Neuroradiology (2008) 50:1–8
DOI 10.1007/s00234-007-0294-1

DIAGNOSTIC NEURORADIOLOGY

Focal laminar cortical infarcts following aneurysmal subarachnoid haemorrhage

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Received: 13 February 2007 / Accepted: 16 July 2007 / Published online: 6 October 2007

Abstract
Introduction The aim of this prospective study was to analyse small band-like cortical infarcts after subarachnoid haemorrhage (SAH) using magnetic resonance imaging (MRI) with reference to additional digital subtraction angiography (DSA).
Methods In a 5-year period between January 2002 and January 2007 10 out of 188 patients with aneurysmal SAH were evaluated (one patient Hunt and Hess grade I, one patient grade II, four patients grade III, two patients grade IV, and two patients grade V). The imaging protocol included serially performed MRI with diffusion- and perfusion-weighted images (DWI/PWI) at three time points after aneurysm treatment, and cerebral vasospasm (CVS) was analysed on follow-up DSA on day 7±3 after SAH.
Results The lesions were located in the frontal lobe (n=10), in the insular cortex (n=3) and in the parietal lobe (n=1). The band-like infarcts occurred after a mean time interval of 5.8 days (range 3–10 days) and showed unexceptional adjacent thick sulcal clots. Seven out of ten patients with cortical infarcts had no or mild CVS, and in the remaining three patients DSA disclosed moderate (n=2) or severe (n=1) CVS.
Conclusion The infarct pattern after aneurysmal SAH includes cortical band-like lesions. In contrast to territorial infarcts or lacunar infarcts in the white matter which develop as a result of moderate or severe proximal and/or distal vasospasm visible on angiography, the cortical band-like lesions adjacent to sulcal clots may also develop without evidence of macroscopic vasospasm, implying a vasospastic reaction of the most distal superficial and intraparenchymal vessels.

Keywords Subarachnoid haemorrhage · Cerebral vasospasm · Cortical infarct · Digital subtraction angiography · MRI

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Introduction

Despite enormous improvement in the acute management of aneurysmal subarachnoid haemorrhage (SAH) including microneurosurgical clipping techniques and endovascular embolization, delayed cerebral vasospasm (CVS) still remains a formidable complication associated with a high morbidity and mortality after initial successful aneurysm treatment [1–3]. Digital subtraction angiography (DSA) discloses CVS of the large proximal or distal arteries in up to 70–95% of patients when performed 7 to 14 days after aneurysm rupture [2, 4, 5]. Furthermore, delayed ischaemic neurological deficits and infarcts due to CVS, i.e. symptomatic vasospasm, occur in 20% to 40% of patients [1, 3, 5, 6]. On cranial computer tomography (CT) common patterns of cerebral infarction following SAH include single territorial infarcts [5, 7, 8] and multiple lesions involving cortical, subcortical and deep white-matter structures [5]. However, the significance of small parenchymal and cortical lesions is underestimated due to limited detection on CT in comparison to MRI especially when using diffusion-weighted imaging (DWI) [9–16].

Review of the literature yielded only a few reports suggesting disturbance of microcirculation after SAH besides known infarct patterns of delayed CVS [17–24]. The key point is that small parenchymal arteries in particular may exhibit vasospasm as shown in animal trials of experimental SAH [18, 24–27]. However, due to the limited resolution even of modern DSA units, CVS of the most distal vessels of the cortical surface and the intraparenchymal segment cannot be detected. In addition, Dreier et al. [21, 28] have postulated that haemolytic cell products after SAH may induce neuronal depolarization waves triggering acute episodes of severe vasoconstriction in the cortical microcirculation due to spreading depression. Cortical lesions were found mostly in areas covered with blood in a fissure or a sulcus [28]. Uhl et al. [17] found decreased capillary density as well as vasospastic vascular narrowing of the arterioles using orthogonal polarization spectral imaging in ten patients during the acute phase of SAH who did not show any signs at all of angiographic CVS.

The aim of this prospective study was to analyse small cortical infarcts in patients suffering from SAH using MRI including DWI and perfusion-weighted imaging (PWI) with reference to additional DSA.

