Infratentorial Cerebral Microbleeds in Patients with Cerebral Amyloid Angiopathy

Dimitri Renard, MD,* Lavinia Tatu, MD,* and Eric Thouvenot, MD, PhD*,†

Background: Cerebral microbleeds (CMBs) observed in hypertension-related arteriolosclerosis tend to occur in the supratentorial deep gray matter, whereas those in cerebral amyloid angiopathy (CAA) typically show a supratentorial lobar distribution. Recently, superficial spontaneous cerebellar intracerebral hemorrhage has been shown to be associated with strictly lobar CMBs. Few data exist on infratentorial CMBs in CAA. The purpose of this study was to describe the incidence, number, and characteristics of infratentorial CMBs in patients with CAA. *Methods:* We performed a retrospective analysis of data derived from a prospectively recruited cohort of patients with possible or probable CAA according to the Boston criteria. *Results:* A total of 115 patients with CAA (59% with CMBs) were analyzed. Eighteen percent of all patients with CAA had at least 1 infratentorial CMB. For patients with CMBs, presence and median CMB number were as follows: brainstem, 8% and 1; deep cerebellum, 4% and 1; superficial cerebellum, 10% and 1.5. Brainstem or deep cerebellum CMB was associated with the presence of and with higher numbers of supratentorial deep gray matter CMBs ($P < .001$ for both) and with hypertension ($P = .048$), whereas superficial cerebellar CMB was associated with the presence of and with higher numbers of supratentorial lobar CMBs ($P < .001$ for both). *Conclusions:* Based on our study, superficial cerebellar CMBs (in low numbers when present) seem to be a CAA-related phenomenon observed in a minority of patients who have CAA with a relatively high supratentorial lobar CMB load. **Key Words:** Infratentorial—cerebral microbleeds—cerebellum—brainstem—cerebral amyloid angiopathy.

Introduction

Cerebral microbleeds (CMBs) are frequently seen in cerebral amyloid angiopathy (CAA) typically showing a predominantly supratentorial lobar distribution, whereas CMBs observed in hypertension-related arteriolosclerosis tend to occur in the supratentorial deep gray matter and the brainstem. In CAA, the posterior fossa (i.e., the brainstem and, to a lesser degree, the cerebellum, which can be involved in end-stage CAA) are less severely involved than the supratentorial brain structures.[1] Recently, superficial spontaneous cerebellar intracerebral hemorrhage (i.e., restricted to the cerebellar cortex or vermis) has been shown to be associated with the presence of strictly lobar CMB (a pathological marker of CAA).[2]

The total number of CMBs in CAA varies considerably between different studies depending on the patient populations studied and the magnetic resonance imaging (MRI) field strength and sequence used (i.e., T2*- or susceptibility-weighted imaging) to detect CMBs.[3-8] Only a few of these studies specifically assessed infratentorial CMBs, showing low incidence of cerebellar CMB (12%) and low infratentorial CMB numbers (overall CMB number of .06 for the brainstem and .18 for the cerebellum) in CAA.[3,8] In these studies, no further analyses were performed for these infratentorial regions.

From the *Department of Neurology, Nîmes University Hospital, Hôpital Caremeau, Nîmes, France; and †Institut de Génomique Fonctionnelle, UMR5203, Université Montpellier, Montpellier, France.
Received April 9, 2018; accepted May 15, 2018.
Address correspondence to Dimitri Renard, MD, Department of Neurology, CHU de Nîmes, Hôpital Caremeau, 4, Rue du Pr Debré, Nîmes 30029 Cedex 4, France. E-mail: dimitrirenard@hotmail.com.
1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.05.015

Our aim was to study in more detail the incidence, number, and characteristics of infratentorial CMBs in patients with CAA.

Methods

We performed a retrospective analysis of data derived from a prospectively recruited (between January 2012 and November 2017) cohort of patients with possible or probable CAA according to the Boston criteria recruited in our center (Nîmes University Hospital, France). Patients with anticoagulant therapy were excluded. MRI including T2*-weighted imaging was required for inclusion. A total of 119 patients were screened. One patient was excluded because movement artifacts did not permit proper MRI analysis and 3 patients because MRI was lacking, leaving 115 patients with CAA for analysis. Demographic and clinical data (history of hypertension, hypercholesterolemia, diabetes, and smoking, and antiplatelet therapy) were collected. MRI scans were acquired on 1.5T or 3T magnets with slightly different TR and TE parameters. CMBs were evaluated according to current consensus criteria, on axial T2*-weighted images.[9] We analyzed CMBs on axial T2*-weighted imaging on the initial MRI performed for CAA-related symptoms. Two experienced readers (D.R. and L.T.) assessed by consensus the presence and the number of CMBs in different brain regions: supratentorial lobar location, supratentorial deep gray matter, brainstem, deep cerebellum (dentate nucleus), and superficial cerebellum (cerebellar cortex or vermis) (Fig 1).

