

Brief Communication

Hemiplegic Migraine Aura Begins With Cerebral Hypoperfusion: Imaging in the Acute Phase

Jakob M. Hansen, MD, PhD; Henrik W. Schytz, MD, PhD; Vibeke A. Larsen, MD, PhD;
Helle K. Iversen, MD, DrMSc; Messoud Ashina, MD, PhD, DrMSc

Imaging studies of spontaneous migraine aura have proved challenging because of the episodic and unpredictable nature of migraine attacks. Two patients with signs of acute ischemic stroke were evaluated for thrombolysis and turned out to suffer from familial hemiplegic migraine. It was possible to record the early phase of the hemiplegic aura with computed tomography with perfusion sequences and magnetic resonance imaging. We found cerebral hypoperfusion in the relevant cortical areas within the first hour after onset of aura symptoms. This report supports the concept that migraine aura across the migraine spectrum is caused by similar mechanisms. In a setting with efficient cooperation between headache and stroke neurologists, thrombolysis centers provide the set-up and opportunity to record aura symptoms at an early phase. Furthermore, in the time of ready access to acute systemic thrombolysis treatment, these cases underscore the importance of an accurate headache history, especially in younger patients.

Key words: familial hemiplegic migraine, migraine aura, cortical spreading depression, magnetic resonance imaging, computed tomography

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INTRODUCTION

Imaging studies of spontaneous migraine aura have proved challenging because of the episodic and

From Danish Headache Center, Department of Neurology, Glostrup Hospital, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark (J.M. Hansen, H.W. Schytz, and M. Ashina); Glostrup Stroke Center, Department of Neurology, Glostrup Hospital, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark (H.K. Iversen); Radiology and Functional Imaging Unit, Glostrup Hospital, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark (V.A. Larsen).

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Address all correspondence to J.M. Hansen, Danish Headache Center, Department of Neurology N01, Glostrup Hospital, Faculty of Health Sciences, University of Copenhagen, Nordre Ringvej 57, DK-2600 Glostrup, Copenhagen, Denmark, email: jmh@dadlnet.dk.

unpredictable nature of migraine attacks. Two patients with signs of acute ischemic stroke were evaluated for thrombolysis and turned out to suffer from familial hemiplegic migraine. It was possible to record the early phase of the hemiplegic aura with computed tomography (CT) with perfusion sequences and magnetic resonance imaging (MRI). We found cerebral hypoperfusion in the relevant cortical areas within the first hour after onset of aura symptoms. This report supports the concept that migraine aura across the migraine spectrum is caused by similar mechanisms.

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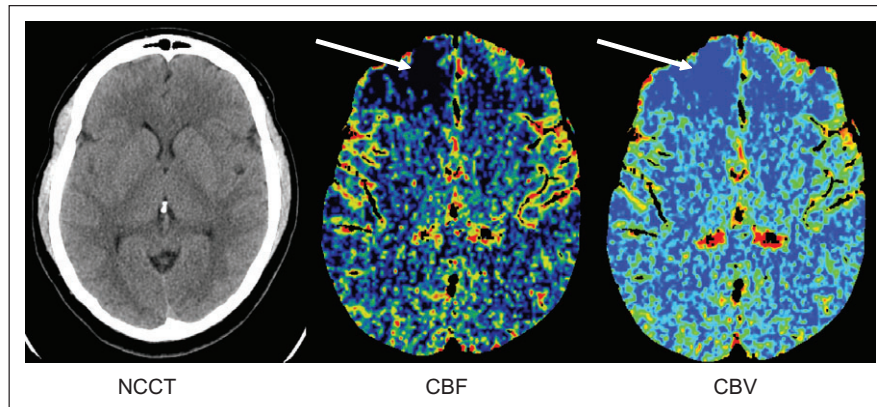


Fig 1.—Non-contrast computed tomography (NCCT) and CT perfusion of patient 1 performed 70 minutes after onset of symptoms. NCCT shows no signs of infarcts. CT perfusion study performed with a 64 multi-detector CT scanner. Sixteen 5-mm slices were performed using 50 mL Iomeron 400 mg I/mL with an injection rate of 5 mL/second. The images show a perfusion defect in the right frontal lobe with decreased cerebral blood flow (CBF) and cerebral blood volume (CBV), indicating a vascular event in that region.

treatment, these cases underscore the importance of an accurate headache history, especially in younger patients.

CASE 1

A 33-year-old man, non-smoker, noted acute onset of anesthesia and paresthesia in the left part of the face and neck. After a few minutes, the symptoms spread to the left arm. Paramedics arrived 10 minutes later and noted reduced motor response of the left leg on ambulation. The patient was referred to the Stroke Center and arrived 55 minutes after onset of symptoms.

On admission, the patient was alert and fully cooperative and reported aggravation of the paresthesia in the left part of the face and arm, but no headache. Physical examination revealed a discrete reduction in the motor response of the left arm and leg (strength 4 of 5), no dysarthria or aphasia (National Institutes of Health Stroke Scale [NIHSS] 1-2). The patient was cardiorespiratory stable.

