Journal of
INTERNATIONAL MEDICAL RESEARCH

Incidence and possible causes of nontraumatic convexal subarachnoid haemorrhage in Chinese patients: A retrospective review

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Abstract

Objective: To explore the incidence and possible underlying pathogenic mechanisms of nontraumatic convexal subarachnoid haemorrhage (cSAH; a rarely reported condition) in a cohort of Chinese patients.

Methods: Medical records from all patients with subarachnoid haemorrhage (SAH) who had been treated at Peking University Third Hospital, China, between January 2010 and December 2014 were retrospectively reviewed to identify cases of cSAH.

Results: Of 144 patients with SAH, cSAH was observed in 14 cases (9.7%). The most frequent presenting symptoms in cSAH cases were severe headache ($n = 8$) and a focal neurological deficit ($n = 8$). The parietal (10/14 patients, 71.4%) and frontal (9/14 patients, 64.3%) lobes were the most common haemorrhage sites. Cause of cSAH was identified in 11 patients: in seven cases (50.0%), significant stenosis or occlusion in the internal carotid artery system, ipsilateral to cSAH, was reported; in four cases, cSAH was caused by cerebral venous sinus thrombosis, cerebrovascular malformation, anticoagulant therapy or possible cerebral amyloid angiopathy.

Conclusion: cSAH is an important subtype of nonaneurysmal SAH, with diverse aetiologies. In the present study, internal carotid artery system atherosclerotic stenosis was the most frequent cause of cSAH.

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Introduction

Nontraumatic convexal subarachnoid haemorrhage (cSAH) is an atypical presentation of subarachnoid haemorrhage (SAH), in which the haemorrhage is located in one or a few cortical sulci of the brain.[1] cSAH remains under-reported in the literature, and to the present authors' knowledge, there are currently no published systematic or comprehensive reviews of the topic.

Causes of cSAH are diverse, and other than aneurysm rupture, include cerebral amyloid angiopathy, reversible cerebral vasoconstriction syndrome, coagulopathy, cerebral venous thrombosis, vascular malformation, vasculitis, posterior reversible leukoencephalopathy syndrome, brain tumours and abscesses, bilateral internal carotid artery stenosis and drug misuse.[2–13]

In the present study, medical records from patients who had been diagnosed with SAH at Peking University Third Hospital, Beijing, China, between January 2010 and December 2014 were retrospectively reviewed to ascertain the prevalence of cSAH, to collate information regarding the main clinical and radiological presentations, and to determine possible underlying pathogenic mechanisms.

Patients and methods

This retrospective, observational cohort study included patients with cSAH, who were admitted to Peking University Third Hospital, Beijing, China between January 2010 and December 2014. The radiology reports of consecutive patients with SAH, who were admitted within the study period, were screened to identify patients with potential cSAH.[1] Eligible patients were ≥ 18 years-of-age and presented with hyperdensity exclusively in a cortical sulci identified by computed tomography (CT SOMATOM Definition Flash; Siemens Medical Systems; Erlangen, Germany) and/or a hyperintensity observed on fluid-attenuated inversion recovery magnetic resonance imaging (MRI; MAGNETOM Sonata™ system; Siemens Medical Systems, Erlangen, Germany), and hypointensity observed using gradient recalled echo T2*-weighted MRI sequences. Patients with traumatic haemorrhage and/or parenchymal bleedings that ruptured into the subarachnoid space were excluded. Medical records including hospital notes, laboratory data (comprising routine blood tests, blood biochemistry, coagulation function, autoimmunity and tumour-related tests), and imaging results (including plain CT, CT angiography, MRI, magnetic resonance angiography, magnetic resonance venography, and digital subtraction angiography) were reviewed. Data relating to patient demographics, clinical presentation, and outcome were documented and collated. Patient follow-up data up to 30 March, 2015 were also reviewed.

The study was approved by the institutional review board of Peking University Third Hospital (Approval No. 2013144). Patient informed consent was not considered to be required due to the retrospective, observational nature of the study.