Patients and methods

In a 5-year period from January 2002 to January 2007, MRI and DSA studies of ten patients with small cortical infarcts and absence of global cerebral vasospasm on DSA were prospectively selected and evaluated out of 188 patients with aneurysmal SAH (one patient Hunt and Hess grade I, one patient grade II, four patients grade III, two patients grade IV, and two patients grade V; three patients grade 2 according to the Fisher classification, and seven patients grade 3). After aneurysm occlusion MRI was performed serially at three time points: within 3 days, between day 4 and day 6, and between day 7 and day 14 after SAH. At the first time point five patients received CT instead of MRI in order to identify therapy-associated lesions. All patients underwent biplane DSA before surgical clipping or endovascular embolization in the first 48 h and on day 7±3 after SAH.

MRI protocol

MR examinations were performed at 1.5 T (Magnetom Vision; Siemens, Munich, Germany). The standardized imaging protocol included native axial T2-weighted (T2-W) images, axial T2*-W images, and axial fluid-attenuated inversion-recovery (FLAIR) sequences. In addition, all patients received biplane DWI and PWI. DWI was performed with a single-shot echo-planar imaging spin echo sequence (TE 123 ms, flip angle 90°, field of view 230×230 mm, matrix 128×128 pixels, 19 slices, slice thickness 6 mm, b=1,000 s/mm^2). Bolus tracking PWI was performed with a gradient-echo echo-planar imaging sequence (TE 60.7 ms, field of view 230×230 mm, matrix 128×128 pixels, slice thickness 5 mm). After standardized intravenous contrast agent injection (0.1 mmol/kg Gd-DTPA) at a flow rate of 5 ml/s, 40 T2*-W images for each of the 12 slices were obtained at intervals of 2 s. In all major vessel territories as well as in adjacent areas with hyperintense signal changes on DWI, time-to-peak (TTP) values and mean transit time (MTT) values were determined in the regions of interest. TTP and MTT delays in the affected hemisphere were compared with those in the other hemisphere.

Selective DSA was used to evaluate proximal and distal vasospasm as well as cerebral circulation time (CCT) of the injected contrast medium bolus. CCT was defined as the time period between intradural arterial inflow of the contrast medium bolus at the level of the C2 segment of the internal carotid artery (ICA) and contrast enhancement of the bridging veins.

For analysis of proximal CVS, the diameter of the M1, A1 and P1 segments and the distal part of the ICA (C1 segment) and the vertebral artery (intradural V4 segment) and the basilar artery (BA) were measured in absolute values and set in relationship to the absolute values of the petrous segment of the ICA or the V3 segment of the VA [29]. These ratios between the baseline and follow-up DSA values were compared and relative diameter changes on the follow-up angiogram expressed in relation to the initial baseline measurement (as a percentage). Vasospasm was classified as none (0–10%), mild (11–33%), moderate (34–66%) or severe (67–100%) luminal reduction when at least one vessel segment was involved. Changes in the diameter of distal vessel segments (A2–A5, M2–M4, P2–P3) were assessed using a qualitative grading score (no arterial narrowing, mild arterial narrowing, moderate arterial narrowing, and severe arterial narrowing) [9]. All measurements were performed by two independent experienced neuroradiologists (S.W., H.L.)

Results

The data from the ten patients (eight women, two men; mean age 57.4 years, range 48–68 years) as well as the location of cortical infarcts, angiographic findings and disturbance of perfusion, i.e. prolongation of CCT on DSA and TTP/MTT delay on MRI as well as type of aneurysm treatment are summarized in Table 1. Aneurysm treatment was performed at a mean of 1.6 days (range 1–

