Crescendo Transient Aura Attacks
A Transient Ischemic Attack Mimic Caused by Focal Subarachnoid Hemorrhage

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Background and Purpose—Diagnosis of transient ischemic attack can be difficult because many mimics exist. We report the clinical and neuroimaging features of a distinct hemorrhagic transient ischemic attack mimic.

Methods—Case series.

Results—We describe 4 elderly patients presenting with a cluster of stereotyped somatosensory migraine auras, initially referred for “crescendo transient ischemic attacks”. Neuroimaging in each patient revealed an unexpected finding of spontaneous focal subarachnoid hemorrhage conforming to a cortical sulcus in the contralateral hemisphere. We postulate that the episodic aura symptoms corresponded to recurrent cortical spreading depression triggered by the presence of subarachnoid blood, and speculate that such episodes could be a presenting feature of cerebral amyloid angiopathy in the absence of typical cerebral microbleeds or history of cognitive impairment.

Conclusions—Focal subarachnoid hemorrhage can present clinically with transient repetitive migraine auras. Awareness of this entity is important because misdiagnosis as cerebral ischemic events could lead to incorrect treatment. We recommend that elderly patients presenting with a cluster of new unexplained migraine auras should be investigated ideally with MRI to detect focal subarachnoid hemorrhage.

Key Words: amyloid angiopathy • migraine • subarachnoid hemorrhage • transient ischemic attack

The clinical diagnosis of transient ischemic attack (TIA) is often inaccurate and many mimics exist.¹ This case series reports the clinical and neuroimaging features of a unique TIA mimic and speculates on the pathophysiological mechanisms. We describe 4 patients presenting with a cluster of repeated migraine aura-like episodes of transient focal neurological symptoms who were referred to our stroke centers for “crescendo TIAs.” Neuroimaging in each patient revealed an unexpected finding of a spontaneous nonaneurysmal focal subarachnoid hemorrhage in a cortical sulcus.

Patient 1
A 77-year-old woman with hypertension presented with 3 stereotyped episodes of hemisensory symptoms over 2 weeks. The episodes began with paresthesias in the left tongue and lips, which spread to the left cheek and then to the left hand over 20 minutes. The episodes were followed by a right hemicranial headache. She was not taking any antithrombotic medication. Neurological examination was normal.

Head CT (Figure 1A) revealed an acute focal subarachnoid hemorrhage in the right central sulcus. CT angiography (Figure 1B) of the extra- and intracranial circulation revealed no vascular occlusion or aneurysm. MRI demonstrated linear T2 fluid-attenuated inversion recovery (FLAIR) hyperintensity (Figure 1C) and susceptibility on gradient imaging (Figure 1D) in the right central sulcus consistent with recent subarachnoid blood. Meningeal hemosiderin staining was present. There were no parenchymal microhemorrhages. Diffusion-weighted images were negative for acute ischemia. There were mild chronic microangiopathic changes. Holter monitor showed sinus rhythm. Electroencephalogram showed a right temporal dysrhythmia but no epileptiform abnormalities. Repeat CT (Figure 1E) and CT angiography (Figure 1F) 1 month later showed resolution of the subarachnoid blood and unchanged vascular appearances.

She was treated empirically with valproate. She had 7 recurrent identical spells over the subsequent 5 months and was asymptomatic thereafter. At follow-up 20 months later, she was asymptomatic and scored 23 out of 30 on the Montreal Cognitive Assessment with points lost for clock drawing, copy of a cube, phonemic fluency, word similarities,
and delayed recall. On repeat MRI 2 years after the index event, no FLAIR signal abnormality was evident (Figure 1G). Susceptibility-weighted brain MRI showed residual meningeal hemosiderin staining in the right central and frontal sulci (Figure 1H). No other new hemorrhage or parenchymal microbleeds were evident.

**Patient 2**

An 85-year-old man with hypertension, coronary disease, and dyslipidemia presented with 6 stereotyped episodes over 2 days. They began with paresthesias in the left hand that traveled up the arm and then down the left leg, each lasting 10 to 15 minutes, without headache. One of the episodes involved transient paresis of the left upper limb. Neurological examination was normal.

CT (Figure 2A) showed hyperdensity in the right central sulcus compatible with acute subarachnoid blood. Intracranial CT angiography was unremarkable (Figure 2B). No aneurysm was identified. MRI revealed subarachnoid FLAIR (Figure 2C) hyperintensity and gradient susceptibility changes (Figure 2D) within the right central and precentral sulci with similar findings in the medial right parietal and occipital sulci. On the diffusion-weighted sequence, there were 2 small lesions (T2 shine-through) that corresponded to the location of hemorrhage on gradient echo imaging, reflecting the acute blood rather than indicating separate areas of restricted diffusion due to ischemia. There were no microhemorrhages. Electroencephalogram showed no epileptiform abnormalities. Echocardiography was unremarkable.