Results

Of 144 patients identified with spontaneous SAH, 14 fulfilled the criteria for nontraumatic cSAH. Demographic and clinical characteristics are shown in Table 1 and Table 2. The study cohort consisted of 10 male and four female patients (median age, 62 years [range 19–87 years]). With the exception of one 19-year-old female, all patients were > 45 years. Medical history data revealed that the most common concomitant condition was hypertension (10 patients). Two patients had experienced a previous transient ischemic attack, one had experienced a cerebral infarction, one had experienced a previous SAH, and the remaining 10 patients had no previous history of cerebral vascular disease (Table 2).

Table 1. Baseline demographic, clinical and radiological data of patients with nontraumatic convexal subarachnoid haemorrhage ($n = 14$).

Characteristic	Value
Age, years	62 (19–87)
Sex, male:female	10:4
Presenting symptom	
Headache	8 (57.1)
Dizziness	1 (7.1)
Sensory or motor symptoms	8 (57.1)
Previous history	
Hypertension	10 (71.4)
Diabetes Mellitus	3 (21.4)
Hyperlipidaemia	7 (50.0)
Hyperhomocystinaemia	5 (35.7)
Ischemic stroke	3 (21.4)
Subarachnoid haemorrhage	1 (7.1)
Image	
Plain computed tomography	14 (100)
Magnetic resonance imaging	11 (78.6)
Vascular imaging	10 (71.4)
Magnetic resonance angiography	5 (35.7)
Magnetic resonance venography	1 (7.1)
Computed tomography angiography	3 (21.4)
Digital subtraction angiography	3 (21.4)
Location of bleeding	
Frontal	9 (64.3)
Parietal	10 (71.4)
Frontoparietal	1 (7.1)
Temporal	1 (7.1)
Unihemispheric	12 (85.7)
Left hemispheric	8 (57.1)
Right hemispheric	4 (28.6)
Bi-hemispheric	2 (14.3)
Concomitant with ischemic stroke	4 (28.6)

Data presented as median (range) or *n* (%) patient prevalence.

Clinical presentation

Headache was one of the most common presenting symptoms (8 patients) and among these patients, two had neck rigidity and none had a history of migraine. One of the patients with headache (patient 10) also had generalized seizures and although there was no history of epilepsy and trauma, the patient responded well to anticonvulsants, and an MRI scan and magnetic resonance venography showed the presence of a sigmoid sinus thrombosis. Three other patients with headache presented with unilateral weakness and numbness.

Eight patients presented with focal neurological deficits as the main symptom. Two of these patients experienced transient weakness of both lower limbs and six patients had unilateral symptoms that persisted over 24 h. Six of the patients with neurological deficits had MRI scan images available, and acute ischemic stroke was confirmed in four patients. One 74-year-old female (patient 3) had reported experiencing dizziness, and the CT scan showed a left parietal lobe cSAH.

Imaging findings

Plain CT scans were available for all 14 patients with cSAH and showed that haemorrhages were typically unilateral (observed in 12 [85.7%] patients) and localized between one to three neighbouring sulci (Table 1). Two patients had bihemispheric involvement: a 56-year-old male (patient 11) who was receiving warfarin for mesenteric vein thrombosis caused by phlebitis; and an 87-year-old male (patient 13), who after 6 months experienced a second cSAH attack involving the right frontal and parietal lobe sulci. The most common haemorrhage sites were the parietal and frontal lobes, observed in 10 patients (71.4%) and 9 patients (64.3%), respectively.

Cranial MRIs were available for 11 patients, of whom 10 had undergone diffusion-weighted MRI. Four patients were found to have scattered acute subcortical infarcts all of which were ipsilateral with the cSAH. Representative scan images from a 53-year-old male (patient 6) with right sided cSAH, acute ischemic stroke and severe (75%) stenosis of the right middle cerebral artery (MCA) are shown in Figure 1. Of nine

Table 2. Clinical features of patients with nontraumatic convexal subarachnoid haemorrhage (*n* = 14).