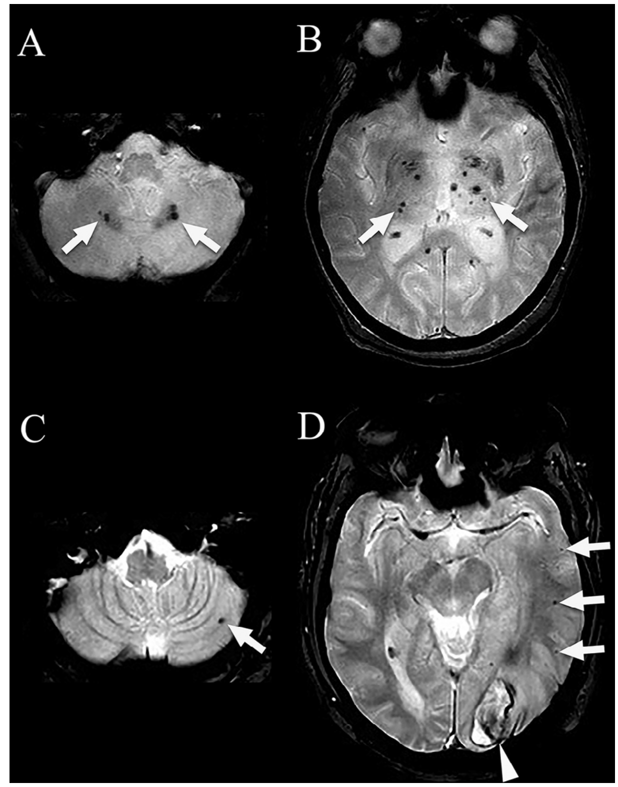

Figure 1. *MRI T2*-weighted imaging of 2 patients (patient 1, A and B; patient 2, C and D) showing in patient 1 the coexistence of deep cerebellar CMBs (A, arrows) and supratentorial deep gray matter CMBs (B, arrows) and in patient 2 the coexistence of superficial cerebellar CMBs (C, arrow), supratentorial lobar CMBs (D, arrows), and a left occipital lobar intracerebral hemorrhage (D, arrowhead). Abbreviations: CMBs, cerebral microbleeds; MRI, magnetic resonance imaging.*

The number of CMBs was expressed as median values with interquartile ranges (IQR) for the different groups. For each of the infratentorial brain regions, we looked for possible association with age, sex, cardiovascular risk factor (hypertension, hypercholesterolemia, diabetes, and smoking), antiplatelet therapy, MRI field strength, and supratentorial deep gray matter and lobar CMBs. Student *t* test was used to compare CMB numbers between different groups. Fisher exact test was used in the presence of 2 nominal variables. Spearman rank correlation coefficient (rho) was used to estimate the correlation between CMB numbers of different groups. A probability value under .05 was considered statistically significant.

The study was performed with the approval of the institutional review board of the hospital. Informed consent was obtained from all patients (or guardians of patients) participating in the study.

Results

A total of 115 patients with CAA (52% men, median age 77) were analyzed, consisting of 84 and 31 patients with initial symptoms related to lobar intracerebral hemorrhage and cortical superficial siderosis, respectively. A 1.5T magnet was used in 77% of patients and a 3T magnet in the remainder. Overall, CMBs were observed in 59% (n = 68) of patients, with a median total CMB number of 6 (IQR 2-19.5). Eighteen percent (n = 21) of all patients had at least 1 infratentorial CMB (including 9 patients with 1 or more brainstem CMBs, 16 patients with 1 or more cerebellar CMBs, and 4 patients with both brainstem and cerebellar CMBs).

In patients with CMBs, the site and median (IQR) CMB number for the different brain regions were as follows: supratentorial lobar location, 52% (n = 60) and 6 (IQR 2-16.5); supratentorial deep gray matter, 20% (n = 23) and 3 (IQR 2-4); supratentorial mixed lobar and deep gray matter, 14% (n = 16) and 5 (IQR 2-19); brainstem, 8% (n = 9) and 1 (IQR 1-2.5); cerebellum (deep or superficial), 14% (n = 16) and 1.5 (IQR 1-3.75); deep cerebellum, 4% (n = 5) and 1 (IQR 1-4); superficial cerebellum, 10% (n = 12) and 1.5 (IQR 1-3.75); and mixed deep and superficial cerebellar location 1% (n = 1) and 3.

The number of supratentorial deep gray matter CMBs in the group with and without brainstem or deep cerebellar CMBs and the number of supratentorial lobar CMBs in the group with and without superficial cerebellar CMBs are shown in Figure 2.