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The clinical and neuroradiological features of patients of coexisting atraumatic convexity subarachnoid hemorrhage and large artery atherosclerosis stroke

A retrospective observational study

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Abstract

Atraumatic convexity subarachnoid hemorrhage (c-SAH) concomitant with large artery atherosclerosis (LAA) stroke has been rarely discussed in the literature. Our aim in this study is to characterize the clinical and neuroradiological features of patients with LAA stroke and c-SAH.

A retrospective study from a single institution was performed between January 2016 and June 2020. Only patients diagnosed with c-SAH and LAA stoke were included in this study. The clinical presentation and neuroimaging finding were summarized by our experienced neurologists.

In total, 12 patients (8 men, 4 women), ranging in age from 45 to 75 years, were identified. All of them had cardiovascular risk factors and hypertension was the commonest (50%). Almost all patients presented hemiparesis (91.7%). Other clinical presentations included, dysarthria (41.7%), hemianesthesia (33.3%), facial palsy (33.3%), aphasia (16.7%), and cognitive impairment (8.3%). Internal border-zone (IBZ) infarction and cortical border-zone (CBZ) infarction occurred in 12 and 3 patients, respectively. c-SAH might occurred in different cortical sulcis. Percentages of frontal lobe, parietal lobe and fronto-parietal lobe were 41.7% (n = 5), 25% (n = 3) and 25% (n = 3), respectively. All ischemic lesions were ipsilateral to the sites of c-SAH. High-grade atherosclerotic stenosis of large artery was detected in all patients. The M1 segment of middle cerebral artery (MCA) is the second most common atherosclerotic artery after internal carotid artery (ICA).

Our data suggest that LAA stroke is always ipsilateral to the site of c-SAH. Severe atherosclerotic changes can also been seen in the M1 segment of MCA apart from extracranial ICA. Moreover, border zone infarction may be a specific form of infarct when c-SAH is confronted with LAA stroke.

Abbreviations: AIS = acute ischemic stroke, CAA = cerebral amyloid angiopathy, CBZ = cortical border-zone, c-SAH = convexity subarachnoid hemorrhage, CT = computed tomography, DSA = digital subtraction angiography, DWI = diffuse-weighted imaging, IBZ = internal border-zone, ICA = internal carotid artery, LAA = large artery atherosclerosis, MCA = middle cerebral artery, MRI = magnetic resonance imaging, PRES = posterior reversible leukoencephalopathy syndrome, RCVS = reversible cerebral vasoconstriction syndrome.

Keywords: atraumatic convexity subarachnoid hemorrhage, border-zone infarction, internal carotid artery, large artery atherosclerosis, middle cerebral artery

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This study was approved by the ethics committee of Jiangxi Provincial People's Hospital Affiliated to Nanchang University. A written informed consent form was obtained from each study participant.

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Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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1. Introduction

Atraumatic convexity subarachnoid hemorrhage (c-SAH), an unusual form of subarachnoid bleeding with a low prevalence ranging from 3% to 6%, is confined to the convexities of the brain without involvement of the adjacent parenchyma, sylvian fissures, basal cisterns, or ventricles.[1–3] Diverse etiologies, including cerebral amyloid angiopathy (CAA), reversible cerebral vasoconstriction syndrome (RCVS), posterior reversible leukoencephalopathy syndrome (PRES), cortical vein occlusions, coagulopathy, cocaine use, lupus vasculitis, cavernoma and brain abscesses, have been proposed for its occurrence.[2] Kumar et al. suggested RCVS and CAA were the 2 most common etiologies for c-SAH. CAA was the commonest cause in patients >60 years old, and RCVS in those <60 years old.[3] Although the coexistence of c-SAH and acute ischemic stroke (AIS) has been increasingly described in case reports, the underlying mechanism of this association is not well understood.[4,5] In previous case series of c-SAH concomitant with AIS, nearly half of patients had severe stenosis or occlusion of large arteries.[5] The most common symptom of c-SAH is headache, but the frequency of headache is low in c-SAH with ischemic stroke. Therefore, asymptomatic c-SAH might always be overlooked in AIS patients. In order to detect recurrent stroke or hemorrhagic complications, it is necessary to perform a repeated computed tomography (CT) or magnetic resonance imaging (MRI) examination. Previously, the clinical characteristics, mechanism, imaging features of c-SAH with AIS are not well elucidated. In the present study, we aimed to characterized the clinical and neuroradiologic features of patients of coexisting c-SAH and large artery atherosclerosis (LAA) stroke.

