Acute Convexity Subarachnoid Hemorrhage Related to Cerebral Amyloid Angiopathy: Clinicoradiological Features and Outcome

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Background: The specificities of acute convexity subarachnoid hemorrhage (cSAH) related to cerebral amyloid angiopathy (CAA) and its evolution are not well known. We aimed to describe the clinicoradiological pattern, the magnetic resonance imaging (MRI) evolution, and the risk of recurrent bleeding in such patients. *Methods:* Among consecutive patients with an acute nontraumatic cSAH, subjects with available MRI who meet the modified Boston criteria for probable CAA were included. Review of medical records, MRI findings, and follow-up data was performed. *Results:* Twenty-three patients (14 women; mean age ± standard deviation: 75.9 ± 7.3 years) were included. cSAH was revealed by transient focal neurological episodes (TFNEs) in 18 of 23 (78.3%) patients. In all patients, acute cSAH appeared as a sulcal fluid-attenuated inversion recovery hyperintensity and GRE T2 hypointensity. Cortical superficial siderosis and cortical microbleeds, respectively, were observed in 21 (91.3%) and 20 (86.9%) patients. Twenty patients (87%) had available follow-up data with a mean duration of 29.8 ± 20.2 months. Recurrent TFNEs occurred in 40% of patients. Acute cSAH evolved into cortical superficial siderosis in all patients. New subarachnoid bleedings defined by recurrent acute cSAH (n = 8) or extension of siderosis (n = 14) were detected in 83.3% of the patients. Lobar intracerebral hemorrhage (ICH) occurred in 7 patients (35%). *Conclusion:* CAA-related cSAH has a specific pattern defined by a high prevalence of TFNEs and cortical superficial siderosis, with a high risk of recurrent bleeding, either cSAH or lobar ICH. The systematic evolution from cSAH to focal cortical superficial siderosis reveals data on siderosis physiopathology. **Key Words:** Cerebral amyloid angiopathy—convexity subarachnoid hemorrhage—superficial siderosis—magnetic resonance imaging.

Sporadic cerebral amyloid angiopathy (CAA) is an age-related common small-vessel disease. In a pathological study, prevalence of CAA reached 50% among patients older than 70 years and 70% among patients older than 90 years[1] (and up to 100% in patients with Alzheimer's disease).[2] CAA is characterized by amyloid-β deposition in the wall of medium and small cortical and meningeal arteries, leading to loss of smooth muscle cells then detachment and delamination of the outer part of the tunica media, fibrinoid necrosis, and microaneurysm formation. The main hypothesis to explain this phenomenon is an impairment of amyloid-β clearance along perivascular drainage pathways.[3] The rupture of these

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abnormally weak, amyloid laden vessels induces both lobar intracerebral hemorrhage (ICH) and cortical cerebral microbleed (CMB), included in the Boston criteria.[4] Thus, CAA is a major cause of lobar ICH in the elderly.[3]

Cortical superficial siderosis (cSS) is characterized by the chronic deposition of hemosiderin in the superficial layers of the cortex. Because of its high prevalence (ranging from 40% to 70%) among CAA patients in imaging and neuropathological studies,[5,6] cSS is now included in the modified Boston criteria.[7] More recently, acute convexity subarachnoid hemorrhage (cSAH) has also been identified in patients with CAA.[8-11] cSAH demonstrates a distinct pattern of subarachnoid bleeding, in which blood is localized in the convexity of the brain, sparing the basal cisterns, sylvian fissures, and ventricles.[12] Various etiologies of cSAH have been described including vasoconstriction syndrome, endocarditis, carcinomatous meningitis, coagulation disorders, cortical vein thrombosis, small arteriovenous fistulae or pial malformations, vasculitis, cervical or intracranial occlusion, or severe stenosis.[10] In young patients, headaches seem to be the most common clinical presentation with vasoconstriction syndrome as the most frequent etiology. Conversely, in patients older than 60 years, several case series have linked cSAH to underlying CAA with a typical clinical presentation of single or recurrent transient focal neurological episodes (TFNEs), also termed "amyloid spells."[9,10,13-19] The high prevalence of cSS among CAA-related cSAH patients and the high prevalence of TFNE in CAA patients with either cSAH or cSS suggest a link between cSAH and cSS.[10,14,20] However, the natural history of cSAH is likely related to CAA, and the risk of recurrent hemorrhage in these patients has not been well established in detail. The evolution from acute cSAH through cSS has not been systematically assessed.

