

# The relevance of MRI blood-sensitive sequences in the diagnostic assessment of late-onset epilepsy

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**Abstract.** – **OBJECTIVE:** Sporadic cerebral amyloid angiopathy (CAA) is a degenerative brain small vessel disease of ageing resulting from progressive amyloid deposition in small arteries and arterioles of the cortex and leptomeninges. CAA may be diagnosed by the mean of Boston criteria, particularly with the use of the blood-sensitive T2\* MRI sequences (GRE and SWI). Epileptic seizures have rarely been reported in CAA.

**PATIENTS AND METHODS:** We describe two patients with late-onset unprovoked seizures due to CAA. A short literature review on this topic is presented.

**RESULTS:** In our two patients with late-onset unprovoked seizures as the first manifestation of CAA, only GRE and SWI sequences lead to a correct diagnosis. In literature, only 15 patients with CAA presenting with seizures have been reported. In these subjects, data on seizures semiology and prognosis are scarce.

**CONCLUSIONS:** Our report highlights the importance to perform blood-sensitive sequences in all subjects with LOE of otherwise unknown etiology, not to miss a diagnosis of CAA.

## Key Words:

Late-onset epilepsy, Cerebral amyloid angiopathy, Cortical superficial siderosis, Blood-sensitive imaging sequences.

and leptomeninges in patients  $\geq 55$  years<sup>1</sup>. While definite CAA may be diagnosed only by full post-mortem examination, probable and possible CAA can be diagnosed antemortem using the validated Boston criteria, that contemplate the use of blood-sensitive T2\* MRI sequences [Gradient echo (GRE); susceptibility-weighted imaging (SWI) sequences] to demonstrate cortical superficial siderosis (cSS), intracerebral hemorrhage (ICH) or subarachnoid hemorrhage (SAH)<sup>2</sup>. Leukoaraiosis may also be evident<sup>2</sup>. CAA is a well-known cause of cognitive impairment, permanent focal neurological deficit due to atypical hemorrhages and transient focal neurological deficits (named amyloid spells)<sup>3,4</sup>. Epileptic seizures have rarely been reported in CAA; thus, CAA is not usually included among causes of late-onset epilepsy (LOE)<sup>5</sup>. The most frequent causes of LOE are stroke, neurodegenerative diseases, and brain tumors<sup>6</sup>. However, despite the use of standard MRI (without the blood-sensitive sequences), the cause of a LOE still remains unknown in ~50% of patients<sup>7</sup>. We report two patients with LOE of otherwise unknown etiology, in whom only MRI with blood-sensitive sequences allowed to pose diagnosis of CAA.