He was treated empirically with phenytoin and continued aspirin and clopidogrel, which he was taking for coronary disease. There were no new or recurrent episodes at 16-month follow-up, and he scored 25 out of 30 on the Montreal Cognitive Assessment test at that time, losing points for copy of a cube, attention tasks, delayed recall, and orientation. MRI at 16 months showed resolution of the subarachnoid FLAIR (Figure 2E) and reduction of central, precentral, and medial parieto-occipital sulcal meningeal hemosiderin staining on susceptibility-weighted imaging (Figure 2F). Interval development of a solitary right deep white matter parietal microhemorrhage was seen on gradient T2* and susceptibility-weighted imaging.

**Patient 3**

A 79-year-old man with a history of lung cancer, coronary disease, peripheral vascular disease, heart failure, and essential thrombocytosis experienced 3 transient episodes over 2 days consisting of “numbness” in the right arm and face along with paresis of the right arm, each lasting 20 to 30 minutes, without associated headache. He was taking aspirin. Neurological examination was normal.

CT revealed focal subarachnoid hemorrhage within the left central sulcus (Figure 3A). MR angiography of the circle of Willis was unremarkable (Figure 3B). No aneurysm was identified. On MRI, sulcal FLAIR hyperintensity (Figure 3C) and gradient susceptibility (Figure 3D) were present in addition to a silent chronic right parietal cortical infarct of
unknown etiology. A small lesion on diffusion-weighted MRI corresponded to the focal hemorrhage, but initially caused clinicians concern regarding an embolic ischemic etiology. There were no microhemorrhages. Electroencephalogram was normal.

Because of a high-grade extracranial left carotid stenosis in the setting of symptoms initially attributed to carotid TIAs, clopidogrel was prescribed and endarterectomy was considered. However, after careful review of the brain MRI findings, the carotid stenosis was reclassified as asymptomatic. An echocardiogram was unremarkable and Holter monitor showed sinus rhythm.

Follow-up CT 2 months later (Figure 3E) demonstrated resolution of subarachnoid blood. FLAIR at 7 months showed resolution of the hyperintensity (F) with residual meningeal hemosiderin staining on susceptibility-weighted imaging (G). At 7 months, there had been no new clinical events. He scored 15 out of 30 on the Montreal Cognitive Assessment test with points lost for visuospatial testing, clock drawing, digit span, serial subtractions, repetition, phonemic fluency, word similarities, and delayed recall. Because he maintained functional independence in daily activities, he did not meet criteria for dementia.

Patient 4

A 68-year-old man with a history of smoking, unruptured 2- to 3-mm intracranial aneurysms, and hyperlipidemia presented with 7 stereotyped episodes of transient principally hemisensory symptoms over 8 weeks. The episodes began with paresthesias in the second and third digits of the right hand, which spread to the entire right hand over 10 seconds, the right arm over 15 seconds, the right trunk and abdomen over 60 seconds, and eventually to the right peri-auricular area and scalp. Occasionally he described concurrent right arm heaviness and weakness. The episodes' duration varied from 15 to 20 minutes and were followed by a left hemispheric headache. He was not taking antithrombotic medication. Neurological and cognitive examinations were normal.

Unenhanced head CT (Figure 4A) demonstrated a 2-mm anterior communicating artery aneurysm and a 3-mm left cavernous carotid aneurysm, unchanged in appearance from historical comparisons, and no other vascular lesion. FLAIR (Figure 4C) demonstrated a small focus of left frontoparietal sulcal hyperintensity consistent with subarachnoid hemorrhage and incidental chronic microangiopathic changes. In addition, gradient T2* revealed 2 foci of susceptibility in the left temporal and subinsular gray–white junction consistent with microhemorrhages. Holter monitor revealed sinus rhythm, and echocardiogram and electroencephalogram were normal. He was treated empirically with gabapentin for 4 weeks without reduction in the frequency of his recurrent transient hemisensory symptoms. Next, he was treated empirically with levetiracetam. He experienced 2 additional recurrent events in the next 3 weeks and then no further
recurrences during the next 4 months. Repeat gradient T2* (Figure 4D) and FLAIR (Figure 4E) imaging 4 months later revealed residual hemosiderin staining with resolution of sulcal FLAIR abnormality. MR angiography revealed no interval change in the pre-existing small intracranial aneurysms.