In the present study, among a cohort of patients with probable CAA-related cSAH, we aimed to (1) describe the clinicoradiological pattern of cSAH; (2) assess the magnetic resonance imaging (MRI) evolution of acute cSAH; and (3) evaluate the risk of recurrent bleeding.

Materials and Methods

Patients

Using our clinical and radiological database we retrospectively identified patients admitted to our institution with acute cSAH. cSAH was defined as a hemorrhage restricted to one or several sulci at the convexity of the brain without recent bleeding in the parenchyma, sylvian fissure, basal cisterns, or ventricles. Traumatic causes were excluded. Patients underwent a systematic workup that typically consisted of brain CT, CTA and MRI, or MRI only. Digital subtraction angiography was performed in 5 patients to exclude a vascular malformation or to confirm cerebral vasoconstriction syndrome, because diagnosis was not obtained by noninvasive examinations. Various diagnoses were established according to published criteria.[12]

Patients were included in the present study if they had available brain MRI demonstrating an acute cSAH and if they met Boston criteria for probable CAA.[7]

Data Collection

Database and medical records were used for demographics, vascular risk factors, clinical presentation, and follow-up information.

TFNEs were defined according to published criteria[14]: a clinical episode of transient focal neurological symptoms including numbness/tingling, weakness, dysarthria, or aphasia lasting for several minutes to 1 hour with subsequent complete resolution. Alternative explanations other than CAA such as ischemia related to atrial fibrillation or artery stenosis, structural brain lesions, and metabolic disorders (e.g., hypoglycemia) were excluded during the initial workup.

Neither institutional review board approval nor informed patient consent was required by the ethics committee of our institution for retrospective analysis of the patients' medical records and imaging data acquired as part of routine clinical care.

Neuroimaging

Magnetic resonance (MR) images were acquired on either 1.5-T Philips Intera (Philips Research, Eindhoven, The Netherlands) or Avanto Siemens (Erlangen, Germany). MRI included at least fluid-attenuated inversion recovery (FLAIR), GRE T2* (Repetition Time (TR) = 917 millisecond, Echo Time (TE) = 26 millisecond, slice thickness = 5 mm, Field of View (FOV) = 230 mm, matrix = 320 × 240), and diffusion-weighted sequences. T1-weighted imaging before and after intravenous administration of gadolinium (.1 mmol/kg body weight of Dotarem; Guerbet, Villepinte, France) was performed in most patients.

MRI scans were reviewed by 2 experienced neuroradiologists (V.C. and F.B.) blinded to clinical data.

Acute cSAH was defined as hyperintensity filling one or more cortical sulci of the cerebral convexities on FLAIR images with corresponding hypointensity on GRE T2* sequences. cSS was defined as superficial hypointense signals on both sides of supratentorial sulci giving a track-like appearance on GRE T2* images without corresponding hyperintense signal FLAIR images. The distribution of cSS and acute cSAH was classified as focal (restricted to ≤3 sulci) or disseminated (≥4 sulci).

The presence and number of chronic ICH (>5 mm in diameter) and CMB (≤5 mm in diameter) were noted.

White matter hyperintensities were assessed with the Fazekas and Schmidt rating scale.[21]

Statistical Analysis

At baseline, the patients were classified according to the presence of cSS, the extension of cSS (focal or