Patient No.	Age, sex	Clinical presentation	cSAH site	History of CVD	Vascular imaging result	cSAH cause
1	58, male	Left arm paraesthesia	Right, F,P	No	Right ACA (A1 segment) stenosis 90%	Stenosis of ICA system
2	60, female	Acute headache	Right, F,P,T	No	Right MCA (M1 segment) occlusion	Stenosis of ICA system
3	74, female	Episodic vertigo	Left, P	TIA	Left ICA (CI stenosis 70%, C6 occlusion)	Stenosis of ICA system
4	82, male	Acute headache	Right, F-P	No	Right MCA (M1 segment) occlusion, right ACA stenosis	Stenosis of ICA system
5	80, male	Both lower limbs paralysis	Left, P	CI	Left MCA and ACA (A1) mild stenosis	Undetermined
6	53, male	Left hemiparesis	Right, F,P	No	Right MCA (M1 segment) stenosis 75%	Stenosis of ICA system
7	60, male	Headache, left hemiparesis and paraesthesia 6 days later	Right, F,P	TIA	Right ICA stenosis 70%	Stenosis of ICA system
8	75, female	Acute headache	Left, P	No	Left MCA occlusion	Stenosis of ICA system
9	19, female	Acute headache, left hemiparesis and paraesthesia	Right, F	SAH	ND	Cerebrovascular malformation
10	46, male	Headache, generalised seizures	Right, P	No	CVST in SLS and right transverse sinus	CVST
11	56, male	Acute headache, left arm paresis and paraesthesia	Bilateral, F,P	No	Left MCA (M1 segment) stenosis 30%	Anticoagulant therapy
12	56, male	Headache	Right, F	No	ND	Undetermined
13	87, male	Both lower limbs paralysis	Bilateral, F,P	No	ND	Possible CAA
14	61, male	Left paraesthesia	Right, F	No	ND	Undetermined