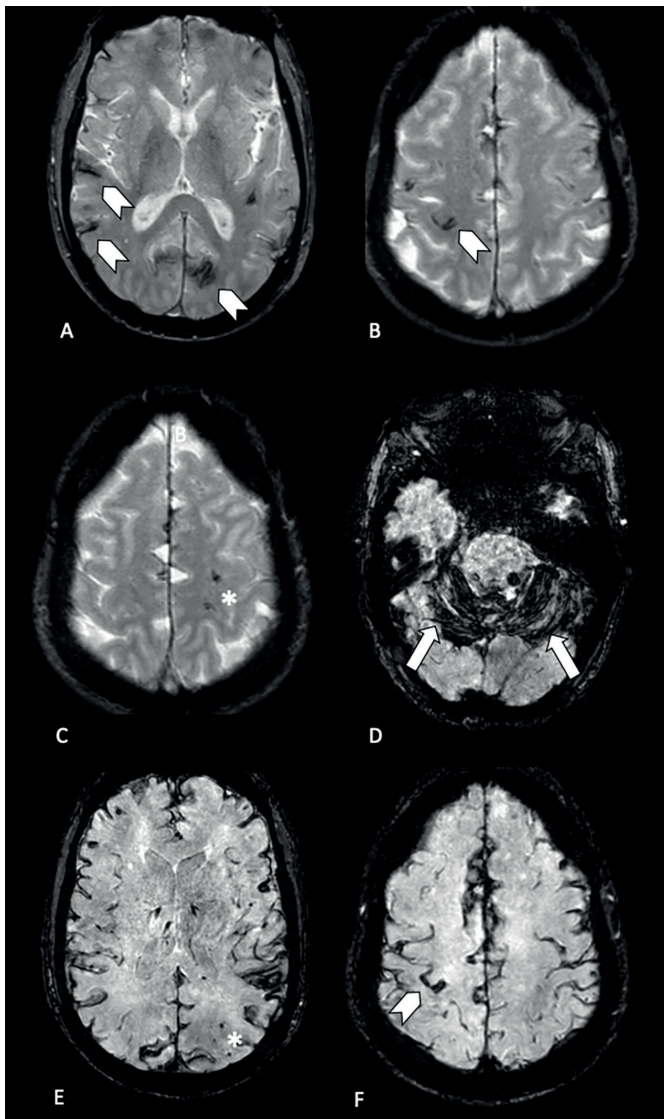
## Introduction

Sporadic cerebral amyloid angiopathy (CAA) is a degenerative brain small vessel disease of ageing resulting from progressive amyloid deposition in small arteries and arterioles of the cortex

## Case Reports

### Patient 1

A 56-year-old man was admitted to our unit for a single focal aware sensory seizure with bi-



**Figure 1.** Brain MRI of 56 years-old male patient. GRE sequences (A, B, C,) and SWI sequences (D, E, F,) showing disseminated cerebral and cerebellar cSS (arrows) and cerebral microbleeds (asterisks).

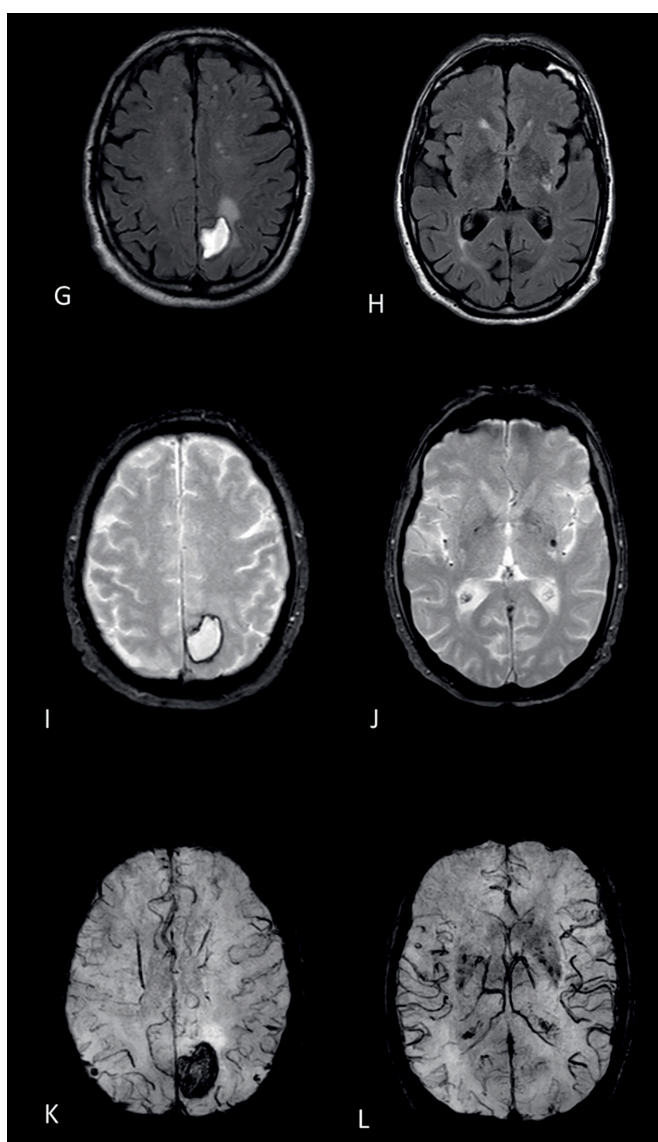
lateral tonic-clonic evolution. Brain CT scan was normal. At brain MRI, T1 and T2 sequences were uninformative. Fluid attenuated inversion recovery sequences (FLAIR) showed mild leukoaraiosis. GRE (Figure 1A, B, C) and SWI sequences (Figure 1D, E, F) showed disseminated cSS involving both cerebral and cerebellar hemispheres. Cerebral microbleeds (cMBs) were also detected (Figure 1C, E). A wide hematological screening, as well as neuropsychological examination, were unremarkable. EEG showed mid-voltage spikes over the right central electrodes. Clinical and neuroradiological findings allowed the diagnosis of probable CAA according to modified Boston criteria<sup>2</sup>. Levetiracetam up to 1000 mg/day was started. At a 6-month follow-up, the patient was

seizure-free. The patient released the informed consent for this report.