3 days) after SAH. In seven out of the ten patients the aneurysms were clipped and the remaining three patients were treated by coil embolization. Initial DSA performed on day 1 after SAH in eight patients (patients 1, 2, 3, 5, 6, 8, 9 and 10) and on day 2 after aneurysm rupture in two patients (patients 4 and 7) did not reveal signs of CVS in any of the patients. On follow-up DSA, three out of the ten patients (Table 1; patients 1, 2 and 9) had no evidence of vasospasm (mean 6.3 days after SAH). In four patients (Table 1; patients 3, 5, 6 and 8), angiography revealed mild proximal vasospasm. However, moderate distal vascular narrowing in the A2 and M2 segments was seen in two patients (Table 1; patients 4 and 10) and in one patient (Table 1; patient 7) DSA showed severe distal vasospasm in the A2 and A3 segments. MTT delay on PWI (mean 1.8 , range 0–6.1 s) was more pronounced than CCT prolongation on DSA (mean 0.8 s, range 0–3.8 s) in comparison to the baseline angiography values.

Cortical laminar infarcts occurred after a mean of 5.8 days (range 3–10 days; Table 1) after SAH. One out of the five patients receiving initial MRI during the first 3 days after SAH showed a cortical infarct (patient 3). Also in two out of the remaining five patients having CT 72 h after SAH instead of first MRI, focal cortical lesions were visible (patients 9 and 10). In all ten patients CT and MRI showed adjacent thick sulcal clots (Figs. 1, 2 and 3). The lesions were located in the frontal lobe beside the interhemispheral fissure in six patients (Figs. 3 and 4; Table 1, patients 4–9). In three patients (Table 1; patients 1, 2 and 10) the insular cortex was affected and one 57-year-old woman (Table 1, patient 3) showed a parietal left-sided band-like laminar infarct pattern. However, in the remaining 111 patients with superficial thick clots no isolated cortical lesions were visible, reflecting an overall occurrence of laminar cortical infarcts of 6.4% in these patients.

MRI revealed additional infarcts in the white matter or in the basal ganglia in seven patients (Table 1, patients 1–7). One patient showed in addition two small subcortical ischaemic lesions with hyperintense signal changes on T2-W and DW images adjacent to the cortical lesions (Table 1, patient 1; Fig. 1a and c). MRI also showed

Table 1 Location, associated angiographic vasospasm and alteration of cerebral perfusion in ten patients with isolated cortical infarcts (*AcomA* anterior communicating artery, *ICA* internal carotid artery, *MCA* middle cerebral artery, *PcomA* posterior communicating artery)

Patient no.	Age (years)	Sex	Hunt & Hess grade	Days after SAH	Infarct location	Vasospasm on DSA	CCT difference on DSA (s)	MTT delay on PWI (s)	Sulcal clots	Aneurysm site	Aneurysm treatment
1	56	F	III	10	Insular left and adjacent subcortical white matter	No	–	Not measured	Yes	PcomA left	Clip
2	64	F	I	5	Insular right	No	0.28	–	Yes	PcomA right	Clip
3	57	F	III	3	Parietal left	Mild proximal (M1 left)	0.78	3.5	Yes	MCA left	Clip
4	52	F	V	6	Frontal right/left	Moderate distal (A2-4 right/left)	0.68 0.68	1.3 right 1.3 left	Yes	AcomA	Clip
5	54	M	IV	8	Frontal right/left	Mild proximal (A1 right/left)	1.0 1.0	– –	Yes	AcomA	Clip
6	51	F	IV	4	Frontal right/left	Mild proximal (A1 right/left)	– –	Right –	Yes	ICA (C2) right	Coil
7	48	F	V	7	Frontal right/left	Mod. proximal (A1 right/left) Severe distal (A2-5 right)	3.8 right 2.7 left	5.1 right 6.1 left	Yes	AcomA	Coil
8	68	F	II	9	Frontal left	Mild proximal (A1 right/left)	–	Not measured	Yes	AcomA	Clip
9	62	M	III	3	Frontal left	No	–[a]	Not measured	Yes	AcomA	Coil
10	62	F	III	3	Insular right	Mild proximal (M1 right) Moderate distal (M2 right)	–[a]	Not measured	Yes	MCA right	Clip

[a] DSA performed on day 7 after SAH.

