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Transient Ischaemic Attack Mimics Revealing Focal Subarachnoid Haemorrhage

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Key Words
Amyloid angiopathy · Subarachnoid haemorrhage · Transient ischaemic attack

Abstract
We describe here 7 elderly patients with a transient neurological deficit due to a focal subarachnoid haemorrhage, identified from the Dijon Stroke Registry over 4 years. These 7 patients presented a clinical pattern marked by focal paraesthesia, with several stereotyped focal episodes (5 of the 7 cases), lasting less than 30 min (6 of the 7 cases), and associated with a cognitive decline (4 of the 7 cases). Headache was present in only 1 case. Neuroimaging revealed focal haemorrhage present in a cortical sulcus contralateral to the symptoms. No vascular lesions nor epileptic mechanisms nor ischemic lesions were observed. This syndrome could be explained by a spreading depression, and the focal subarachnoid haemorrhage could reflect possible cerebral amyloid angiopathy, suggested by the cognitive decline present in more than 50% of our series. Our observations suggest that focal subarachnoid haemorrhage may be diagnosed by MRI in the absence of acute headache and it may be revealed by transient focal and repetitive sensory perturbations. In medical practice, it is important to evoke this diagnosis in the elderly to avoid inappropriate treatment.

Introduction

Transient ischaemic attack (TIA) mimics have recently been reported as unusual clinical manifestations of focal subarachnoid haemorrhage (SAH) and it has been suggested that cerebral amyloid angiopathy (CAA) may be associated with this type of lesion [1–3]. The clinical diagnosis of CAA is currently based on the Boston criteria, which requires the presence of intracerebral haemorrhage, whereas focal SAH is not considered [4].

We report here 7 cases of TIA mimics caused by focal SAH in elderly people with the possible implication of cerebral amyloid angiopathy.

Case Reports

Patient 1

A 76-year-old man with treated hypertension presented in October 2006, with paraesthesia in the left arm that developed progressively over 15 min, without headache. The first unenhanced head CT scan revealed hyper-density in the right central sulcus compatible with acute subarachnoid blood, without vascular arterial or venous abnormalities on CT angiography. FLAIR and gradient-recalled echo MRI confirmed the hyperintensity and gradient susceptibility changes respectively, consistent with focal SAH within the right central sulcus. No microbleeds were observed. MRI angiography showed no vascular abnormalities, and electro-

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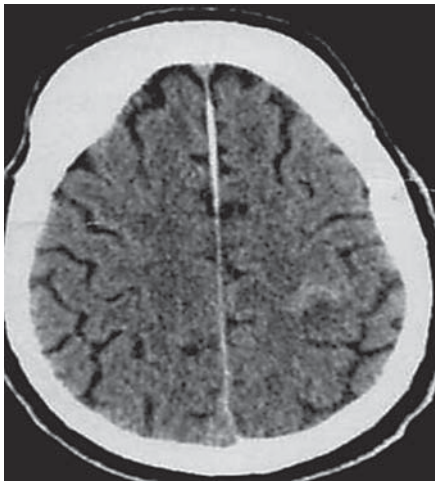

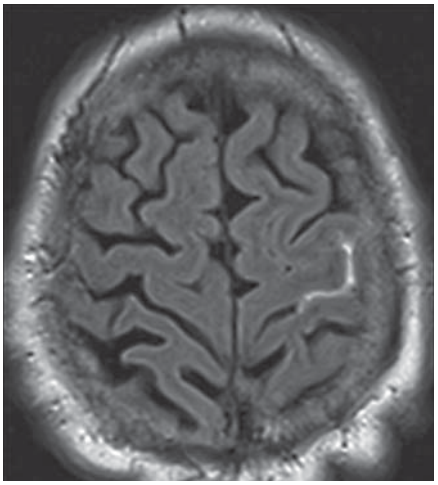

Fig. 1. Unenhanced CT scan showing a focal subarachnoid haemorrhage in the left median sulcus (patient 4).
Fig. 2. Axial brain T2 FLAIR-weighted MRI showing the left central sulcus subarachnoid haemorrhage (patient 4).

encephalography (EEG), electrocardiogram (EKG), transoesophageal echocardiography (TEE) and biological screening showed no abnormalities either. Treatment of the hypertension was reinforced. There was no new event at 36 months of follow-up, but a cognitive decline was observed, with a Mini-Mental-Score (MMS) of 24/30, associated with executive dysfunction and anterograde memory trouble.

