Study**

<table>
<thead>
<tr>
<th></th>
<th>OR for dementia</th>
<th>Adj for age</th>
<th>Adj for age/path</th>
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<tbody>
<tr>
<td>(-) severe CAA (n=168)</td>
<td>1.0</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>(+) severe CAA (n=41)</td>
<td>7.7 (3.3-20.4)</td>
<td>9.3 (2.7-41.0)</td>
<td></td>
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*Lancet 2001;357:169*
CAA and Dementia

Conclusions

Advanced CAA is

- Common in AD
- Associated with white matter lesions
- Independently associated with cognitive impairment
In Vivo Detection of CAA in Mice
Dynamic Multiphoton Imaging

Robbins J Neurosci
2005;26:365
Imaging β-amyloid with PiB

Bacskaio Arch Neurol 2007;64:431
PiB in CAA

Normal Control

Alzheimer’s Disease

Cerebral Amyloid Angiopathy
PiB Retention in Global ROI

\[ p = 0.0009 \]

\[ p = 0.002 \]

\[ p = 0.0009 \]
Occipital PiB in CAA

AD

CAA

Occipital cortex

p=0.003
CAA-related Inflammation

Subset of CAA cases
- Subacute cognitive changes or seizures
- MRI with microhemorrhages and extensive white matter lesions
- Severe CAA, perivascular inflammation, multinucleated giant cells, focal cortical infarctions

Eng Ann Neurol 2004;55:246
Reversal and Relapse in Inflammatory CAA

Baseline

Post-treatment (+3 mos)

Relapse (+15 mos)

Relapse + ICH (+18 mos)

Kinnecom Neurology 2007;68:1411
1st autopsied case of Aβ vaccine-related inflammation

Nicoll Nat Med 2003;9:448
Thanks to...

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AA IIRG-06-26331