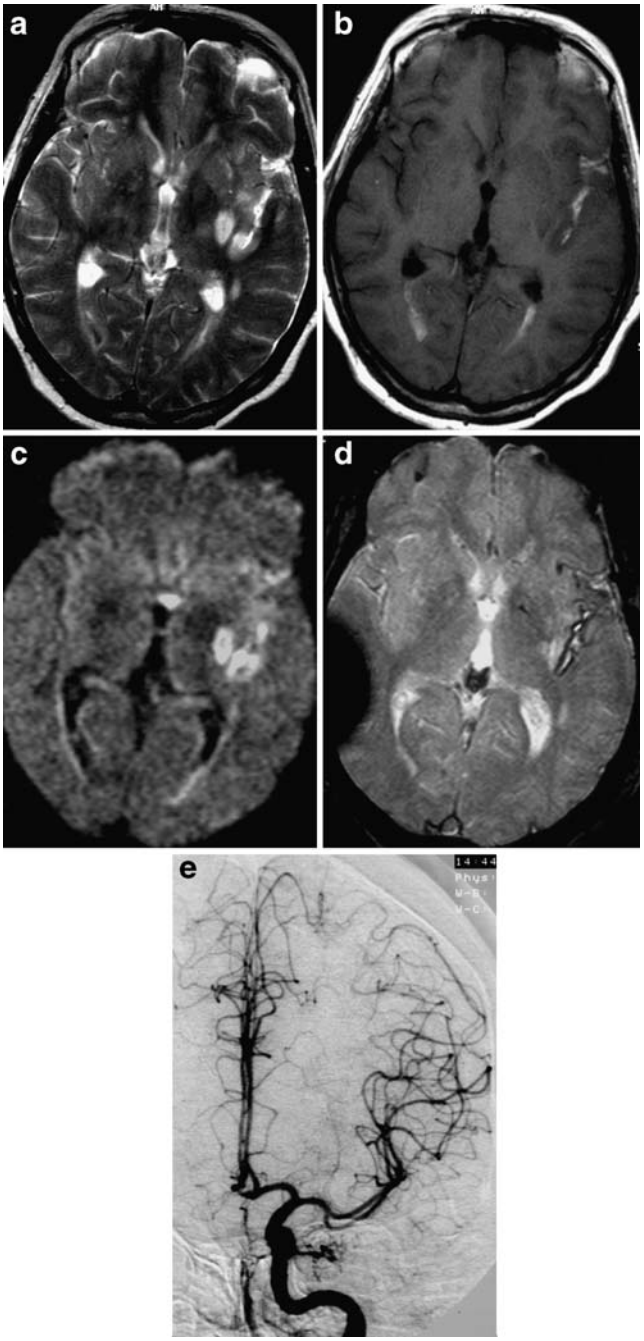
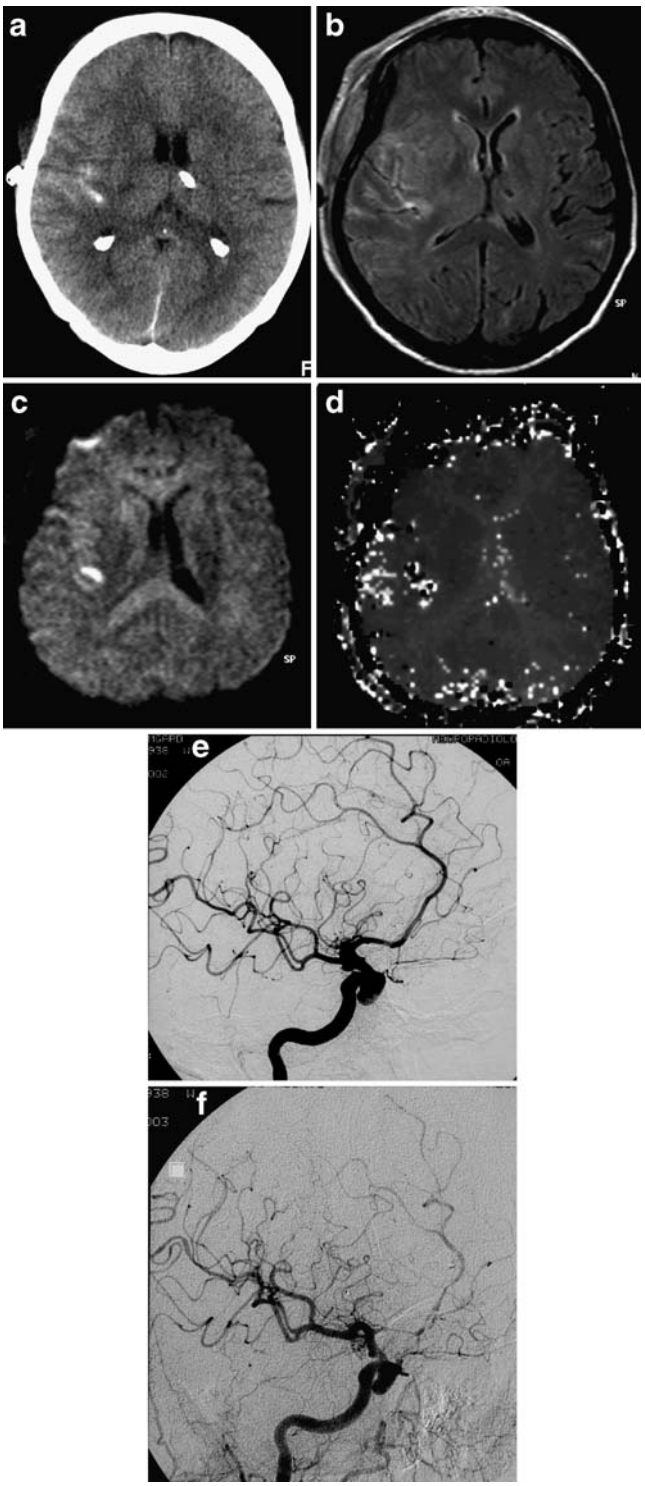


