Relations of Blood Inflammatory Marker Levels With Cerebral Microbleeds

Kaori Miwa, MD; Makiko Tanaka, MD; Shuhei Okazaki, MD; Shigetaka Furukado, MD; Manabu Sakaguchi, MD; Kazuo Kitagawa, MD

Background and Purpose—Cerebral microbleeds (CMB) are observed in the elderly and have been regarded as one of the manifestations of small vessel disease. Although inflammatory processes have attracted much attention not only in large-artery disease, but also in small vessel disease, their involvement in CMB remains to be determined. The purpose of this study is to clarify relations between inflammatory marker levels and CMB.

Methods—Four hundred thirty-one patients without histories of cerebrovascular diseases were prospectively enrolled. The presence and number of CMB were assessed on gradient-echo magnetic resonance imaging. As common inflammatory markers, serum levels of high-sensitivity C-reactive protein (hsCRP), interleukin-6 (IL-6), and interleukin-18 (IL-18) were evaluated.

Results—CMB were found in 65 patients (15%). In 35 patients, at least one CMB was found in deep locations, but 30 patients had strictly lobar CMB. Levels of hsCRP, IL-6, and IL-18 were higher in patients with CMB than in those without. Logistic regression analyses showed that each 1SD increase in each inflammatory marker level was significantly associated with the presence of CMB after adjustment for age and sex, and after additional adjustment for cardiovascular risk factors, silent lacunar infarction, and white matter hyperintensity. The OR (95% CI) of hsCRP, IL-6, and IL-18 was 1.81 (1.35–2.46), 1.73 (1.18–2.61), and 2.41 (1.44–4.52), respectively. Furthermore, the inflammatory marker levels were associated with both deep and lobar CMB.

Conclusions—Higher levels of hsCRP, IL-6, and IL-18 are associated with CMB, in both deep and lobar locations, suggesting the involvement of inflammation in CMB. (Stroke. 2011;42:3202-3206.)

Key Words: cerebral microbleeds ■ inflammation ■ high-sensitivity C-reactive protein ■ small vessel disease

Cerebral microbleeds (CMB) are seen as small, round foci of hypointensity on gradient echo (GRE) T2*-weighed MRI. They represent perivascular collections of hemosiderin-containing macrophages on histopathologic examinations.1 CMB are associated with hypertensive vasculopathy mainly in the basal ganglia, and cerebral amyloid angiopathy in the lobar location, which have been implicated in small vessel disease (SVD).2 CMB are commonly observed not only in patients with ischemic and hemorrhagic stroke, but also in normal elderly individuals.2 More importantly, CMB might predict future risk of stroke, especially hemorrhagic stroke under antithrombotic therapy.3 Age and hypertension have been closely associated with CMB,4 and the APOEe4 allele is associated with lobar CMB,4 but whether inflammatory processes are involved in CMB remains to be determined.

Recently, inflammatory processes have been recognized 1 of the most important pathways in the development of atherosclerosis.5 In particular, the levels of circulating inflammatory markers, such as high-sensitivity C-reactive protein (hsCRP), interleukin-6 (IL-6), and interleukin-18 (IL-18), could predict future risk of stroke and cardiovascular events.6—8 Several studies have demonstrated the association of inflammatory markers with the severity of vessel lesions in the carotid and intracranial arteries,9,10 as well as with silent lacunar infarction (SLI) and white matter hyperintensities (WMH),11,12 suggesting the involvement of inflammatory processes in SVD. Although a relationship between hsCRP, matrix metalloproteinase-9, and CMB was examined in acute stroke patients,13 the relationship between CMB and inflammatory marker levels has not been investigated in individuals without a history of stroke.

In this study, we examined the associations of hsCRP, IL-6, and IL-18 with CMB in deep or lobar locations, in neurologically asymptomatic patients with cardiovascular risk factors, to explore the involvement of inflammatory processes in CMB.

