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CORRESPONDENCE

Teaching Neuroimages: Inflammatory CAA

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Inflammatory cerebral amyloid angiopathy (CAA) includes a spectrum of inflammatory diseases with similar clinical and imaging features, e.g. CAA-related inflammation (CAA-ri) and Aβ-related angiitis (ABRA). The CAA-ri is histologically characterized by focal accumulation of amyloid-β (Aβ) in leptomeningeal and parenchymal blood vessels associated with segmental perivascular inflammatory infiltrates and ABRA by the presence of intramural granulomas and regions of vessel wall destruction [1, 2]. Patients with inflammatory CAA typically present with rapid cognitive decline, focal neurologic deficits, headache, and/or seizures. Diagnostic criteria have recently been proposed for CAA-ri (Table 1; [5, 6]). The differential diagnosis of inflammatory CAA includes posterior reversible encephalopathy syndrome (PRES), acute disseminated encephalomyelitis (ADEM), reversible cerebral vasoconstriction syndrome (RCVS), chronic hypertensive encephalopathy, primary angiitis of the central nervous system (PACNS), autoimmune encephalitis, malignancies (such as primary neoplasms, CNS lymphoma and carcinomatous meningitis) and infections (especially progressive multifocal leukoencephalopathy). Inflammatory CAA is characterized by patchy or confluent T2 or fluid attenuation inversion recovery (FLAIR) hyperintensity which is usually asymmetric with or without leptomeningeal or parenchymal enhancement on magnetic resonance (MR) imaging. Infarcts are lacking and the edema is confluent, differentiating it from PACNS. Vascular imaging findings can also help differentiate PACNS and inflammatory CAA where PACNS can produce a pattern of multifocal narrowing and irregularity of middle to distal cerebral arteries. The edema can be unifocal or multifocal but is typically asymmetric when multifocal, distinguishing it from PRES [5]. Chronic hypertensive encephalopathy, also known as

Table 1 Proposed diagnostic criteria for CAA-related inflammation. (From Chung et al. [6])

Probable CAA-ri (all of the following)
1. Acute or subacute onset of symptoms
2. 40 years of age or older
3. At least one of the following clinical features: headache, mental status or behavioral changes, focal neurological signs, and seizures
4. MRI shows patchy or confluent T2 or fluid attenuation inversion recovery hyperintensity which is:
(a) Usually asymmetric
(b) With or without mass effect
(c) With or without leptomeningeal or parenchymal enhancement
5. Evidence of pre-existing CAA on susceptibility-weighted MRI sequences:
(a) Multiple cortical and subcortical hemorrhages or microhemorrhages and/or
(b) Recent or past lobar hemorrhage
6. Absence of neoplastic, infectious, or other causes
Definite CAA-ri (all of the above plus histopathological confirmation with)
1. Perivascular, transmural, and/or intramural inflammation
2. Amyloid deposition within vessels of affected area in the cortex and leptomeninges

CAA-ri CAA-related inflammation

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Table 2 Summary of demographic data, clinical and MRI findings in three cases of CAA-ri and in one case of ABRA

Age (years), gender	CSF	Clinical presentation	Pathologic diagnosis	MRI findings
52, male	NA	Focal impaired awareness	CAA-ri	Multifocal subcortical edema with U-fiber involvement Cortical and subcortical microbleeding Faint leptomeningeal contrast enhancement
73, male	NA	Nonconvulsive status epilepticus for 6 days Worsening of baseline cognitive impairment EEG: right centroparietal sharp waves	CAA-ri	Biparietal subcortical edema with U-fiber involvement Cortical and subcortical microbleeding Faint leptomeningeal contrast enhancement
76, male	OP: normal, Pr: 504 mg/l, WC: 0, lactate in CSF: normal	Transient focal neurological episode (TFNE) with temporary dysphasia Focal impaired awareness EEG: NA	CAA-ri	Right parietal subcortical edema with U-fiber involvement Right parietal hemorrhage Right parietal enhancing lesion Cortical and subcortical microbleeding
75, female	OP: normal, Pr: 499 mg/l, WC: 0, lactate in CSF: 20.40 mmol/l	New organic psychosyndrome Acute onset aphasia Left-sided weakness	ABRA	Right parietal subcortical edema with U-fiber involvement Right leptomeningeal enhancement Enhancing basal ganglia lesions SWI/T2*: NA

