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ORIGINAL ARTICLE

Cerebral amyloid angiopathy-related inflammation: A potentially reversible cause of dementia with characteristic imaging findings

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Summary
Background and purpose: Cerebral amyloid angiopathy with inflammation (CAA-I) is a less well-recognized clinically and radiologically distinct subtype of CAA. We aim to describe the imaging manifestations of this uncommon entity.
Materials and methods: A retrospective review of the medical records and imaging database yielded 9 patients with clinical and radiological findings compatible with CAA-I. The neurological findings at presentation, MRI findings including the presence of white matter involvement, mass effect, microhemorrhages and contrast enhancement, treatment provided and outcome were evaluated. Brain biopsy specimens, when available were also reviewed.
Results: All patients presented with subacute cognitive decline. In all 9 patients, confluent white matter lesions with mass effect were observed. Eight out of 9 patients demonstrated foci of microhemorrhage, while in 1, the microhemorrhages appeared 12 weeks after the initial examination. No significant parenchymal or meningeal enhancement was present in any patient. In 4 patients, brain biopsy was consistent with CAA-I. Immunosuppressive therapy was initiated in all patients, leading to full recovery in 5.

Abbreviations: CAA, cerebral amyloid angiopathy; CAA-I, inflammatory cerebral amyloid angiopathy; PACS, Picture Archiving and Communication System; ADL, activities of daily living.

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Conclusion: CAA-I is characterized by the subacute onset of dementia, a distinct pattern of confluent white matter signal abnormality with mass effect and response to immunosuppressive therapy. Prompt recognition may help obviate brain biopsy and initiation of treatment.

Introduction

Amyloid is an eosinophilic, insoluble, extracellular protein, first discovered in the brain in 1909. Cerebral amyloid angiopathy (CAA) is a disorder characterized by amyloid deposition in the tunica media and adventitia of the walls of leptomeningeal and cortical arteries and arterioles [1]. CAA is a frequent pathological finding in the elderly, present in 10—40% of elderly brains and in >80% of brains with concomitant Alzheimer's dementia [2,3]. It is estimated to be present in 2.3% of 65—74 year-old brains, 8% of 75—84 year-old brains and 12.1% of >85 year-old brains [4]. The disease is classically diagnosed by the yellow-green birefringence of amyloid protein on Congo red staining of pathological specimens under polarization microscopy. Amyloid deposition within the vessel walls leads to loss of elasticity and increased fragility resulting in a tendency to rupture and bleed more frequently [5].

The clinical course of CAA is very variable with no pathognomonic features. Cognitive decline is well described and focal neurological deficits may ensue due to hemorrhage or infarction [2]. The radiological signs of CAA are also non-specific. Microhemorrhages, best detected on susceptibility-weighted sequences [5,6], lobar intraaxial hemorrhage [7], subarachnoid hemorrhage and superficial siderosis [8,9], are all well described as radiological features of CAA [10].

A less well-known feature of CAA is white matter involvement, either patchy and ill-defined or confluent, and even tumefactive and mass-like [11—13], an entity termed CAA associated inflammation (CAA-I). CAA-I presents with subacute cognitive decline and is important to recognize because its symptoms may be reversible with immunosuppressive therapy [14]. The mass-like appearance of white matter abnormalities in CAA-I often leads to a misdiagnosis of neoplasm, which is why, traditionally, CAA-I is a histopathology diagnosis. In this work, we aim to describe the characteristic radiological features of CAA-I that, in the correct clinical setting, are specific enough to avoid brain biopsy.

Materials and methods

Institutional review board approval was obtained and the requirement for informed consent was waived in this HIPAA compliant retrospective study. Nine patients (2 M, 7 F; age range: 60—87; median age: 75) with a suspected diagnosis of CAA-I in the period between 01/01/2005 and 12/31/2014 were identified using the PACS and dictation systems. All patients had one or more MRI brain studies on 1.5 T or 3 T systems. Sequences obtained included T1 pre- and post-contrast, T2, FLAIR, diffusion, susceptibility imaging, or gradient echo. The type and extent of any white matter abnormality present on imaging was reviewed and described. Hemorrhagic foci were assessed on gradient echo (Siemens, Erlangen, Germany, Magnetom TrioTim syngo MR TR 620 ms, TE 20 ms, FA 20 degrees, slice thickness 4 mm, FOV read 220 mm, FOV phase 100%, base resolution 256) or susceptibility-weighted images (Siemens, Erlangen, Germany, Magnetom TrioTim syngo MR, parameters — TR 27 ms, TE 20 ms. FA 15 degrees, slice thickness 1.5 mm, base resolution 256, bandwidth 120 Hz/Px, FOV read 230 mm, FOV phase 75%, Integrated Parallel Acquisition [IPAT] factor-2). The electronic medical records were reviewed for demographic data, clinical presentation, treatment and outcomes. The use of steroids or immunosuppressants as treatment for CAA was recorded.

Results

Diagnosis of CAA

CAA-I was confirmed on brain biopsy in order to definitively exclude a neoplasm in four patients. These patients were deemed to be in the category ''probable CAA with supporting pathological evidence'' described by the Boston criteria for CAA [15]. In the other five patients, a combination of MRI brain findings (confluent white matter abnormality with mass effect, multiple microhemorrhages, intracranial hemorrhage, subarachnoid hemorrhage [10]) and clinical features (subacute cognitive decline, personality change) strongly suggested the diagnosis of CAA, but no brain biopsy for neuropathological confirmation of the diagnosis was obtained. However, reasonable differential diagnoses such as hypertensive encephalopathy, progressive multifocal leukoencephalpathy and vasculitis were considered and excluded based on their clinical, laboratory and radiological findings. All of these patients were diagnosed as ''probable CAA'' by the Boston criteria [15]. If one were to apply the modified criteria proposed by Chung et al., the four patients who underwent confirmatory biopsy would be categorized as ''definite CAA-I'', while the five that did not would meet the criteria required for ''probable CAA-I'' [13]. One patient had an established clinical diagnosis of Alzheimer's disease. APO-E4 status was not available in any of the nine patients.

Microhemorrhages

Microhemorrhages were present in 8/9 patients at presentation. In one patient, they were undetectable at presentation but appeared on follow-up examination after 12 weeks. Microhemorrhages tended to colocalize with the areas of abnormal white matter signal discussed below. None of the patients presented with a lobar hemorrhage. In four patients, superficial siderosis was present.