Patient 2

On February 12, 2007, a 73-year-old man with no medical history, experienced transient dysarthria followed 5 min later by a sensory deficit in the right arm lasting for 30 min without an associated headache. A second and third stereotyped episode occurred on March 10, 2007. The first unenhanced head CT scan performed 3 h after the first TIA was normal. FLAIR and gradient-recalled echo MRI performed 4 h after the second TIA confirmed focal SAH in the left central and precentral sulci. No microbleeds were noted. CT and MRI angiography showed no arterial or venous abnormalities. EEG, Holter-EKG, TEE and biological screening were normal. He was treated empirically with carbamazepine. There were no new events and no cognitive decline during 24 months of follow-up.

Patient 3

In February 2008, a 75-year-old woman with no medical history presented 3 stereotyped episodes of transient paraesthesia in the left face and, 10 min later, in the left arm lasting 15, 10 and 15 min, respectively, over 3 weeks, without a headache. The first unenhanced CT scan after the first episode was normal but MRI after the third episode confirmed focal SAH within the right frontoparietal sulcus. No microhaemorrhage was found. CT and MRI arterial and venous angiographies were normal, as were Holter-EKG, TEE, EEG and biological screening. The MMS after the third transient event was 25. She was treated empirically with gabapentin. There were no new events and the MMS remained stable during 12 months of follow-up.

Patient 4

A 65-year-old man, with tobacco abuse, presented in April 2008 with 2 transient episodes of dysarthria with progressive paraesthesia on the right face and 10 min later in the right arm, without a headache or aphasia. The episodes lasted between 3 and 5 min and occurred over 3 days. The first unenhanced head CT performed after the first episode showed a focal SAH within the left central sulcus with no microhaemorrhage (fig. 1). MRI performed after the sixth episode revealed focal SAH within the left central sulcus (fig. 2). CT and MRI angiography, EEG and Holter-EKG and TEE were normal. He was treated empirically with gabapentin and the outcome was normal, with no recurrent events or cognitive decline (MMS = 28) during 8 months of follow-up.

Patient 5

An 80-year-old man, with treated hypertension and hypercholesterolemia, experienced 3 transient episodes of stereotyped paraesthesia on the left face and arm, with dysarthria and right hemicranial headache, lasting 10 to 20 min over 30 days. Unenhanced head CT after the first episode revealed a focal SAH within the right parietal sulcus confirmed by MRI performed after the third episode, with no microhaemorrhage. CT and MRI angiographies showed no vascular malformation and complete cardiac, EEG and biological tests were normal. One month later, the patient presented left hemiplegia induced by a right fronto-parietal hematoma. The second CT angiography revealed neither aneurysm nor venous abnormalities. A cognitive decline was observed 6 months later (MMS = 24), with no recurrent episodes.

Patient 6

A 76-year-old woman, with a history of past tobacco use, presented 3 stereotyped episodes of paresthesia of the left face, which diffused 15 min later to the left arm and lasted between 1 and 16 h, without headache. CT scan showed a focal SAH within the right central and parietal sulci, confirmed by MRI. Head CT and MRI angiographies showed no vascular changes, and no microhaemorrhages were found. The EEG and complete cardiac and biological tests were normal. No recurrent events were observed