2. Materials and methods

2.1. Patient selection and definition of c-SAH

This study was approved by the ethics committee of Jiangxi Provincial People's Hospital Affiliated to Nanchang University. Patients were prospectively screened from the electronic case database at Jiangxi Provincial People's Hospital Affiliated to Nanchang University between January 2016 and June 2020. Only patients with concomitant c-SAH and LAA stroke were included in this study. LAA stroke were fulfilled with the criteria as follows:

1. the clinical features met the criteria of cerebral infarction;
2. diffusion-weighted imaging (DWI) showed an acute infarction;
3. ischemic stroke with significant (>50%) stenosis of the large cerebral artery by angiography according to the TOAST classification.

c-SAH was defined as the hemorrhage restricted to ≥1 adjacent cortical sulci at the convexity of the brain without involvement of the adjacent parenchyma or extension into the interhemispheric fissures, basal cisterns, or ventricles. c-SAH due to CAA, RCVS, PRES, aneurysm, thrombolysis, endovascular treatment, cortical vein occlusions, coagulopathy, cocaine use, lupus vasculitis, cavernoma, and brain abscesses were excluded. All patients underwent both brain CT and magnetic resonance imaging (MRI) on admission. Besides, those patients routinely underwent follow-up CT or MRI during the hospital stay to detect recurrent stroke as well as hemorrhagic complications. As the aim of this study was to assess acute c-SAH in LAA stroke patients, c-SAH was detected 14 days or more after admission were excluded. c-SAH was detected by CT and susceptibility-weighted imaging (SWI).

2.2. Data collection and evaluation

Clinical data, including demographics (gender and onset age), cardiovascular risk factors, clinical presentations, National Institute of Health Stroke Scale score, and radiological findings (site of infarct lesion, site of c-SAH and the responsible parent artery), were independently collected by 2 of our authors (YS and JC). Risk factors for stroke were defined as:

1. hypertension, systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg during the hospitalization, previously diagnosed hypertension or previously treated hypertension;
2. diabetes mellitus, use of oral hypoglycemic agents or insulin, or glycosylated hemoglobin level (National Glycohemoglobin Standardization Program) ≥6.5%;
3. dyslipidemia, use of cholesterol-lowering drugs, or serum low-density lipoprotein-cholesterol >140 mg/dL;
4. Drinking, defined as having a history of chronic alcoholism for 10 years; and
5. smoking, defined as having smoked at least 10 cigarettes daily for at least 2 years. CT angiography or digital subtraction angiography was utilized to evaluate extracranial and intracranial vascular status.

The site of arterial stenosis was divided into the extracranial internal carotid artery (ICA), the intracranial ICA, and the middle cerebral artery (MCA). Clinical presentation and the National Institute of Health Stroke Scale scoring (NIHSS) were documented at the time of admission.

2.3. Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (version 21.0, IBM, Armonk, NY). Descriptive statistics were reported using percentages for categorical variables, and mean ± standard error (SE) for continuous variables.

3. Results

3.1. Clinical presentation

The clinical summary of included cases was demonstrated in Table 1. The included 12 patients had an average age of 64.2 ± 8.7 years (age range: 45–75 years), and proportion of males was 66.7% (8 males). All patients had cardiovascular risk factors, including hypertension (n = 6/12, 50%), smoking (n = 5/12, 41.7%), diabetes mellitus (n = 5/12, 41.7%), hyperlipemia (n = 4/12, 33.3%), and drinking (n = 3/12, 25%). On admission, all patients presented with neurological symptoms. The overwhelming majority of the included patients presented with hemiparesis (n = 11/12, 91.7%). Other clinical presentations included, dysarthria (n = 5/12, 41.7%), hemianesthesia (n = 4/12, 33.3%), facial palsy (n = 4/12, 33.3%), aphasia (n = 2/12, 16.7%), and cognitive impairment (n = 1/12, 8.3%). The average scores of NHISS on admission was 5.8 ± 3.0 (range: 3–12 scores).

