Cnm-positive *Streptococcus mutans* is associated with distribution pattern of cerebral microbleeds.

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**Background & Purpose**

Recently, in a stroke cohort, we reported that hypertensive intracerebral hemorrhage (ICH) and deep cerebral microbleeds (CMBs) are associated with Cnm-positive *Streptococcus mutans* (Cnm-positive *S. mutans*) which express collagen binding protein called Cnm on the bacterial surface (Tonomura S, et al. *Sci Rep* 2016). However it remains unknown whether Cnm-positive *S. mutans* is associated with distribution pattern of CMBS.

**Results**

We enrolled 165 patients (mean age 70.3 ± 12.1 years; 60.6% male). *S. mutans* was found in 111 patients (67.2%) and Cnm-positive *S. mutans* was found in 31 patients (27.9%).

**Table 1. Baseline Characteristics**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Strictly deep CMBS n=36</th>
<th>Mixed CMBS n=36</th>
<th>Strictly lobar CMBS n=11</th>
<th>No CMBS n=82</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>mean (±SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>n (%)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>sBP (mmHg)</td>
<td>median (IQR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CCR (ml/min)</td>
<td>median (IQR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICH</td>
<td>n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lacuna</td>
<td>n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PVWMH &gt; grade 2</td>
<td>n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSWMH &gt; grade 2</td>
<td>n (%)</td>
<td></td>
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</tbody>
</table>

Af, Atrial fibrillation; CCR, creatinine clearance; CMBS, cerebral microbleeds; sBP, diastolic blood pressure; DSWMH, deep subcortical white matter hyperintensity; ICH, intracerebral hemorrhage; PVWMH, periventricular white matter hyperintensity; sBP, systolic blood pressure.

Study design: A single hospital based, retrospective observational study

202 patients with cerebrovascular disease registered in our cohort study and collected sample of saliva.

18 cases excluded
(7 cases: asymptomatic ICS, 2 cases: dementia, 2 cases: epilepsy, and 7 cases: other causes)

184 patients with acute cerebrovascular disease
(4 cases: contra-indication for MRI and 15 cases: 1.5Tesla MRI)

165 patients with 3 Tesla MRI

Assessment of CMBS distribution on T2*WI

Evaluate the number and locations of CMBS using previously reported scale.

1. Strictly deep CMBS
2. Strictly lobar CMBS
3. Mixed CMBS
4. No CMBS

We investigated the relationship between the distribution of CMBS and Cnm-positive *S. mutans*

Wilcoxon signed rank test was used to analyze differences in the median of continuous variables between groups. Analysis of variance (ANOVA) was used to analyze differences in the means of groups. Statistical Analysis was done using JAMP 11 (SAS Institute Inc. Chicago, USA).

**Discussion**

**Cnm-positive *S. mutans* and pathology of CMBS**

- Genetic factors (APOE, etc)
- Aging
- Vascular risk factors (e.g. hypertension)
- Amyloid-β deposit in vessel wall, causing inflammation (angiitis), oxidative stress, apoptosis, etc
- Cerebral amyloid angiopathy mainly in lobar region
- Fibrohyalinosis
- Hypertensive vasculopathy mainly in deep region
- BBB dysfunction
- Antithrombotic therapy
- BBB leakage
- Microbleeds

In this study, we showed that Cnm-positive *S. mutans* is significantly associated with deep CMBS caused by hypertensive vasculopathy but not with lobar CMBS caused by CAA. Different associations with the oral microbe among each distribution patterns of CMBS may highlight the different pathogenesis.

**Conclusion**

The distribution pattern of CMBS is associated with Cnm-positive *S. mutans*.

**Conflict of Interest**

The authors have no conflicts of interest to declare.

**Acknowledgement**

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