NA not available, *OP* opening pressure, *Pr* protein, *WC* white cells, *EEG* electroencephalography, *CAA-ri* CAA-related inflammation, *ABRA* Aβ-related angiitis, *CSF* cerebrospinal fluid, *MRI* magnetic resonance imaging, *SWI/T2** susceptibility-weighted imaging/T2* sequences

hypertensive microangiopathy, can be excluded based on patient history, examination, and imaging studies, which typically results in microhemorrhages in the basal ganglia, pons, and cerebellum. Vascular and nonvascular imaging findings can help differentiate inflammatory CAA and RCVS. The RCVS is a clinical and radiologic syndrome characterized by the hyperacute onset of severe headache and reversible segmental vasoconstriction of the cerebral arterial vasculature with either normal neuroimaging study or watershed infarct/vasogenic edema, differentiating it from inflammatory CAA [7]. This article describes the magnetic resonance imaging (MRI) spectrum in three men with histologically verified CAA-related inflammation and one woman with ABRA (Table 2) (Fig. 1). The MRI shows multifocal subcortical edema with U-fiber involvement (Figs. 2 and 3). It also shows multiple cortical and subcortical microbleeds (Figs. 2, 3 and 4); however, only some areas with microbleeding show subcortical edema. There is faint leptomeningeal contrast enhancement in all patients (Figs. 2, 3 and 5). Interestingly and not unreported, one patient with a CAA-ri showed an enhancing parenchymal lesion (Fig. 4) and the ABRA patient also showed enhancing basal ganglia lesions (Fig. 5; [2–4]). Characteristic are a subcortical edema with U-fiber involvement in regions with microbleeding and a faint leptomeningeal enhancement. The parietal lobes are preferentially involved. CAA-related inflammation and ABRA cannot be distinguished clinically or on MRI. If the enhancing basal ganglia lesions found in patients with pathologically confirmed CAA-ri, since the basal ganglia are tipically devoid of amyloid, PCNSV should be considered in the differential diagnosis. In the latter case, PACNS is a relevant differential diagnosis.

Conflict of interest I.E. Duman, V.A. Coenen, S. Doostkam and H. Urbach declare that they have no competing interests.

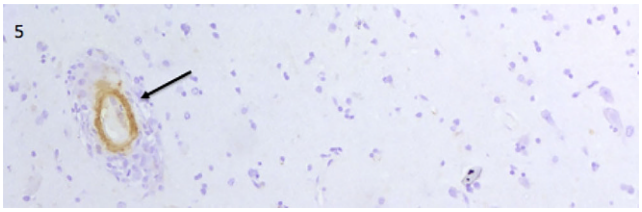

Fig. 1 Photomicrograph of brain specimen (amyloid β, ×200) stained with an antibody to Aβ. Brown stain corresponding to ring-like Aβ deposition (*black arrow*) in the vessel wall consistent with CAA

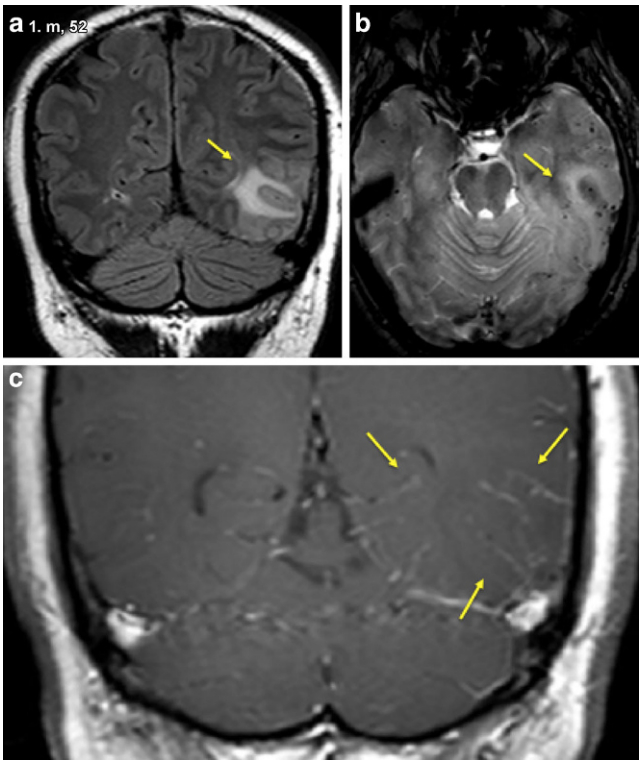

Fig. 2 52-year-old man with CAA-related inflammation (case 1). Coronal FLAIR (**a**) imaging with multifocal subcortical oedema with U-fiber involvement (*yellow arrows*), axial susceptibility-weighted (**b**) imaging with multiple bilateral cortical-subcortical microbleeds (*yellow arrows*), and coronal contrast-enhanced spin-echo T1-weighted (**c**) imaging with faint leptomeningeal contrast enhancement (*yellow arrows*)