Methods

Patients
Subjects were prospectively enrolled from the consecutive outpatients age ≥45 years who visited the Department of Neurology at Osaka University Hospital between April 2002 and August 2010. The majority

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of patients had been referred from another hospital or department for risk assessment and primary or secondary prevention of stroke. At the time of referral, comprehensive neurological evaluations were performed by stroke neurologists, including measurement of the carotid intima-media thickness (IMT), which reflects the severity of atherosclerosis; patients also underwent MRI, which indicates imaging evidence of stroke. When neither neurological symptoms nor a history of stroke or transient ischemic attack were identified, the patient was considered to be eligible for this study. Most MRIs were performed to evaluate suspicious neurological symptoms (eg, headache, vertigo, dizziness, numbness, syncope, or subjective memory impairment). During the study period, 804 patients were identified as candidates (Figure 1). We then excluded 49 patients in whom MRI examinations were not completed. Patients with a history of stroke or transient ischemic attack (n=275), or brain surgery (n=8), were excluded to eliminate any effects of clinical evident disease on CMB and the inflammatory markers. In addition, patients with collagen disease (n=7) or malignant disease (n=12) and those who were receiving hemodialysis (n=3) were excluded because such conditions could increase inflammatory marker levels. Patients whose hsCRP levels were higher than 3 mg/dL were also excluded because of the possibility of acute viral infection (n=19). Consequently, all analyses were based on 431 patients. Final diagnoses were tension-type headache (n=48), vestibular vertigo or dizziness (n=54), orthostatic hypotension (n=33), cervical spondylosis (n=32), mild cognitive impairment (n=11), subclavian artery stenosis (n=7), retinal artery occlusion (n=6), Bell’s palsy (n=3), or migraine (n=2), while the remaining individuals (n=235) were diagnosed as normal despite transient nonspecific symptoms. Baseline characteristics are summarized in Table 1, which demonstrates a higher prevalence of vascular risk factors. The study was approved by the local ethical review board, and all patients gave written informed consent.

**MRI Protocol**

MRI was performed with a 1.5T Signa Horizon (GE Medical System). The image protocol included: T1-weighted, fluid-attenuated inversion recovery, T2-weighted, and proton density images. In addition, diffusion-weighted images were obtained to assess for acute ischemic stroke.

![Figure 1. Description of the study population. hsCRP indicates high-sensitivity C-reactive protein.](http://stroke.ahajournals.org/)