Fig. 1 Patient 1. **a–c** Axial T2-W image (**a**) and axial DW image (**c**) 10 days after SAH show a subacute hyperintense band-like insular and a temporal cortical infarct and a small subcortical ischaemic lesion on the left side with adjacent thick hyperintense clots on the T1-W image (**b**) in the lateral Sylvian fissure. **e** DSA on day 9 shows no vasospasm. **d** Follow-up T2*-W MR image 9 months later shows focal hypointense superficial siderosis

ischaemic lesions in the deep white matter (centrum semiovale; patients 2 and 3; Fig. 4b), and in the left recurrens Heubner artery territory (patients 5 and 7; Fig. 4e and g). Patients 4 and 6 showed small hyperintense lesions beside the cortical infarcts in the frontal part of the right capsula interna (Fig. 4d and f).

Neurological features

Initial loss of consciousness occurred in five patients (Table 1, patients 1, 5, 6, 9 and 10) and one patient (Table 1, patient 6) had seizures. Another 48-year-old woman (Table 1, patient 7) suffered a cardiac arrest but with immediate successful resuscitation and no evidence



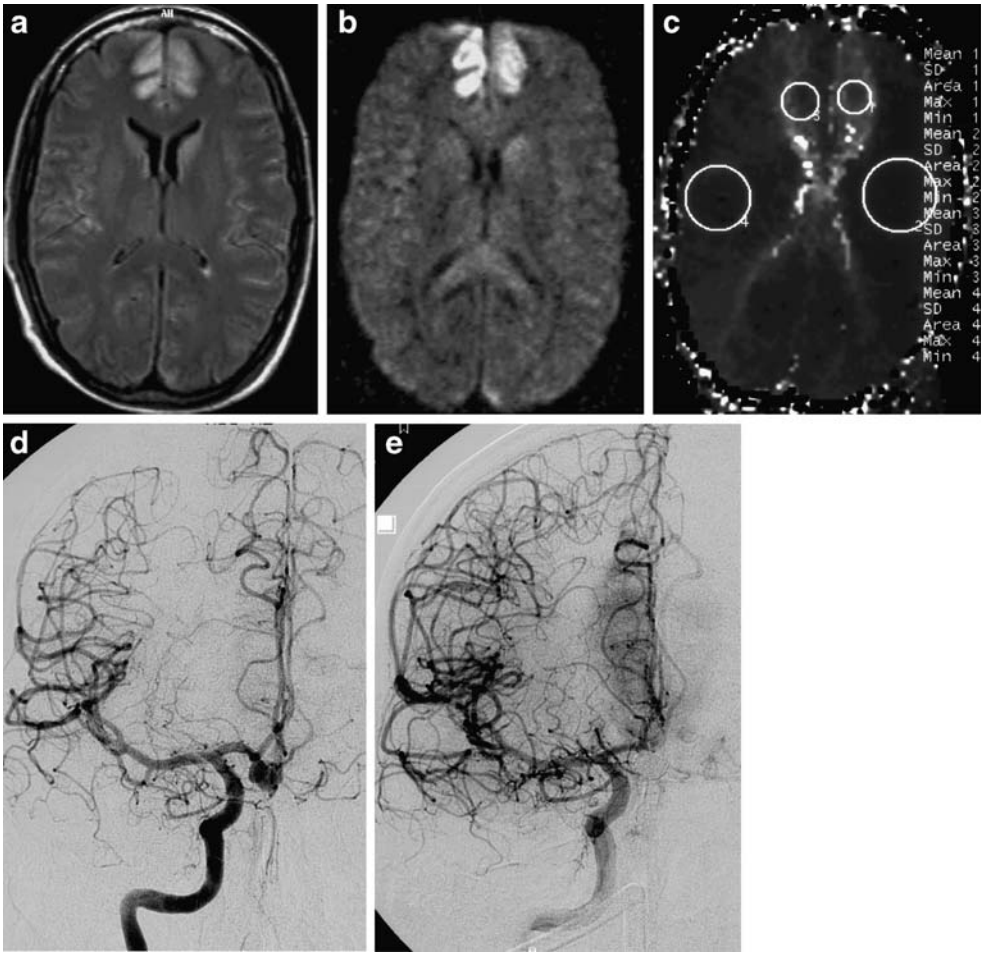


Fig. 3 Patient 7. **a–c** Axial FLAIR image (**a**) and axial DW image (**b**, b 1,000 s/mm^2; mean±SD ADC values 0.23±0.11×10^{-3} mm^2/s, normal appearing cortical tissue 0.97±0.12×10^{-3} mm^2/s) 7 days after rupture of an anterior communicating artery (AcomA) aneurysm show nearly symmetrical bilateral paramedian frontal band-like hyperintense cortical lesions and (**c**; PW image, TTP map) an additional TTP delay of 5.1 s in the right and 6.1 s in the left anterior cerebral artery (ACA) territory. **d**, **e** DSA (**d** initial angiography, PA projection, **e** follow-up angiography on day 7 after coiling of the AcomA aneurysm) show moderate proximal vasospasm of the right A1 segment and severe distal vascular narrowing in the A3–A5 segments. Note accentuated capillary blush in the paramedian frontal lobe on the right side (ACA territory)

of hypoxia or medical complications. Symptoms related to the cortical infarcts were seen in patient 1 (left insular infarct) with slight aphasia and in patient 3 (left parietal infarct) with right-sided ataxic hemiparesis, dyscalculia and dyslexia.

The clinical outcome was excellent in two patients (patients 7 and 9), one patient (patient 6) suffered drowsiness, and four patients (patients 2, 5, 6 and 8) showed mild to moderate confusion. In patient 4 neurological examination revealed slight left-sided hemiparesis.

◀ **Fig. 2** Patient 2. **a** CT image on day 3 after SAH due to rupture of a distal ICA aneurysm shows a sulcal clot in the lateral right Sylvian fissure. **b–d** MRI images on day 5 show small hyperintense signal changes of the dorsal right insular cortex (**b** axial FLAIR image, **c** axial DW image, b 1,000 s/mm^2) with low ADC values (mean±SD 0.63±0.64×10^{-3} mm^2/s) in relation to the normal appearance of the cortical tissue (mean±SD ADC value 0.92±0.07×10^{-3} mm^2/s) and without additional perfusion deficit on the PW image (**d** TTP map). **e**, **f** DSA (**e** initial DSA, oblique projection; **f** follow-up on the same day as PW imaging) of the right ICA reveals normal vessel diameter and no vasospasm of the right M1–M3 segments