### **Patient 2**

A 67-year-old man with arterial hypertension was admitted for multiple focal motor seizures involving the right limbs with bilateral tonic-clonic evolution. The patient had no previous history of seizures. A CT scan (not showed) showed a left superficial occipital hyperdense lesion, compatible with cerebral hemorrhage. Angio-CT scan was normal. At brain MRI, T1 and T2 sequences (Figure 2G, H) showed the same hyperdense lesion and widespread leukoaraiosis. GRE (Figure 2I, J) and SWI (Figure 2K, L) sequences were also performed and showed hypointensities com-

**Figure 2.** Brain MRI of 67-year-old man. T1 and T2 sequences (G, H) show a lobar cortical haemorrhage. GRE (I, J) and SWI (K, L) sequences show hemosiderin deposition at the site of the hemorrhage and at right parietal and bilateral nucleocapsular site.



patible with hemosiderin deposition at the site of the hemorrhage, and also, at right parietal and bilateral nucleocapsular site. Hematological screening was unremarkable. EEG showed theta-delta waves over the left parietal region. Levetiracetam 1000 mg/day was started. At a 7-month follow-up, the patient was seizure free. The patient released the informed consent for this report.

### Discussion

We describe two patients with late-onset unprovoked seizures as the first manifestation of CAA.

Clinical features of seizures due to CAA have not been accurately described in the literature.

To date, only 15 patients with CAA and epileptic seizures have been reported (Table I). In these subjects, data on seizures semiology and prognosis are scarce (Table I). Differential diagnosis between seizures and amyloid spells may sometimes be challenging<sup>8</sup>. However, in our two patients, the semiology of the episodes undoubtedly suggested their epileptic nature.

In CAA, the epileptogenic role of cSS, ICH and SAH has been postulated<sup>1,9</sup> (Table I). It may be due to the epileptogenic role of blood degradation products on the adjacent cortex. In patients with LOE, MRI may show leukoariosis in the absence of overt potential epileptogenic lesions. The epileptogenic role of leukoariosis is still a matter of debate<sup>10,11</sup>. We assume that some pa-

**Table I.** Summary of the main literature data on seizures in patients with CAA.

References	N° of included subjects	Age	Sex	Semeiology	Early/Late	MRI	Prognosis
Sreedharan et al <sup>1</sup> , 2020	3	NA	NA	NA	Late	cSS	NA
		NA	NA	NA	Late	cSS	NA
		NA	NA	NA	Late	cSS	NA
Ladisich et al <sup>13</sup> , 2020	1	69	M	NCSE	Late	EM	NA
Lummel et al <sup>14</sup> , 2015	4	NA	NA	Focal to bilateral	Late	cSS	NA
		NA	NA	Focal to bilateral	Late	cSS	NA
		NA	NA	Focal to bilateral	Late	cSS	NA
		NA	NA	Focal to bilateral	Late	cSS	NA
Garcia Estevez et al <sup>15</sup> , 2015	3	67	M	Focal to bilateral	Early	SAH	NA
		79	M	Focal to bilateral	Early	SAH	NA
		71	F	Focal to bilateral	Early	SAH	NA
Katoh et al <sup>9</sup> , 2007	2	74	F	Focal to bilateral	Early	SAH	NA
		74	M	Focal	Early	SAH	NA
Maia et al <sup>16</sup> , 2004	1	92	F	Focal	Late	cSS	NA
Silbert et al <sup>17</sup> , 1992	1	74	F	Focal to bilateral	Early	ICH	NA

cSS: cortical superficial siderosis; EM: encephalomalacia; ICH: intracerebral hemorrhage; NA: not available; NCSE: nonconvulsive status epilepticus; SAH: subarachnoid hemorrhage.

tients with LOE may have unrecognized CAA. Indeed, in our two patients, only the blood-sensitive T2\* MRI sequences allowed to pose the correct diagnosis. Of note, ILAE Neuroimaging Task force<sup>12</sup> suggests the use of blood-sensitive sequences only in patients in whom tumor, vascular malformations or infectious process are suspected.

### Conclusions

Our report highlights the importance to perform blood-sensitive sequences in all subjects with LOE of otherwise unknown etiology, in order not to miss a diagnosis of CAA. Further studies evaluating the prevalence of CAA in patients with LOE are warranted.

### Conflict of Interest

The Authors declare that they have no conflict of interests.

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