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LETTER TO THE EDITOR

Sporadic cerebral amyloid angiopathy as a cause of relapsing lobar hemorrhage, convexal subarachnoid hemorrhage and cortical superficial siderosis

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Dear Editor,

A 78 year-old female affected by headache and right lateral hemianopsia, on MR images she showed areas of pathologic signal, in left occipital lobe, suggestive of hemorrhage (Fig. 1a1, a2 axial T2W; Fig. 1a3, a4 FLAIR W; Fig. 1a5, a6 ADC map images), in right frontal lobe, in different phases (Fig. 1b1, b2 axial T2W; Fig. 1b3, b4 FLAIR W; Fig. 1b5, b6 images ADC map), and a third known frontal convexity hemorrhage (Fig. 1c1, c2 axial T2W; Fig. 1c3, c4 FLAIR W; Fig. 1c5, c6 images ADC map). MR control showed a subarachnoid hemorrhage in the right rolandic cortical sulcus with edema of pre- and post-rolandic convolutions, following a subcortical hemorrhage in right frontal region. A recurrent subarachnoid hemorrhage in the frontal sulcus might have been a warning sign of a huge subcortical hemorrhage. In the aging society, a radiological prediction of cerebral amyloid angiopathy (CAA) is important. Although it is generally thought to be very difficult, GRE T2*W sequence may be useful for predicting CAA. In GRE T2W, cortico-meningeal "track-like" lines of absent signal, both next to the hemorrhagic cortical lesions and in the contralateral cerebral hemisphere. This last feature is indicative of old residual subclinical superficial bleeding, characteristic of CCA. GRE T2W imaging revealed subarachnoid siderosis and cortical superficial siderosis, defined as linear blood residues, in the superficial cortical layers of the brain, due to recurrent bleeding [5].

CAA is characterized by the accumulation of amyloid-β (Aβ) in the walls (media and adventitia) of medium and small arteries, arterioles and occasionally veins, preferentially affecting occipital lobe, followed by either frontal, temporal or parietals lobes [1]. Amyloid deposits have been also observed in the capillaries of central nervous system, parenchyma and leptomeninges [2]. CAA mostly occurs in the sporadic form in the elderly, while rare familial forms occur in younger patients and are generally lead to more severe clinical manifestations [3–5]. CAA is considered the third most common cause of spontaneous intracerebral hemorrhage after hypertension and subarachnoid aneurysmal hemorrhage [1–3]. The formation and deposition of insoluble oligomeric structures, trigger a cascade of events including release of inflammatory components, activation of the complement system, oxidative stress, alteration of the blood–brain barrier permeability, and cell toxicity [3, 4]. At the initial stage, the vessel wall structure is intact, but as the disease progresses, there is pan-mural amyloid accumulation and loss of smooth muscle cells. In severe CAA, detachment and delamination of the outer part of the tunica media result in the so-called 'double barrel' appearance; fibrinoid necrosis and microaneurysm formation also occur in advanced disease. There may also be microbleeding with perivascular deposition of erythrocytes and blood breakdown products. Endothelial cells are usually preserved, even in vessels severely affected by CAA. Occasionally Aβis deposited in the surrounding brain parenchyma immediately adjacent to an affected vessel (called 'dysphoric CAA') [3]. CAA is also associated with cerebral ischemic damage, including cortical microinfarcts, white matter irreversible leukoacariosis (demyelination and

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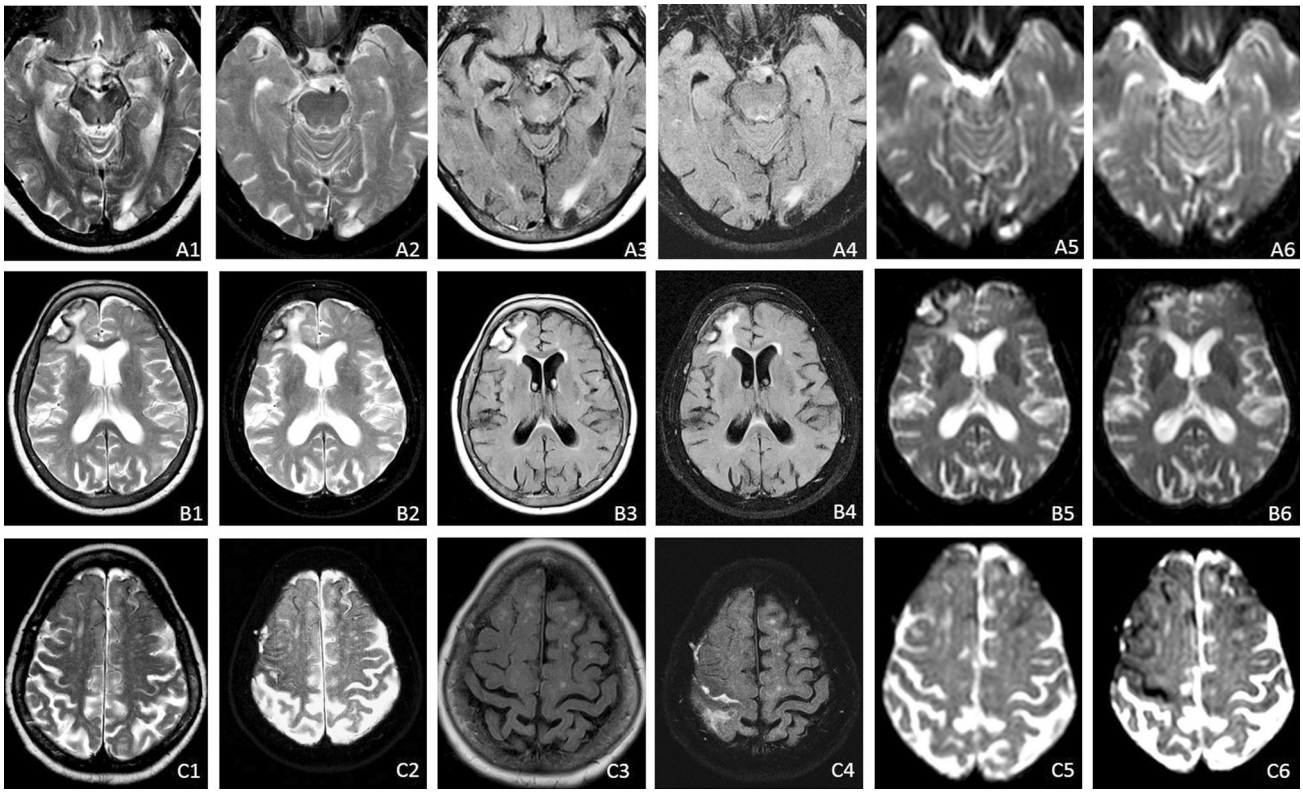