3.2. Radiological findings

The neuroradiological features of included 12 patients were characterized in Table 1. In these patients, c-SAH that was confirmed by CT and SWI might occurred in different cortical sulcis (Fig. 1C, Fig. 2B-C). Percentages of frontal lobe, parietal

Table 1

Clinical and neuroradiological findings of 12 patients with c-SAH and LAA stroke.

Demographics	
Age (yr)	64.2±8.7
Male gender	8 (66.7%)
Cardiovascular risk factor	
Smoking	5 (41.7%)
Drinking	3 (25%)
Hypertension,	6 (50%)
Hyperlipidemia	4 (33.3%)
Diabetes mellitus	5 (41.7%)
Clinical presentation	
Hemiparesis	11 (91.7%)
Dysarthria	5 (41.7%)
Hemianesthesia	4 (33.3%)
Cognitive impairment	1 (8.3%)
Facial palsy	4 (33.3%)
Aphasia	2 (16.7%)
Neurological deficit	
NIHSS score	5.8±3.0
Infarction location	
IBZ	12 (100%)
CBZ	3 (25%)
BG	4 (33.3%)
Site of c-SAH (lobe)	
Frontal lobe	5 (41.7%)
Parietal lobe	3 (25%)
Fronto-parietal lobe	3 (25%)
Responsible parent artery	
Extracranial ICA	8 (66.6%)
M1 segment of MCA	4 (33.3%)

BG = basal ganglia, CBZ = cortical border-zone, c-SAH = convexity subarachnoid hemorrhage, IBZ = internal border-zone, ICA = internal carotid artery, M = male, MCA = middle cerebral artery, NIHSS = National Institute of Health Stroke Scale (NIHSS).

lobe and fronto-parietal lobe were 41.7% (n=5), 25% (n=3) and 25% (n=3), respectively. c-SAH occurring in parietal-occipital lobe was observed in only 1 case. After carefully scanning DWI, it was not difficult to find that the sites of infarction were almost distributed in border zone. All patients had cigar-shaped or rosary-like infarction in the corona radiata and centrum semiovale, which were in accordance with internal border-zone (IBZ) infarction (Fig. 1B, Fig. 2A). Moreover, 3 patients had scattered and dot-like ischemic lesions in the cortical territories between MCA and posterior cerebral artery, which were consistent with cortical border-zone (CBZ) (Fig. 1A). In addition, basal ganglia infarct was noted in 4 (33.3%) patients. CTA or digital subtraction angiography examination was performed to evaluate the severity of the stenosis in main arteries. All of the included patients had occlusion/severe stenosis of large artery. Eight and 4 patients had severe atherosclerotic changes in the extracranial ICA and the M1 segment of MCA, respectively (Fig. 1D, Fig. 2D). Occlusion or stenosis of a major artery was almost ipsilateral to the site of c-SAH in all included patients.

4. Discussion

Previous studies have been performed to investigate the association between c-SAH and AIS. In an retrospective study of 4953 patients with acute stroke or transient ischemic attacks, Nakajima et al found the incidence of c-SAH was estimated to be 0.14%.[5] Sato et al screened 382 AIS patients, c-SAH was identified within 4.5 hours of ischemic stroke onset in 2 patients (0.5%).[6] Hence, the occurrence rate of c-SAH is extremely low in AIS patients. However, another retrospective study reviewed 24 patients with c-SAH, 5 patients showed acute ischemic infarcts distant from the c-SAH.[3] It is suggested that there was a relatively high rate of AIS in patients with c-SAH.