Table 1. Clinical and radiological characteristics of the patients

Patient No.	Sex	Age years	Vascular risk factors	Clinical characteristics	Brain CT scan	Brain MRI	Follow-up
1	male	76	hypertension	*Oct 2006:* paraesthesia in left arm that developed progressively over 15 min, without headache	hyperdensity in the right central sulcus compatible with acute subarachnoid blood, without vascular arterial or venous abnormalities on CT angiography	SAH within right central sulcus; no microbleeds or vascular abnormalities observed	cognitive decline, but no new event at 36 months
2	male	63	none	*Feb 2007*: transient dysarthria followed 5 min later by a sensory deficit in right arm lasting for 30 min without associated headache *March 2007*: 2nd and 3rd stereotyped episodes	normal	focal SAH, in left central and precentral sulci; no microbleeds noted; MRI angiography showed no arterial or venous abnormalities	no new event at 24 months
3	female	75	none	*Feb 2008*: 3 stereotyped episodes of transient paraesthesia in left face and 10 min later in left arm lasting 15, 10 and 15 min, respectively, over 3 weeks, without headache	normal	focal SAH within right frontoparietal sulcus; no microhaemorrhage found; CT and MRI arterial and venous angiographies normal	no new event at 12 months
4	male	65	tobacco abuse	*April 2008*: 6 transient episodes of dysarthria with progressive paraesthesia on right face and 10 min later in right arm, without headache or aphasia.	focal SAH within left central sulcus with no microhaemorrhage	focal SAH within left central sulcus	no new event at 8 months
5	male	80	hypertension, hyperchol-esterolemia, tobacco abuse	*June–July 2008*: 3 transient episodes of stereotyped paraesthesia on left face and arm, with dysarthria and right hemicranial headache, lasting 10–20 min, over 30 days	focal SAH within right parietal sulcus	focal SAH within right parietal sulcus; no microhaemorrhage; no vascular malformation	*August 2008:* left hemiplegia revealing right frontoparietal intracerebral haemorrhage; cognitive decline at 6 months
6	female	76	tobacco abuse	*June 2007*: 3 stereotyped episodes of paresthesia on left face, which diffused 15 min later to left arm and lasted 1–16 h, without headache	focal SAH within right central and parietal sulci	focal SAH within the right central and parietal sulci; no vascular changes; no microhaemorrhage	cognitive decline, but no new event at 24 months
7	female	82	hypertension	*Feb 2009*: 2 transient episodes of paraesthesia of right arm in same day, each lasting 10 min	focal SAH in left parietal sulcus	focal SAH in left parietal sulcus	no new event at 6 months

over 24 months of follow-up, but a disorder in executive function was noted with an MMS of 28.The patient was empirically treated with gabapentin.

Patient 7

An 82-year-old woman, with a history of treated hypertension, presented in February 2009 with 2 transient episodes of paraesthesia of the right arm in the same day, each of which lasted 10 min. There was neither motor failure nor aphasia nor headache. Head CT scan and MRI showed a focal SAH in the left parietal sulcus. CT and MRI angiographies were normal, as were the EEG, and complete cardiac and biological tests. The outcome at 6 months was normal.

Discussion

We report 7 well-defined cases of stereotyped, recurrent and transient somatosensory deficits secondary to spontaneous focal, contralateral, non-traumatic and non-aneurysmal SAH. These 7 cases were identified in a series of 11 cases of focal SAH recorded in the Dijon Stroke Registry, the methodology of which has been described elsewhere [5]. Briefly, the diagnosis of focal SAH was made if neuroimaging demonstrated acute blood in the subarachnoid space of a cortical sulcus without asso-

ciated intracerebral haemorrhage. The 4 other cases not reported here were diagnosed after neuroimaging performed for isolated headache.

Our 7 cases presented a characteristic clinical pattern, occurring in elderly patients and marked by focal sensory trouble with predominant paraesthesia (7 of the 7 cases), occurring in a progressive migratory way (5 of the 7 cases), lasting less than 30 min (6 of the 7 cases) corresponding to the usual duration of TIA [6] and associated with a cognitive decline in the outcome (4 of the 7 cases). Headache was present in only 1 case. Neuroimaging revealed acute subarachnoid blood in a cortical sulcus consistent with focal SAH contralateral to the symptoms. Brain and vascular imaging did not reveal aneurysm, angioma, cavernoma or cortical vein thrombosis. Patients had no history of cranial trauma, migraine or epilepsy, and antiplatelets or anticoagulants had not been used before the first TIA mimic. None of the 7 patients had a history of cognitive impairment before the first TIA mimic.

We assume that focal SAH may be related to CAA. Several arguments are in favour of this hypothesis. The age of the patients ranged from 63 to 82 years, and it is well recognized that the prevalence of CAA increases dramatically with age. Other possible causes of intrasulcal bleedings – including venous thrombosis, arteriovenous malformations and oral anticoagulants – were ruled out by complementary explorations. In addition, from a clinical point of view, 3 of our 7 patients developed cognitive impairment during follow-up, and lobar intracerebral haemorrhage occurred in 1 patient. These features are commonly associated with CAA. Nevertheless, our observations were limited by the fact that no anatomopathological evidence of CAA was available. However, previous studies have suggested that focal SAH, as superficial siderosis, may be associated with CAA confirmed by autopsy [2, 3, 7–9]. In a recent study, superficial siderosis was detected in 60% of the 38 patients with histopathologically proven CAA compared with none of the 22 control patients with non-CAA forms of intracerebral haemorrhage [9]. For the authors, the inclusion of superficial siderosis in the Boston criteria for CAA-related intracerebral haemorrhage may increase its sensitivity. Surprisingly, none of our patients had microbleeds on T2* gradient-recalled echo MRI whereas such lesions were found in 47% of patients with confirmed CAA [9].