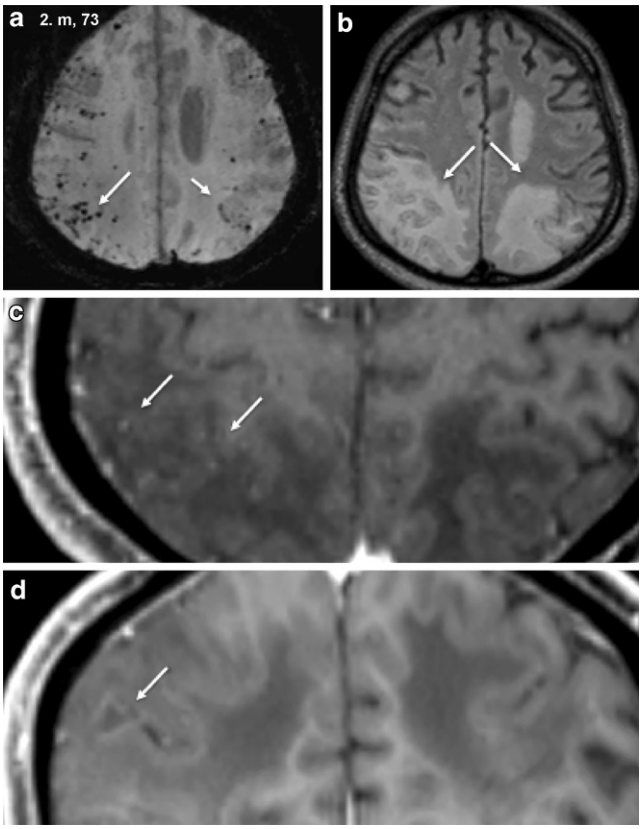

Fig. 3 73-year-old man with CAA-related inflammation (case 2). Axial susceptibility-weighted (**a**) imaging with multiple bilateral cortical-subcortical microbleeds (*white arrows*), axial FLAIR (**b**) imaging with bi-parietal subcortical oedema with U-fiber involvement (*white arrows*), axial (**c**) and coronal (**d**) contrast-enhanced spin-echo T1-weighted images with faint leptomeningeal contrast enhancement (*white arrows*)

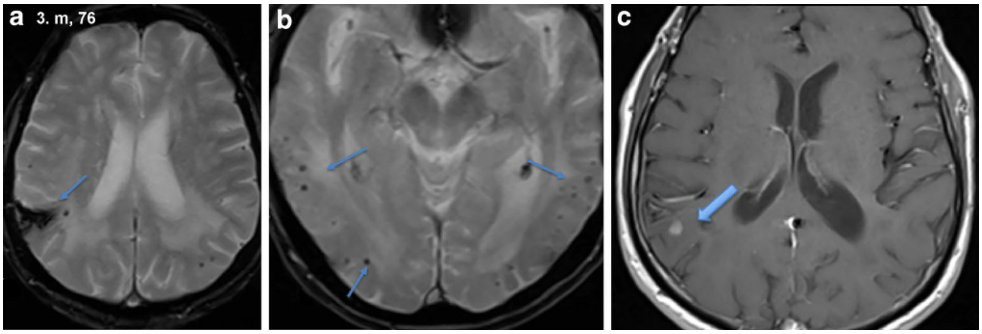

Fig. 4 76-year-old man with CAA-related inflammation (case 3). Axial T2*-weighted gradient echo images (**a**, **b**) show right parietal hemorrhage and multiple bilateral microbleeds (*blue arrows*) with right parietal subcortical oedema. Axial contrast-enhanced spin-echo T1-weighted MR image (**c**) shows right parietal enhancing lesion (*blue thick arrow*)

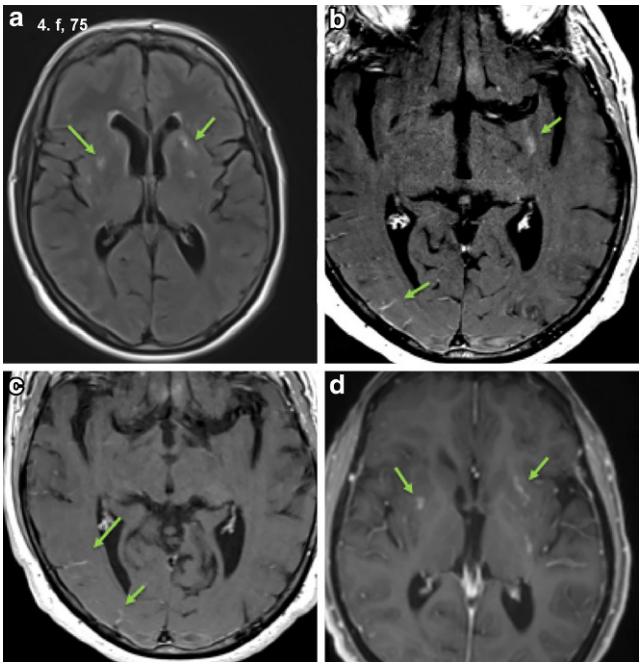

Fig. 5 75-year-old female with amyloid β–related angiitis (case 4). Axial FLAIR (**a**) imaging with multiple FLAIR hyperintense lesions (*green arrows*). Axial contrastenhanced spin-echo T1-weighted (**b–d**) MR images show right leptomeningeal enhancement and enhancing basal ganglia lesions (*green arrows*)

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