**Table 1. Baseline Characteristics According to CMB Status**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All</th>
<th>No CMB</th>
<th>CMB</th>
<th>Deep CMB</th>
<th>Lobar CMB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n</td>
<td>431</td>
<td>366</td>
<td>65</td>
<td>35</td>
<td>30</td>
</tr>
<tr>
<td>Age, y</td>
<td>69.3 (8.6)</td>
<td>68.9 (8.6)</td>
<td>71.7 (8.6)*</td>
<td>71.7 (8.1)</td>
<td>71.8 (9.2)</td>
</tr>
<tr>
<td>Male, %</td>
<td>52</td>
<td>51</td>
<td>60</td>
<td>67</td>
<td>53</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>23.0 (3.0)</td>
<td>23.0 (2.9)</td>
<td>23.4 (3.3)</td>
<td>24.4 (3.2)*</td>
<td>22.4 (3.1)</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>15</td>
<td>15</td>
<td>19</td>
<td>15</td>
<td>24</td>
</tr>
<tr>
<td>Alcohol intake, %</td>
<td>19</td>
<td>19</td>
<td>17</td>
<td>15</td>
<td>4</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>71</td>
<td>68</td>
<td>76</td>
<td>85</td>
<td>67</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>134 (16)</td>
<td>134 (16)</td>
<td>134 (17)</td>
<td>136 (18)</td>
<td>131 (17)</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>76 (11)</td>
<td>77 (11)</td>
<td>75 (12)</td>
<td>76 (14)</td>
<td>73 (10)</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>19</td>
<td>19</td>
<td>16</td>
<td>21</td>
<td>10</td>
</tr>
<tr>
<td>Fasting glucose, mg/dl</td>
<td>107 (25)</td>
<td>106 (23)</td>
<td>114 (31)*</td>
<td>120 (33)†</td>
<td>109 (29)</td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>5.5 (0.7)</td>
<td>5.5 (0.7)</td>
<td>5.6 (0.7)</td>
<td>5.8 (0.7)</td>
<td>5.4 (0.6)</td>
</tr>
<tr>
<td>Hyperlipidemia, %</td>
<td>37</td>
<td>37</td>
<td>33</td>
<td>39</td>
<td>27</td>
</tr>
<tr>
<td>HDL, mg/dl</td>
<td>58 (16)</td>
<td>59 (16)</td>
<td>55 (16)</td>
<td>54 (15)</td>
<td>56 (18)</td>
</tr>
<tr>
<td>LDL, mg/dl</td>
<td>122 (31)</td>
<td>122 (30)</td>
<td>123 (31)</td>
<td>119 (33)</td>
<td>128 (33)</td>
</tr>
<tr>
<td>Triglycerides, mg/dl</td>
<td>125 (65)</td>
<td>122 (64)</td>
<td>143 (72)*</td>
<td>158 (82)†</td>
<td>126 (56)</td>
</tr>
<tr>
<td>eGFR, ml/min/1.73 m²</td>
<td>67.8 (18.5)</td>
<td>69.6 (17.6)</td>
<td>62.6 (13.8)†</td>
<td>59.7 (15.3)†</td>
<td>66.1 (11.1)</td>
</tr>
<tr>
<td>Antiplatelet/Warfarin use, %</td>
<td>35/3</td>
<td>33/2</td>
<td>41/6</td>
<td>42/8</td>
<td>40/4</td>
</tr>
<tr>
<td>IHD/PAD, %</td>
<td>8/4</td>
<td>8/3</td>
<td>9/8</td>
<td>9/11*</td>
<td>10/4</td>
</tr>
<tr>
<td>IMT, mm</td>
<td>1.01 (0.5)</td>
<td>0.99 (0.5)</td>
<td>1.14 (0.5)*</td>
<td>1.23 (0.5)†</td>
<td>1.06 (0.5)</td>
</tr>
<tr>
<td>SLI, %</td>
<td>36</td>
<td>30</td>
<td>67†</td>
<td>82†</td>
<td>50*</td>
</tr>
<tr>
<td>PVH, median (IQR)</td>
<td>2 (1–4)</td>
<td>2 (1–3)</td>
<td>3 (2–6)†</td>
<td>5 (2–6)†</td>
<td>3 (1.75–6)†</td>
</tr>
<tr>
<td>DWMH, median (IQR)</td>
<td>4 (2–9)</td>
<td>4 (1–6)</td>
<td>8 (3–12)†</td>
<td>8 (3–12)†</td>
<td>8 (2.75–11)†</td>
</tr>
<tr>
<td>hsCRP, mg/dl, median (IQR)</td>
<td>0.05 (0.02–0.11)</td>
<td>0.04 (0.02–0.09)</td>
<td>0.08 (0.05–0.18)†</td>
<td>0.11 (0.06–0.22)†</td>
<td>0.07 (0.03–0.16)*</td>
</tr>
<tr>
<td>IL-6, pg/dl, median (IQR)</td>
<td>1.40 (0.83–2.38)</td>
<td>1.34 (0.81–2.13)</td>
<td>2.02 (0.99–3.73)*</td>
<td>2.35 (0.91–3.83)†</td>
<td>1.78 (1.11–3.13)†</td>
</tr>
<tr>
<td>IL-18, pg/dl, median (IQR)</td>
<td>188.7 (143.3–269.4)</td>
<td>188.7 (135.8–257.6)</td>
<td>224.7 (171.8–296.7)†</td>
<td>249.0 (192.3–304.4)†</td>
<td>212.4 (165.2–292.1)†</td>
</tr>
</tbody>
</table>

CMB indicates cerebral microbleeds; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; eGFR, estimated glomerular filtration rate; IHD, ischemic heart disease; PAD, peripheral artery disease; SLI, silent lacunar infarction; IMT, intima-media thickness; PVH, periventricular hyperintensities; IQR, interquartile range; DWMH, deep white matter hyperintensities; hsCRP, high-sensitivity C-reactive protein; IL, interleukin.

*P<0.05.
†P<0.01 compared with the CMB-negative group.
recovery sequence (FLAIR), T2-weighted, and GRE. GRE parameters were as follows: 22 axial images; field of view, 220 mm; slice thickness, 5 mm; interslice gap, 1.5 mm; 256×256 matrix; echo time, 20 ms; repetition time, 640 ms; and flip angle, 20°.