The mechanism that links focal SAH and TIA mimics is unclear. The hypothesis of an ischemic lesion induced by an arterial spasm within the focal SAH was not observed in any of our 7 cases or in the 4 cases of Izenberg et al. [1]. A focal epileptic seizure induced by the focal SAH is not possible because the duration of the episode is too long, close to 30 min. Only 1 patient had a short episode lasting approximately 5 min. As in the 4 cases of Izenberg et al., the EEG was normal in our patients [1]. The 30-min episodes of migratory and stereotype paraesthesia and other sensory symptoms were thought to be compatible with a migrainous aura [10, 11]. The link between aura and SAH has already been reported in cases of transient visual and somato-sensory symptoms, associated with severe aneurysmal SAH [12]. Izenberg et al. hypothesized that the spreading depression underlying migraine with aura may be the mechanism of the episodic symptoms triggered by the presence of SAH [1, 13]. This hypothesis is strengthened by animal studies demonstrating cortical spreading depression with induced SAH, and by human cases [1, 14]. Aura without headache does exist, and the fact that 5 of the 7 cases in our series experienced several stereotyped auras suggests that the presence of blood in the subarachnoid spaces may trigger recurrent cortical spreading depression. The question is about whether only acute bleeding in the subarachnoid spaces is responsible for the cortical spreading depression. In their study, Izenberg et al. identified 3 patients who experienced multiple repeated auras over months after SAH, without proof of re-bleeding. This suggests that cortical haemosiderin may also trigger recurrent cortical spreading depression for a prolonged time after an initial SAH [1].

Three of our patients were treated with gabapentin. This anti-epileptic drug has been shown to be efficient in the prevention of chronic migraine [16]. From a pathophysiological point of view, it has been shown that the phenomenon of cortical spreading depression can be induced by elevated extracellular potassium, glutamate, and inhibition of Na/K ATPase [17]. Calcium signalling in astrocytes may lead to the induction of epileptiform hypersynchronous activity in adjacent neuronal networks as a result of glutamate released from the astrocytes, and gabapentin is known to effectively suppress calcium signalling in astrocytes. These observations are particularly relevant to the issue of the commonality between migraine and epilepsy, and may explain why astrocytes are an important target for antiepileptic drugs, and particularly gabapentin, in the prophylaxis of cortical spreading depression.

The 7 observations, collected over 3 years, show the relatively high frequency of this clinical presentation. Our series highlights the fact that a transient sensory progressive focal and recurrent episode in elderly people may mimic a classical TIA, and may be associated with a con-

tralateral SAH that is not systematically detectable by non-enhanced or enhanced head CT. Indeed, the sensitivity of CT scans for the detection of SAH is lower than that of MRI, especially T2 FLAIR images [18, 19], and it has been suggested that CT scanning is unreliable for revealing the subarachnoid blood produced by a small bleed. Indeed, the depiction of SAH with CT depends on the attenuation values of the blood in the CSF spaces, whereas that of MRI mainly depends on the difference of the T1 and T2 relaxation times of the SAH relative to those of the CSF and brain parenchyma. The CT attenuation value of blood is related linearly to haematocrit and haemoglobin [20]. Although CSF protein concentration also shows a linear relationship with the CT attenuation value, the normal and pathologic ranges show only a minimal change. Therefore, CT is not sensitive for detecting pathologic alterations in CSF protein [19, 20]. The pathologic alterations are related predominantly to the haemoglobin molecule, not to the iron or protein content. Hence, CT often fails to reveal minor leaks: at low haematocrit levels, the CT values become progressively less than those of normal cortex, and therefore leaks are more difficult to see [19].

As a consequence, MRI appears to be necessary in patients with transient neurological deficits, so as to eliminate focal SAH, to avoid misdiagnosis as a classical TIA and the subsequent treatment with antiplatelets or anticoagulants.

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