Discussion

Animal trials with different experimental SAH models [18, 19, 22–27] and also histopathological studies in humans including light microscopic as well as electron microscopic investigations [17, 20] after SAH showed spastic constrictions of the most peripheral vasculature. Whereas Nihei et al. [25] found no significant histopathological changes in the small extraparenchymal pial arteries and arterioles in the subarachnoid space of rabbits after experimental SAH, Ohkuma et al. [18, 26] found an impressive decrease in luminal diameter of the intraparenchymal portion 7 days after experimental SAH using a two-haemorrhage model. In addition, there was a significant increase in wall thickness. The authors suggested that the pia mater at the level of the origins of the perivascular spaces might be permeable to vasoactive molecular substances after SAH [18, 26]. However, in line with the results of Nihei et al. [25], morphometric analysis demonstrated no relevant vasoconstriction of the extracerebral portion of the perforating arteries.

As well as the vasospastic constriction especially of the intraparenchymal portion of the perforating vessels, Dreier et al.

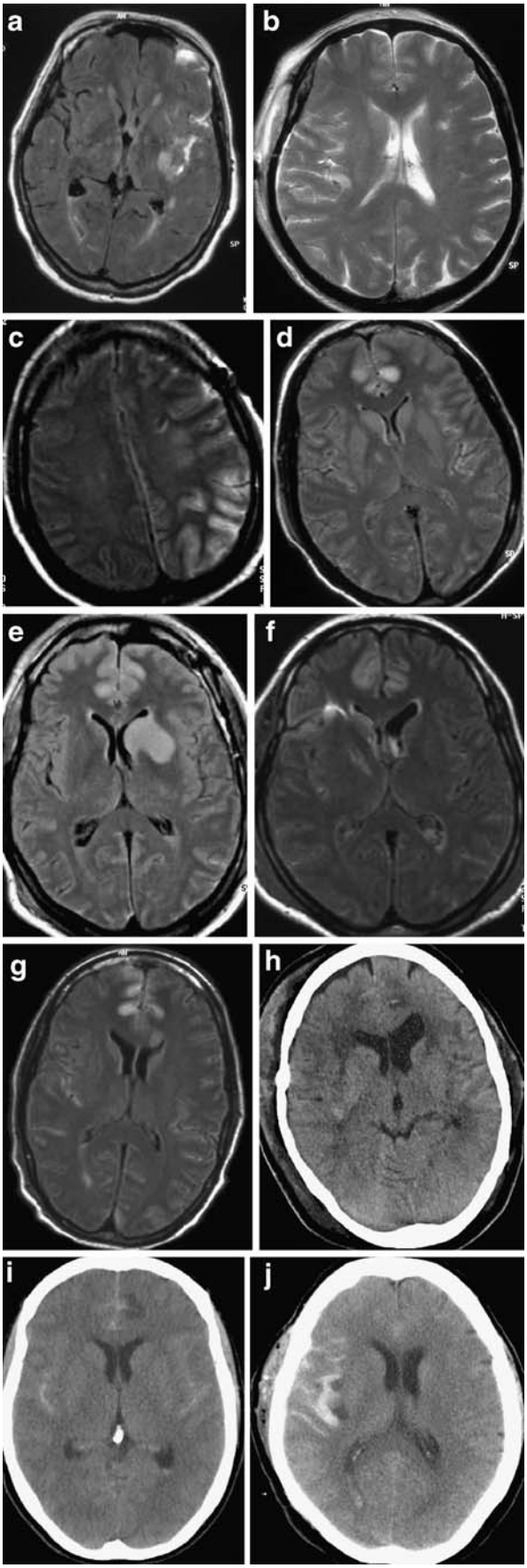


Fig. 4 Images (**a**–**j** patients 1–10; **a**, **c**–**g** axial FLAIR images; **b** axial T2-Wimage; **h**–**j** CT images) showing the infarct patterns in ten patients with small cortical partially band-like lesions of the left (**a**) and right (**b**, **j**) insular cortex, the parietal cortex (**c**), and the frontal paramedian cortex (**d**–**i**)