MRI Assessment
MRI assessment was performed by 2 trained observers who were blinded to clinical information. CMB were defined as punctate hypointense lesions <10 mm on GRE. Location and number of CMB were assessed. The locations of CMB were classified as: lobar (cortex, subcortex, and white matter), or deep or infratentorial (basal ganglia, thalamus, brain stem, and cerebellum). Microbleed mimics (eg, vessels, mineralization, air-bone interfaces, partial volume artifact at the edges of the cerebellum) were excluded.2,14 SLI were defined as focal lesions >3 mm and <15 mm with the hypointense lesion with a hyperintense rim on FLAIR images (when located supratentorially), with corresponding hyperintensity on T2-weighted images and corresponding hypointensity on T1-weighted images. The degree of WMH was visually rated on FLAIR images using the Scheltens scale with slight modifications; ie, scores of 0 to 6 were given for deep WMH of the frontal, temporal, parietal, and occipital lobe (DWMH; range, 0–24) and scores of 0 to 2 were given for 3 periventricular hyperintensities (PVH; range, 0–6).15 In a random sample of 10%, interrater reliability for the presence of CMB was κ = 0.86 and for the number of CMB was intraclass correlation coefficient = 0.84.

Risk Factors
Hypertension was defined as blood pressure ≥140/90 mm Hg on measurements taken on at least 2 occasions, or use of antihypertensive medications. Diabetes was defined as fasting plasma glucose level ≥126 mg/dL, HbA1c level ≥6.1%, or use of antidiabetic therapy. Hyperlipidemia was defined as low-density lipoprotein cholesterol level ≥140 mg/dL, total cholesterol level ≥220 mg/dL, or triglycerides level ≥150 mg/dL; or use of cholesterol-lowering therapy. Estimated glomerular filtration rate (eGFR) was used as the Modification of Diet in Renal Disease method modified by the Japanese coefficient.17 Body mass index was calculated as weight [kg]/height [m]². Smoking was classified as current. Habitual alcohol intake was defined as alcohol drinking of >20 g/d.

Measurement of Inflammatory Markers
After MRI examination, blood was drawn with minimally traumatic venipuncture for measurement of serum inflammatory markers. Blood was centrifuged at 3000 rpm at 4°C for 15 minutes, and aliquots were stored at −80°C. Circulating hsCRP was measured by the latex turbidimetric immunosassay with a sensitivity of 0.01 mg/dL (Shionogi Biomedical Laboratory Inc). Serum IL-6 and IL-18 were measured by enzyme-linked immunosorbsent assay (High-sensitivity Quantikine Kit, R&D System; and Human IL-18 enzyme-linked immunosorbsent assay Kit, MBL Co., Ltd., respectively). The detection limit was 0.10 pg/mL for IL-6, and 12.5 pg/mL for IL-18. The intraassay variation was 7.8% for IL-6 and 5.6% for IL-18; corresponding interassay coefficients were 7.2 and 7.6%, respectively.

Evaluation of Carotid Atherosclerosis
The carotid intima-media thickness was measured as previously described. Briefly, we calculated IMT by averaging the thickness at each measurement. All analyses were performed with SAS-8.1, with statistical significance inferred as 2-sided values < 0.05.

Results
Patient Characteristics
CMB were observed in 65 of 431 patients (15%); 32 patients had single CMB, and 33 patients had multiple CMB (Table 1, Figure 2). The presence of CMB were most commonly found in deep location (35/65 [54%]), followed by lobar location (30/65 [46%]; Table 1). All CMB (n = 339) of 65 patients were equally distributed in lobar (55%) and deep areas (45%; Figure 2).

Relations Between CMB and Inflammatory Marker Levels
By univariate analysis, age, fasting glucose and triglyceride levels, IMT, prevalence of SLI, and degrees of PVH and DWMH were higher in patients with CMB than in those without, and eGFR was lower in patients with CMB than in those without. Similar associations were observed between traditional risk factors and deep CMB, but no association was observed between CMB and inflammatory markers levels. All inflammatory marker levels were also higher in patients with deep CMB (median, 0.08 for hsCRP, 2.02 for IL-6, and 224.7 for IL-18) than in those without (median, 0.04, 1.34, 188.7 respectively; Table 1, Figure 2).

Logistic regression analyses showed that each 1SD-increase in each inflammatory marker level was significantly associ-
ated with the presence of CMB after adjustment for age and sex (Model 1), and after additional adjustment for hypertension, diabetes, hyperlipidemia, eGFR, PVH, DWMH, SLI, and IMT (Model 2). The OR (per 1SD increase; 95% CI) of each inflammatory marker (hsCRP, IL-6, IL-18) for the presence of CMB was 1.81 (1.35–2.46), 1.73 (1.18–2.61), and 2.41 (1.44–4.52), respectively (Model 2).