cSAH, convexal subarachnoid haemorrhage; CVD, cerebral vascular disease; F, frontal; P, Parietal; T, temporal; ACA, anterior cerebral artery; MCA, middle cerebral artery; ICA, internal carotid artery; CVST, cerebral venous sinus thrombosis; SLS, superior longitudinal sinuses; TIA, transient ischemic attack; CI, cerebral infarction; SAH, subarachnoid haemorrhage; CAA, cerebral amyloid angiopathy; ND, not detected.
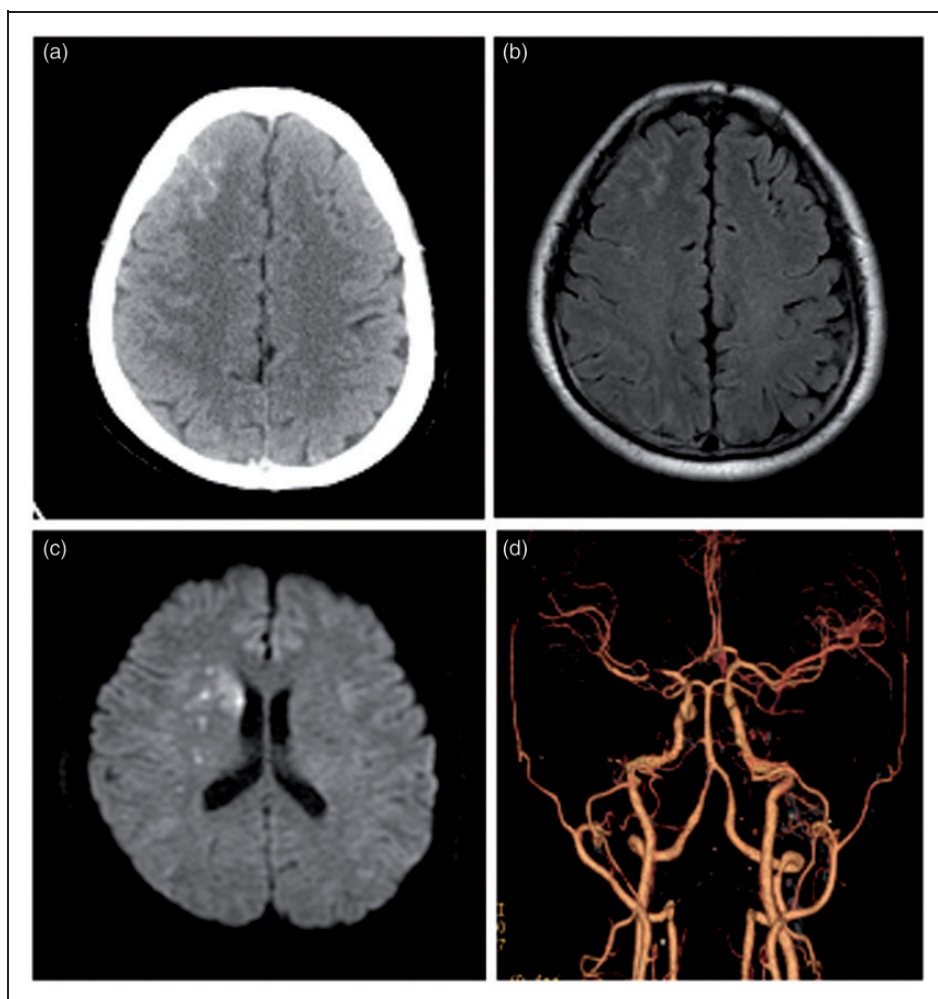
Figure 1. Representative scans from a 53-year-old male (patient 6) with convexal subarachnoid haemorrhage (cSAH), acute ischemic stroke and severe (75%) stenosis of the right middle cerebral artery. (a) Cranial computed tomography (CT; transverse section) scan showing multiple subarachnoid haemorrhages of frontal and parietal lobe; (b) Fluid-attenuation inversion recovery magnetic resonance imaging (MRI; transverse section) showing high signal in corresponding cerebral sulcus of the right middle cerebral artery region; (c) Diffusion-weighted MRI (transverse section) showing acute ischemia in the same vascular region as the cSAH; and (d) CT angiography image showing significant stenosis of the right middle cerebral artery.

patients with available gradient recalled echo T2*-weighted MRI scans, only one 60-year-old male (patient 7) showed small microbleeds in the basal ganglia.

Vascular imaging was performed on 10 patients and included magnetic resonance angiography, magnetic resonance venography, CT angiography and digital subtraction angiography. Following review of the images (JH), no evidence of reversible cerebral vasoconstriction syndrome was found. Seven patients showed significant arterial stenosis ($\geq 70\%$) or occlusion affecting the anterior cerebral artery (ACA), MCA,
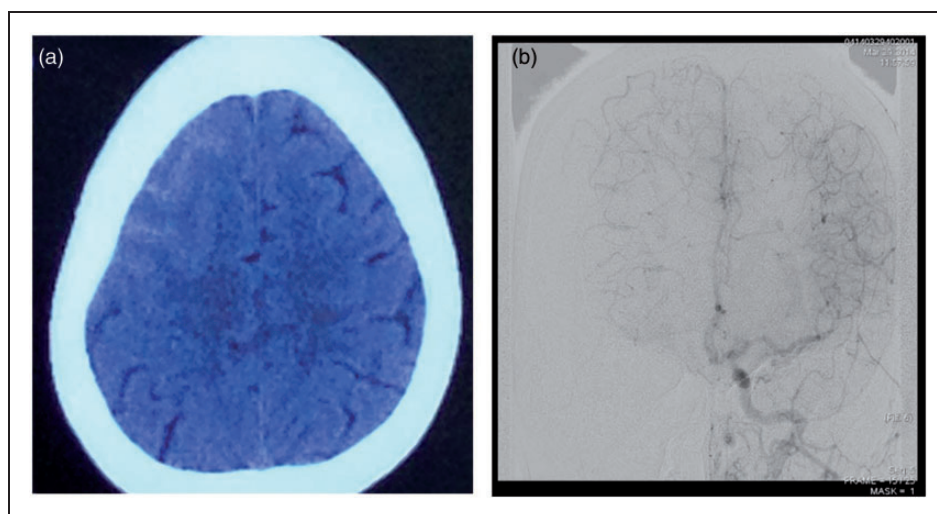
Figure 2. Representative scans from a 60-year-old female (patient 2) with convexal subarachnoid haemorrhage, occlusion of the right middle cerebral artery (MCA) and compensatory flow from the ipsilateral anterior cerebral artery (ACA) via the meningeal artery. (a) Cranial computed tomography (transverse section) showing multiple subarachnoid haemorrhages in the right MCA region; and (b) Digital subtraction angiography showing occlusion of the right MCA and compensatory flow from the ipsilateral ACA via the meningeal artery.