Fig. 1 The MR showed areas of pathologic signal, in left occipital lobe, suggestive of hemorrhage (**a1**–**a2** axial T2W; **a3**, **a4** FLAIR W; **a5**–**a6** ADC map images), in *right frontal lobe*, in different phases (**b1**, **b2** axial T2W; **b3**, **b4** FALIR W; **b5**, **b6** images ADC map), and a third known frontal convexity hemorrhage (**c1**, **c2** axial T2W; **c3**, **c4** FALIR W; **c5**, **c6** images ADC map)

gliosis) and cognitive impairment, including acute progressive dementia. Microinfarcts are predominantly lobar (cortical-subcortical), usually in patients with severe CAA. One possible mechanism for these ischemic lesions is occlusion or reduced perfusion in amyloid laden cortical vessels affected by CAA [3, 4]. CAA-related intracerebral hemorrhages (ICH) increased with age. Previous reports indicated that the incidence of ICH in patients with CAA increased after the age of 50 years. It had also been reported that 5 % occurred in the seventh decade, 43 % in the eighth decade, and 57 % in persons over 90 years old. Transient focal neurological episodes are recognized in cerebral amyloid angiopathy and may herald a high risk of intracerebral hemorrhage. Another characteristic clinical presentation associated with CAA, is the transient focal neurological episodes, termed "amyloid spells" [5]. The spells are typically brief and are characterized by recurrent, stereotyped episodes of 'positive' spreading sensory symptoms (paresthesia). The spells are related to hemorrhagic components of CAA, for example cortical microbleeds, cortical subarachnoid hemorrhage, or cortical superficial siderosis.

Our case represents a patient with typical events, that are the most important markers of CAA, that is a complex disease, which requires a careful evaluation of symptoms and neuroimaging findings. The GRE T2* sequence is less sensitive than the FLAIR sequence for the detection of acute subarachnoid hemorrhage (SAH) and parenchymal changes. The better lesion/tissue contrast achieved by the suppression of the signal intensity of cerebrospinal fluid on the FLAIR sequence, not only in the subarachnoid space, but also in the cerebral parenchyma, can be especially useful for the evaluation of CAA-related white matter lesions and SAH. In addition to these sequences, DW sequence, with apparent diffusion coefficient (ADC) maps can be useful to distinguish CAA-related silent infarctions from other white matter lesions, including vasogenic edema and leukoaraiosis [2–5]. In our patient, FLAIR sequence showed a new SAH recurred in the right rolandic cortical sulcus that would have gone hardly recognized without the execution of that sequence.

MR aspects, highly indicative of SAH due to CAA, allow the diagnosis, even in the absence of histopathological examination; for this type of disease the surgery is sometimes even contraindicated. So, for final diagnosis, an invasive brain biopsy is not required. A relationship between SAH convexity in elderly patient and CAA, in the absence of hypertension or risk factors for venous

thrombosis, could be considered the most likely etiology, in patients over 55 years. Moreover, MR GRE T2* and FLAIR W sequences, previous micro-hemorrhages, ICH and cortical superficial siderosis, support the diagnosis, and a non-invasive diagnostic approach to patient. Therefore, it is necessary to combine with other CAA-related imaging findings for the diagnosis. Amyloid PET can be an important clue to differentiate CAA from other disease, such as hypertension, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy and bleeding diatheses, which cause similar and mistakable hemorrhagic imaging findings.

Computed tomography is the imaging study of choice for evaluation of suspected acute cortical hemorrhage, which may be accompanied by subarachnoid, subdural, or intraventricular hemorrhage. Magnetic resonance imaging is best suited for identification of small or chronic cortical hemorrhages and ischemic sequelae of this disease, exclusion of other causes of acute cortical-subcortical hemorrhage, and assessment of disease progression. MR GRE T2*W images is the best technique for diagnosis of CAA with identification of ICH, SAH and hemosiderosis in elderly patients, that have become the main marker of this disease, with a good correlation with histological findings, even without performing an invasive brain biopsy.

Compliance with ethical standards

Conflict of interest Patients gave consent for treatment and use of figures and cases. None of the authors has any financial interest in the materials and methods used, nor in any of the manufacturers mentioned in this report.

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