Furthermore, the associations between each inflammatory marker level and deep CMB or lobar CMB remained significant after adjustment for age and sex (Model 1) and after additional adjustment for traditional risk factors, IMT, eGFR, and other MRI findings (Model 2; Table 2).

### Discussion

We found that the levels of hsCRP, IL-6, and IL-18 were higher in patients with CMB than in those without. All these associations were independent of cardiovascular factors, IMT, WMH, and SLI, which have been partly shown to be associated with inflammatory markers as well.5,11,12

In our study, there was no location-specific association of CMB with inflammation. This indicates that CMB is a marker for the general severity of SVD and also can be seen as the common downstream product of 2 separate pathways: hypertensive vasculopathy and cerebral amyloid angiopathy. Our data raise the possibility that inflammation may be important to pathogenesis of any CMB.

Numerous studies have shown associations of inflammation markers with myocardial infarction and stroke. However, a few studies examined stroke subtype, even less hemorrhagic stroke. The predictive value of hsCRP for hemorrhagic stroke has not been confirmed.19,20 Moreover, in the prospective study, CMB were shown to be indicative of a higher recurrent ischemic stroke risk.21 Therefore, CMB could be considered better as part of spectrum of SVD rather than as only hemorrhagic representation.

Endothelial dysfunction and disruption of blood–brain barrier (BBB) has been suggested as a main initial pathogenetic feature in SVD. In severe WMH, inflammatory cells accumulated around vessels, in which the presence of hypoxia inducing factor-1α, macrophages, and matrix metalloproteinases support an inflammatory etiology.22 In the elderly, hemosiderin deposits occurred around capillaries, which might represent age-related vulnerability in BBB.23 Furthermore, CMB of severe cerebral amyloid angiopathy could be confirmed as the presence of β-amyloid in the vessel wall, where activated microglia and T lymphocytes expressing heme oxygenase-1 activity and late complement activation were prominent.24 They also reported that extravasated hemosiderin migrates through enlarged Virchow-Robin spaces, propagates an inflammatory reaction, and contributes to the formation of lacunar infarcts.24 These findings support our speculation that inflammation reflects vascular dysfunction leading to SVD, including CMB.

In this study, both IL-6 and IL-18 levels are associated with CMB. Although both cytokines are expressed in carotid atheromatous plaque, IL-6, but not IL-18, was associated with risk of recurrent ischemic stroke.19 IL-6 is a multifunctional cytokine that plays important roles in the regulation of the immune responses and inflammation, and is a main inducer of hepatic production of CRP. In contrast, IL-18 was originally

### Table 2. Odds Ratios (95% CI) for CMB Status per 1SD Increase in Inflammatory-Marker Levels

<table>
<thead>
<tr>
<th>CMB, Dichotomous</th>
<th>CMB, Location</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Deep</td>
</tr>
<tr>
<td></td>
<td>Model 1*</td>
</tr>
<tr>
<td></td>
<td>CMB Positive</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Model 1*</td>
</tr>
<tr>
<td>hsCRP</td>
<td>1.85 (1.41–2.45)§</td>
</tr>
<tr>
<td>IL-6</td>
<td>1.97 (1.36–2.90)§</td>
</tr>
<tr>
<td>IL-18</td>
<td>2.48 (1.40–4.49)§</td>
</tr>
</tbody>
</table>

Values were log transformed for analysis.
CMB indicates cerebral microbleeds; SD, standard deviation; CI, confidence interval.
*Model 1: Adjusted for age and sex.
†Model 2: Adjusted for age, sex, hypertension, diabetes, hyperlipidemia, eGFR, IMT, the presence of SLI, and the WMH (PVH, DWMH) grade.
§P<0.05.
‡P<0.01 compared with the CMB-negative group.
identified as an interferon-γ-inducing factor, and can enhance the production of other inflammatory molecules such as IL-1β, tumor necrosis factor-α, and the inducible form of nitric oxide synthase.23 The precise pathway between inflammation process and SVD is largely unknown and needs additional investigation.