Varies reasons for this association, such as RCVS, CAA, ICA stenosis or occlusion, artery dissection, and cardioembolism, have been proposed.[4,7,13–15] However, the underlying mechanism of this association is still unclear. Large artery occlusive disease causing c-SAH has been described previously.[8,9] Graff-Radford et al performed a retrospective study of 88 patients with c-SAH, 4 individuals had large artery diseases, which consist of carotid occlusion, MCA occlusion, and carotid dissection, and high-grade carotid artery stenosis.[10] Several explanations have been proposed for the association between carotid stenosis and c-SAH. The mainstream theory is that long-standing severe stenosis or occlusion of ICA results in rupture of dilated fragile collateral pal vessels, accompanied by emboli entering into marginally perfused vessels leading to necrosis and rupture.[8,11,12] Another possible explanation is that systemic disturbances, such as a sudden rise in blood pressure or a coagulation disorder in the predamaged vessels, may promote the occurrence of c-SAH.[3] The site of the severe stenosis or occlusion of large artery may occur both intracranially and extracranially, especially for

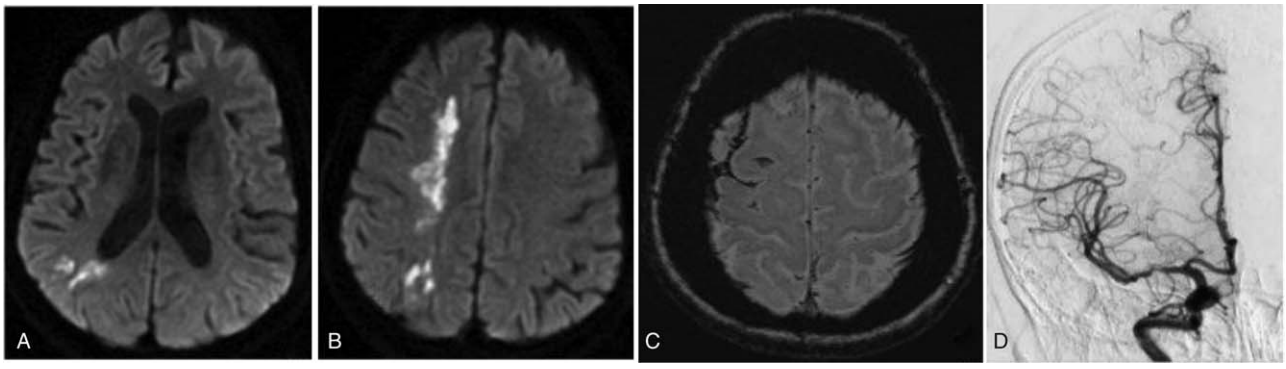

Figure 1. Axial DWI showed right cortical border-zone (CBZ) infarction between the territory of the middle cerebral artery (MCA) and the posterior cerebral artery (PCA) (A), and right internal border-zone (IBZ) infarction in the centrum semiovale (B). SWI demonstrated right frontal c-SAH (C). DSA revealed severe stenosis of the M1 segment of right MCA. DSA = digital subtraction angiography, SWI = susceptibility weighted imaging.

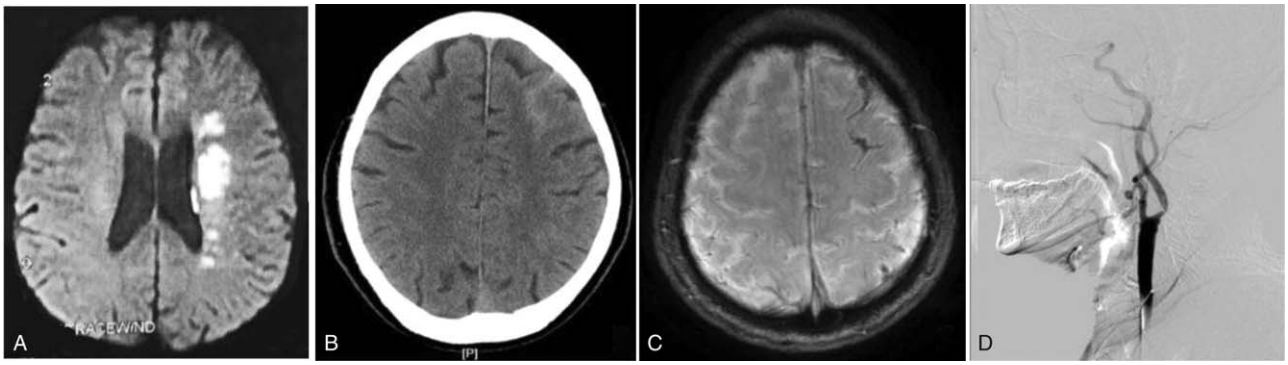

Figure 2. Axial DWI revealed left internal border-zone (IBZ) infarcts in the corona radiata (A). CT and SWI showed Left frontal c-SAH (B, C). DSA illustrated high-grade atherosclerotic stenosis of the C1 segment of the left internal carotid artery (ICA) (D).

