Spontaneous ARIA-like Events in Cerebral Amyloid Angiopathy–Related Inflammation

A Multicenter Prospective Longitudinal Cohort Study

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Study Question
What are the natural history and outcomes after treatment for spontaneous amyloid-related imaging abnormalities (sARIA) in patients with cerebral amyloid angiopathy–related inflammation (CAA-ri)?

What Is Known and What This Paper Adds
CAA-ri is a rare autoimmune encephalopathy characterized by transient focal areas of swelling and bleeding (sARIA-H) on brain MRI associated with increased anti–β-amyloid autoantibodies in the CSF. Evidence suggests that CAA-ri is a potentially reversible condition, responsive to corticosteroids, but this is limited to anecdotal and retrospective observations from small case series. The present study confirms the transient and potentially relapsing inflammatory nature of sARIA and suggests corticosteroids for preventing relapse.

Methods
For this multicenter, hospital-based, longitudinal, prospective observational study, the investigators analyzed data from 113 inpatients meeting CAA-ri diagnostic criteria (10.6% definite, 71.7% probable, and 17.7% possible CAA-ri) consecutively recruited through neurology clinics of the iCAlβ International Network Cohort Registry. A protocol for systematic data collection at presentation and at the 3-, 6-, 12-, and 24-month follow-up, including centralized reading of T1-weighted, gradient recalled echo–T2*, and fluid-suppressed T2-weighted images, was used. The reading was blinded for clinical and therapeutic information. Main outcomes were survival, clinical and radiologic recovery, intracerebral hemorrhage (ICH), and recurrence of CAA-ri.

Results and Study Limitations
The mean age of the patients was 73 (±7) years; 43% were women; 36% had a history of Alzheimer disease and 34% had radiologic evidence of a prior ICH; and 37% were APOEε4 allele carriers (23% heterozygotes, 14% homozygotes). Symptoms at presentation were cognitive changes (72%), focal neurologic deficits (58%), seizures (35%), and headache (22%); 37% had a single symptom at presentation. Among MRI hallmarks of sARIA-H, 16% had ≤4 microbleeds (CMBs), 81% had >4 CMBs, and 3% had only cortical superficial siderosis.

The incidence probability of clinical recovery, radiologic recovery, and relapse is reported in the Table. All recurrences occurred in patients with >10 CMBs. After clinicoradiological resolution of the first-ever episode, 38% (95% CI, 23–59) had at least 1 recurrence within the following 24 months. Recurrence was more likely if IV high-dose corticosteroid pulse therapy was suddenly stopped compared to slow oral tapering off (hazard ratio 4.68, 95% confidence interval 1.57–13.93, p = 0.006). The main limitation was the lack of validated clinical and radiologic rating scales to quantify CAA-ri severity and outcomes.

Study Funding and Competing Interests
The Alzheimer’s Association and Cariplo Foundation funded this study. Some authors report receiving consulting and other fees from health care companies. Go to Neurology.org/N for full disclosures.

Table: Outcome Probability After First-Ever Onset of CAA-ri

<table>
<thead>
<tr>
<th>Follow-up, mo</th>
<th>Clinical recovery</th>
<th>Radiologic recovery</th>
<th>Relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>70.3 (61.6–78.5)</td>
<td>45.1 (36.4–54.8)</td>
<td>Landmark for recovery</td>
</tr>
<tr>
<td>6</td>
<td>80.2 (72.2–87.1)</td>
<td>59.3 (50.1–68.7)</td>
<td>6.9 (2.9–15.8)</td>
</tr>
<tr>
<td>12</td>
<td>84.1 (76.2–90.6)</td>
<td>77.4 (67.7–85.9)</td>
<td>16.2 (9.3–27.6)</td>
</tr>
<tr>
<td>24</td>
<td>84.1 (76.2–90.6)</td>
<td>77.4 (67.7–85.9)</td>
<td>38.3 (22.9–59.2)</td>
</tr>
</tbody>
</table>

Abbreviations: CAA-ri = cerebral amyloid angiopathy–related inflammation; CI = confidence interval. Relapse, defined as a new recurrent episode of CAA-ri (new-onset symptoms associated with new MRI findings consistent with CAA-ri) in participants with previously ascertained clinical and radiologic recovery of the first event.
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