Our results have some limitations. First, the cross-sectional design limits causal inferences. Second, our results are limited to the cohort of elderly individuals with highly prevalent vascular risk factors, and therefore they are not generalized to the general population. Although the prevalence of CMB (15%) in this study is higher than that in the general population,26 it is in line with other estimates of elderly4 and hypertensive subjects.27 The significance of CMB and inflammation in patients with a history of stroke remains unclear and needs additional investigation. Third, hsCRP levels were low because of ethnic differences and of reflecting the prevalence of relatively controlling vascular risk factors. The differences in hsCRP levels probably indicate the difficulty of determining thresholds and replication. Fourth, the sample size was relatively small, and most patients with CMB had only 1.

In conclusion, our study demonstrated that higher inflammatory marker levels were evident in subjects with CMB, regardless of location. If inflammation can be proven to be a component of CMB in the prospective study, patients with inflammatory pattern may be more prone to bleeding complications in addition to hypertension treatment; a selective screening of this process may warrant and specific treatment reducing the level of inflammation might be tested.

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None.

References
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血中炎症マーカー値と脳内微小出血の関連

Relations of Blood Inflammatory Marker Levels With Cerebral Microbleeds

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Department of Neurology, Osaka University Graduate School of Medicine.

背景および目的：脳内微小出血（CMB）は高齢者にみられ、小血管病変の微候の 1 つと考えられている。炎症過程は、大血管病変のみならず小血管病変においても非常に注目されているが、CMB に対する関与は明らかにされていない。本研究の目的は、炎症性マーカー値と CMB との関連を明らかにすることである。

方法：脳血管疾患の既往のない患者 431 例を前向きに登録した。CMB の有無および数を、ブラドニアーエコー MRT により評価した。一般的な炎症マーカーとして高感度 C 反応性蛋白 (hsCRP)，インターロイキン 6 (IL-6)，インターロイキン 18 (IL-18) の血清中濃度を評価した。

結果：CMB は 65 例（15%）で認められた。35 例では 1 篇以上の CMB を深部に認めたが、30 例では脳葉に限局した CMB であった。CMB を有する患者の hsCRP，IL-6，および IL-8 濃度は、CMB のない患者と比較して高かった。年齢および性別について補正後、さらに心血管疾患リスク因子、無症状性ラクナ梗塞，および白質高信号域について補正したロジスティック回帰分析では、各炎症マーカー値の 1 SD の上昇は CMB の存在と有意に関連していることが示された。hsCRP，IL-6，および IL-8 の OR (95% CI) は、それぞれ 1.81 (1.35 ～ 2.46)，1.73 (1.18 ～ 2.61)，および 2.41 (1.44 ～ 4.52) であった。さらに炎症マーカー値は、深部および脳葉の両方の CMB と関連していた。

結論：高濃度の hsCRP，IL-6，および IL-8 は、深部および脳葉の両方の CMB と関連しており、CMB への炎症の関与が示唆される。

図 3

各炎症マーカー値の中央値および 10，25，75，および 90 パーセンタイル値を、CMB の有無 [CMB (―) 対 CMB (+)]，部位 [CMB (―) 対深部 CMB または脳葉 CMB]，および三値 [CMB (―) 対 CMB 1 篇所または CMB 複数範囲 (≥ 2) ] に従って示す。

表 2

炎症マーカー値の 1 SD 上昇あたりの CMB 状態のオッズ比 (95% CI)

<table>
<thead>
<tr>
<th></th>
<th>CMB 有</th>
<th>CMB 有</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>深部</td>
<td>脳葉</td>
</tr>
<tr>
<td>hsCRP</td>
<td>1.85(1.41 ～ 2.45)</td>
<td>1.81(1.35 ～ 2.46)</td>
</tr>
<tr>
<td>IL-6</td>
<td>1.97(1.36 ～ 2.90)</td>
<td>1.73(1.18 ～ 2.61)</td>
</tr>
<tr>
<td>IL-18</td>
<td>2.48(1.40 ～ 4.49)</td>
<td>2.41(1.44 ～ 4.52)</td>
</tr>
</tbody>
</table>

数値は解析用対照変数値。
CMB：脳内微小出血；SD：標準偏差；CI：信頼区間。

モデル 1：年齢および性別について補正。

モデル 2：年齢、性別、高血圧、糖尿病、高脂血症、推定系球体過濾率、内中膜複合体厚、無症状性ラクナ梗塞率、および自質高信号域 (脳葉周囲、深部) グレードについて補正。

"p < 0.05.

"p < 0.1。