[21] also found spreading ischaemia of the cortex with cortical necrosis due to haemolytic products after experimental SAH. Therefore, impairment of cerebral perfusion with possible subsequent infarcts might not only be a result of delayed cerebral vasospasm visible on angiography in the proximal and distal vessel segments of the large leptomeningeal arteries of the circle of Willis [19]. The results of the experimental studies indicate that disturbance of the microcirculation caused by luminal reduction of the intraparenchymal portion of the small perforating arteries may also contribute to the prolongation of the CCT [7, 19, 30–32].

The present study showed that circumscribed cortical infarcts can develop after aneurysmal SAH without angiographic evidence of relevant proximal or distal cerebral vasospasm. Seven out of ten patients with cortical infarcts had no or mild CVS, and only in the remaining three patients did DSA show moderate or severe CVS. However, all patients had local thick subarachnoid sulcal clots adjacent to the cortical infarcts, suggesting two different pathophysiological mechanisms: (1) the band-like lesions might be due to local toxic effects of the haemolytic cell products after SAH, and (2) they are caused by a circumscribed disturbance of microcirculation [17–24, 28]. The results of the experimental investigations [18, 22–27] favour the second hypothesis, whereas our study allowed no further differentiation between infarcts due to vascular narrowing of the small perforating arteries [18, 26] and spreading ischemia [21, 28]. However, the focal cortical lesion pattern was different from those caused by increased intracranial pressure with diffuse cortical hypoperfusion [10, 33] or hypoxia [34], or by postictal cortical abnormalities associated with partial status epilepticus [35].

Analysis of the time-course of cerebral infarcts due to vasospasm suggested that the band-like cortical lesions occurred earlier after SAH [18, 26] than ischaemic lesions due to proximal and/or distal vasospasm visible on angiography (mean 5.8 days vs. 8.6 days) [1, 2, 4, 9]. Moreover, in four out of ten patients the cortical infarcts were detected on days 3 and 4 after aneurysm rupture. These findings are in line with experimental findings reported by Ohkuma et al. [26]. Microvascular casts of intraparenchymal arterioles in dogs showed vasospastic luminal narrowing with folding on day 3 up to day 7 after experimental SAH with cisternal blood injection [26]. One explanation therefore might be a quicker induction of reactive intraparenchymal vessel constriction caused by accumulation of spasmogenic substances in the perivascular spaces adjacent to superficial thick clots. The occurrence of

cortical laminar infarcts in our study was 6.4% in patients with superficial thick subarachnoid clots representing an additional but uncommon infarct pattern after SAH.

Another sequela of affected small pial and intraparenchymal vessels with a vasospastically narrowed luminal diameter might be a dysfunction of cerebral autoregulation [36–39], which may result in a lower ischaemic tolerance of the brain parenchyma when regional cerebral blood flow is disturbed by proximal vasospasm [18, 19, 32, 40–42]. Further investigations are required to assess impairment of cerebral autoregulation after SAH. As the values of TTP and MTT delay derived from MRI PWI studies are usually determined by comparing the affected hemisphere with the other hemisphere, one limitation of this method is the global presence of vasospasm, resulting in underestimation of MTT and TTP prolongation. However, no patient in our study showed evidence of global CVS on DSA.

In conclusion, the infarct pattern after aneurysmal SAH also includes cortical band-like lesions. In contrast to territorial infarcts or lacunar infarcts in the white matter which develop as a result of moderate or severe proximal and/or distal vasospasm visible on angiography, the cortical band-like lesions adjacent to sulcal clots may also develop without evidence of macroscopic vasospasm, implying a vasospastic reaction of the most distal superficial and intraparenchymal vessels. In addition to CVS of the major arteries, vascular narrowing of the distal perforating arteries may contribute to cerebral ischaemia during the vasospastic period after SAH. However, cortical spreading ischaemia as shown in experimental trials is an alternative pathophysiological model for these circumscribed lesions.

Conflict of interest statement We declare that we have no conflict of interest.

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