extracranial segment of ICA.[11] Furthermore, the high-grade atherosclerotic artery is always ipsilateral to the site of c-SAH,[10] but rarely contralateral.[7] In our study, severe atherosclerotic changes can also been seen in the M1 segment of MCA apart from extracranial ICA. Moreover, LAA is always ipsilateral to the c-SAH. More large-scale prospective studies are needed to elucidate the association between c-SAH and LAA stroke.

Previously, the distribution characteristic of infarcts in patients with c-SAH has rarely been discussed. In current study, only patients with c-SAH and LAA stroke were included. Border zone infarction can occurred in all patients. To our knowledge, IBZ infarction is characterized by multiple lesions arranged in a linear fashion parallel to the lateral ventricle in the corona radiata or centrum semiovale. Compared with CBZ infarction, IBZ infarction are caused mainly by stenosis or occlusion of large artery, or hemodynamic compromise.[16] The IBZ is supplied by deep perforating lenticulostriate arteries and medullary penetrating vessels of the middle and anterior cerebral arteries. As the medullary penetrating arteries are the most distal branches of the ICA sharing the minimum perfusion and the deep perforating lenticulostriate arteries have rarely collateral circulation. When confronted with hemodynamic compromise, the centrum semiovale and corona radiata are more susceptible to ischemic insults. Perfusion studies have confirmed that paraventricular white matter is most vulnerable to hemodynamic compromise in patients with occlusive carotid artery diseases. In our study, the M1 segment of MCA is the second most common atherosclerotic artery after ICA. In contrast to patients with ICA diseases, the ischemic area might be smaller in patients with MCA disease. In addition, Combined CBZ and IBZ infarcts can also be found in 3 patients. Although the mechanism of CBZ infarction is controversial in previous studies, embolic mechanism plays a crucial role in the pathogenesis of CBZ infarcts. Large artery disease reduces cerebral perfusion resulting in impairment of the washing out of microemboli, which preferentially involves border-zone areas. According to the above-mentioned analysis, the border zone infarcts are the consequence of hemodynamic compromise and embolization. It is worth noting that those 2 main pathophysiological mechanisms are in accordance with the mainstream theory of LAA stroke concomitant with c-SAH.

In the setting of AIS associated with c-SAH, we can not ignore 2 major causes (RCVS and CAA). RCVS is well characterized by severe headaches, with or without other acute neurological symptoms. It has been reported predominantly in middle-age and the syndrome is more common in women.[14,17] Neuroradiological features of RCVS include c-SAH, intracerebral haemorrhage (ICH), cerebral infarction and PRES. Diffuse segmental vasoconstriction of cerebral arteries that resolves within 3 months confirms the diagnosis.[14,18] CAA, a common small vessel disease of the brain frequently in elderly, is characterized by progressive vascular amyloid-ß deposition in the cerebral cortex and leptomeninges. DWI-positive lesions were noted in about half of patients with CAA-related c-SAH. Lesions were mostly small, located in cortico-subcortical areas and often recurred on repeated MRI.[13,19]

Some limitations need to be acknowledged in our study. It was not possible to make statistical analysis due to the low number of cases. In addition, as this is a retrospective study, selection bias is unavoidable. To better evaluate the association between c-SAH and LAA stroke, a multicenter prospective study with larger sample sizes should be further performed.

In conclusion, LAA stroke is always ipsilateral to the site of c-SAH. Severe atherosclerotic changes can also been seen in the M1 segment of MCA apart from extracranial ICA. Border zone infarction may be a specific form of infarct when c-SAH is confronted with LAA stroke. Further investigations are needed to elucidate the precise mechanism and the association between c-SAH and LAA stroke.

Author contributions

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