Discussion

We report a distinct syndrome of transient, recurrent somatosensory auras secondary to spontaneous focal non-aneurysmal subarachnoid hemorrhage within the contralateral cerebral hemisphere. Neuroimaging in each patient revealed a characteristic pattern of focal siderosis conforming to a cortical sulcus consistent with acute subarachnoid blood and in a neuroanatomical location appropriate to the symptoms. Brain and vascular imaging did not reveal a responsible aneurysm, vascular malformation, vasculitis, or cortical vein thrombosis. Our patients had no antecedent trauma or thunderclap headache, and history was negative for stroke, seizures, and migraine. None of our patients had a history of cognitive impairment at presentation. One of the 4 patients had evidence of prior parenchymal microbleeds on baseline MRI, raising the possibility of cerebral amyloid angiopathy.

The episode duration, stereotyped nature, slow evolution, and migratory nature of the “positive” sensory symptoms were felt to be most compatible with migraine aura rather than focal epileptic seizure (which tends to be of shorter duration) or TIA (which typically produces “negative” symptoms without migration). Moreover, 2 of the patients experienced headaches immediately after the episodes. A link between migraine aura and subarachnoid hemorrhage has been previously observed with reports of transient migratory symptoms (visual and somatosensory) after onset of severe aneurysmal subarachnoid hemorrhage. It is widely accepted that migraine aura symptoms are related to cortical spreading depression. We postulate that the episodic aura symptoms in our patients corresponded to recurrent cortical spreading depression triggered by the presence of subarachnoid blood. Animal studies have demonstrated cortical spreading depression in rats with induced subarachnoid hemorrhage and in rats with hemolysis products applied to the subarachnoid space. In humans, spreading depolarization has been demonstrated in patients with subarachnoid hemorrhage, occurring maximally with neurological deterioration. Cortical spreading depression causes headache in migraineurs by means of activating the trigeminovascular reflex. The well-described clinical syndrome of migraine equivalents (aura without headache) clearly indicates that this reflex is not activated in all patients, including 2 of the 4 patients in this series. The fact that some of our patients experienced multiple repeated auras over months suggests that the cortical hemosiderin may trigger recurrent cortical spreading depression for a prolonged time after an initial subarachnoid hemorrhage. None of our patients had evidence of new or recurrent symptomatic intracranial hemorrhages, but longer follow-up is needed to determine if such patients are at elevated risk for recurrent intracranial hemorrhage.

The finding of spontaneous focal subarachnoid hemorrhage in these elderly patients, especially in conjunction with lobar microhemorrhages in one of the patients, prompted consideration of amyloid angiopathy and subsequent evaluation for cognitive impairment. Focal subarachnoid hemorrhage has been reported as a presenting feature of amyloid angiopathy, and superficial siderosis on MRI has been observed as an early imaging finding in amyloid angiopathy patients with Alzheimer disease. There is also evidence on autopsies that subarachnoid hemorrhage, particularly in cerebral sulci, may be a primary source of hemorrhage in amyloid angiopathy. Indeed, the suggestion to include focal subarachnoid hemorrhage in the diagnostic criteria for cerebral amyloid angiopathy has been made. Moreover, there are reports of transient neurological symptoms in amyloid angiopathy, including a patient with focal seizures with accompanying perirolandic subarachnoid hemorrhage and 4 patients with episodes of migratory neurological symptoms and evidence of corresponding cerebral hemorrhage. Kleining et al reported 4 patients with focal subarachnoid hemorrhage in a cortical sulcus presenting with contralateral aura-like symptoms similar to our patients and all of their patients had lobar microbleeds evident at initial presentation. Histopathologic confirmation would be required to determine whether the 3 patients without microbleeds in our series represent a forme fruste of amyloid angiopathy.

In summary, this unique hemorrhagic stroke syndrome represents a rare but important TIA mimic. The incidence at our high-volume stroke centers was approximately one case detected per year over 4 years. Without careful history-taking, the clinical presentation can be easily misinterpreted as TIA rather than migraine aura. Misdiagnosis as a cerebral ischemic event could result in a very different, and potentially detrimental, treatment plan. Anticoagulant and antiplatelet agents may pose a risk of recurrent or worsening intracranial hemorrhage in such patients, although the natural history is unknown. In one of our patients, carotid endarterectomy was felt to be required at first because of restricted diffusion on MRI that was initially misinterpreted as representing acute embolic cerebral ischemia. CT detection of subtle subarachnoid blood can be difficult (or impossible if CT is delayed several days after the ictus). MRI is the test of choice for detection of small hemorrhages with susceptibility-weighted sequences being more sensitive than gradient echo. We recommend that elderly patients presenting for the first time with a cluster of new, unexplained, migraine aura-like episodes should be investigated ideally using MRI with gradient echo or susceptibility-weighted sequences to screen for focal subarachnoid hemorrhage.

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Disclosures

None.

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