posterior cerebral artery (PCA), or internal carotid artery. For two of these patients, scattered acute ischemic stroke was confirmed by MRI and the stroke infarcts and cSAH were in the same region of the narrow arteries. Three patients had patent meningeal arteries confirmed by digital subtraction angiography. One patient (patient 1), a 58-year-old male, had A1 segment narrowing in the left ACA to > 90% without opening of the anterior communicating artery; the second patient (patient 2) was a 60-year-old female with scans showing occlusion of the right MCA and compensatory flow from the ipsilateral ACA via the meningeal artery (Figure 2). This patient had total occlusion from the M1 segment of the right MCA. The left ACA obtained blood supply from the right internal carotid artery via the anterior communicating artery. The right MCA received compensatory feeding from the ipsilateral ACA via the meningeal artery, and from the ipsilateral PCA via the

meningeal artery. The third patient (patient 3) was a 74-year-old female who had significant stenosis (70%) of the left internal carotid artery at C1 and C6 segments. The left posterior communicating artery and anterior communicating artery were patent and the left MCA region was supplied by the left PCA via the meningeal artery and the left ophthalmic artery through the recurrent meningeal branch artery.

Laboratory findings

For all patients, platelet counts during the hospital stay were within a normal range ($120–350 \times 10^9$/l). Ten patients received coagulation function screening and in one patient (patient 7), the serum D-dimer level was elevated to 0.65 µg/ml (normal range, 0–0.3ug/ml) but autoimmunity (including thyroid function, erythrocyte sedimentation rate, rheumatoid factor, antinuclear antibodies, extractable nuclear antigens, double-

stranded DNA and anticardiolipin antibodies) and tumour-related test results (including [see] cancer antigen [CA]125, CA199, carcinoembryonic antigen, alpha-fetoprotein and squamous cell carcinoma) for this patient were normal.

Patient follow-up

Follow-up data was available for all patients, and showed that in the one patient (patient 11) who was taking anticoagulant medications (warfarin) prior to the cSAH, these were subsequently terminated. The cause of cSAH in patient 10 was cerebral venous sinus thrombosis, and consequently this patient began taking anticoagulants following the cSAH. Patient 14 had a repeat cerebral infarction one week after the first event and received aspirin as antiplatelet treatment. Patient 8 had a repeat cSAH in the same occlusion artery region approximately two years following the first cSAH. Patient 13, who had a cSAH in the bilateral frontal parietal lobe, had a repeat cSAH in the right parietal lobe approximately six months later.

The cause of cSAH was identified in 11 patients and remained undetermined in three (patients 5, 12, 14). Significant internal carotid artery system atherosclerosis was the most common cause of cSAH ($n = 7$, 50.0%). For the remaining four patients, cSAH was caused by cerebral venous sinus thrombosis (patient 10), cerebrovascular malformation (patient 9), anticoagulant therapy (patient 11) or possible cerebral amyloid angiopathy (patient 13).

Discussion

Of 144 patients with SAH who attended Peking University Third Hospital between January 2010 and December 2014, cSAH was observed in 14 cases (9.7%). This prevalence is higher than previously reported (6.0–7.5%),[1,4,6] possibly due to a number of factors including the retrospective nature of the present study, which may have led to selection bias. In addition, a radiologic database was used to identify patients with cSAH in the present study, rather than a diagnostic code, because the authors believe that cSAH could easily be missed, as coding may be inaccurate and lead to an underestimation of the condition. Overall, however, the present data agree with other reports that show nontraumatic cSAH is a relatively rare condition in patients with SAH.[2–13]

Internal carotid artery system atheromatous disease was the most common cause of cSAH in the present study, affecting 50% patients, and was higher than the previously reported prevalence of 33%.[1] All of the present cohort were acutely symptomatic suggesting that cSAH may derive from an acute alteration in haemodynamics (e.g., plaque rupture and/or further atherothrombotic narrowing or acute hypertension). In addition, all the present cases of cSAH were associated with significant ipsilateral intracranial disease. Although a few cases of cSAH associated with symptomatic intracranial stenosis or occlusion have been reported,[1,9,10] the pathologic mechanisms remain unclear. Despite carefully reviewing all imaging studies, no evidence of reversible cerebral vasoconstriction syndrome was found in the present patient cohort.

In an observational study of 24 patients with cSAH, five cases with concurrent ischemic lesions were reported.[14] In another study involving 15 patients with cSAH, five cases of concomitant carotid artery stenosis were described.[1] In a retrospective review of 4 953 patients with acute stroke/transient ischemic attack involving eight (0.16%) patients with cSAH, five patients had occlusion of major arteries and three were suggested as having cerebral amyloid angiopathy.[5] Several studies have suggested that cerebral amyloid angiopathy is a common cause of cSAH.[1,3,5,6] In the present study, nine patients had gradient

recalled echo T2*-weighted MRIs and none fulfilled the criteria for possible or probable cerebral amyloid angiopathy (including multiple haemorrhages of varying sizes/ages with no other explanation, or a single lobar, cortical, or cortical/subcortical haemorrhage without another cause, multiple haemorrhages with a possible but not a definite cause, or some haemorrhage in an atypical location).[15] One patient in the present study, however, an 87-year-old male with recurrent cSAH, may have had cerebral amyloid angiopathy, but this could not be confirmed due to lack of MRI scan or vessel imaging. Antithrombotic drug use has also been suggested to be associated with an increased risk of SAH,[16] however, only one patient was found in the present study, for whom antithrombotic drug use may have accounted for the cSAH.

The results of the present study may be limited by several factors. First, the observations were from a single tertiary care centre using a small sample of patients, and thus, may have been influenced by selection bias. Secondly, this was a retrospective study and not all patients had undergone cerebral angiography and MRI, which meant data may have been incomplete. Moreover, some small vascular malformations, small aneurysms, focal venous thromboses, malignant tumours or vasculitis may have been missed. Finally, although no patients died during the hospitalisation period in the present study, the lack of systematic follow-up for these patients made it difficult to infer accurate prognostic data for the present cohort. The outcome of cSAH appears to depend on the underlying aetiology of the disease and age.[6] Thus, a well-designed, prospective, case-controlled, double-blind, multicentre study is required to overcome the shortcomings of the present small study.

In conclusion, internal carotid artery system atherosclerotic stenosis or occlusion was the most common cause of cSAH in the present study of 14 patients with cSAH.

The authors suggest that vascular radiographic evaluation, particularly cervical vessel imaging, should be performed in all patients with cSAH so that a potentially fatal underlying vascular abnormality may not be missed. Further prospective studies are needed to substantiate the present results and to investigate whether patients with cSAH and significant atheromatous disease should be treated with antiplatelet therapy.

Declaration of conflicting interests

The authors declare that there are no conflicts of interest.

Funding

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