In 2004, the patient was diagnosed with hemiplegic migraine. He described his usual hemiplegic attacks as acute right-sided migraine headache followed by a left-sided hemiparesis lasting up to 1 hour. The previous diagnostic work-up, including cerebral CT, MRI, lumbar puncture tap and ultrasound of the heart, revealed no pathology. The last attack was 6 years before the current admission.

As the patient described a different quality to the symptoms than his previous attacks of hemiplegic migraine, he was taken to acute CT with perfusion sequences (Fig. 1).

Computed tomography was performed 70 minutes after start of symptoms and showed a small perfusion defect in the right frontal lobe with increased cerebral blood volume (CBV), reduced cerebral blood flow (CBF), and increased mean transit time (MTT) (Fig. 1). Based on imaging, headache history and the gradual evaluation of symptoms, no thrombolysis was given. Ninety minutes after onset, the symptoms remitted gradually over 30 minutes. Approximately 3 hours after onset, the patient reported a bilateral mild and pressing headache (Intensity 2 on visual analog scale). The patient needed no analgesic treatment, and reported no nausea, photo, or phonophobia.

Two days after ictus, the headache had resolved spontaneously. The MRI with diffusion and angio sequences 3 days after ictus showed no signs of stroke or other pathology. Ultrasound of the carotid arteries was normal.

CASE 2

A 25-year-old non-smoking man noted foggy vision and dizziness quickly followed by acutely beginning anesthesia and paresthesia in the right hand spreading slowly proximally. After 10 minutes the patient noted aphasia and difficulties controlling

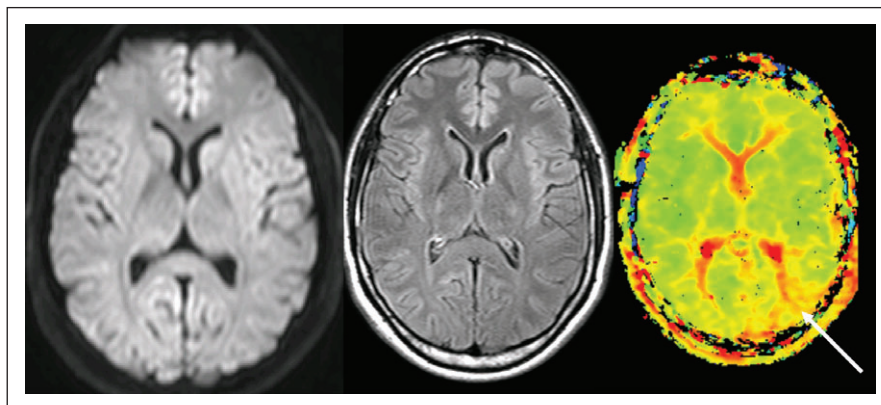


Fig 2.—Diffusion-weighted imaging and fluid-attenuated inversion recovery magnetic resonance imaging (MRI) performed 20 minutes after onset of symptoms in patient 2 is normal without signs of ischemia or infarct. MR perfusion measurement with time-to-peak map showing delayed arrival of the contrast bolus in the left occipitoparietal region. The measurement was performed on a 3T Philips scanner with the dynamic susceptibility contrast MRI.

the right arm. The patient was near the hospital and was rushed there for an acute evaluation. Twenty minutes after start of symptoms, the patient underwent 3 Tesla dynamic susceptibility contrast MRI (Fig. 2).

Magnetic resonance imaging showed normal diffusion and no signs of infarction; diffusion-weighted imaging (DWI) and fluid-attenuated inversion recovery (FLAIR) were normal but MR perfusion showed increased time to peak (TTP) in an area posteriorly in the left hemisphere, indicating hypoperfusion in this area (Fig. 2). The aura symptoms gradually resolved within 20 minutes. Fifty minutes after start of symptoms, the patient reported left-sided headache, described as pressing and aggravated after physical strain, intensity 7 on visual analog scale. The headache was associated with photophobia only. The headache resolved spontaneously within 12 hours.

The patient had never previously experienced similar episodes and only suffered from episodic tension-type headache less than 2 days per month. His mother, however, has had several similar episodes and had been diagnosed with hemiplegic migraine.

DISCUSSION

We describe 2 cases of spontaneous hemiplegic migraine aura, where imaging was carried out in the acute phase 20-70 minutes after symptom onset. We found signs of acute cerebral hypoperfusion similar to what has been reported in migraine with typical aura.

Cortical spreading depression (CSD), described by Leão,¹ has been linked to migraine aura pathogenesis in both observational,² animal,³ and human studies.^{4,6} In patients with migraine with typical aura (MA), the regional cerebral blood flow (rCBF) has been measured during the aura by single-photon emission computed tomography (SPECT), MRI, and positron emission tomography (PET).⁷⁻⁹ During the aura, spreading oligemia moves from posterior to anterior brain areas,⁷⁻⁹ with a focal blood flow decrease of 16-53% compared with the symmetrical contralateral region.⁹⁻¹¹ During the ensuing headache phase, regional CBF gradually changes from abnormally low to abnormally high without apparent parallel changes in headache,⁶ but the hyperperfusion often persists beyond the duration of the clinical headache.¹² Cerebral imaging in the acute phase of the aura in MA show cerebral hypoperfusion.^{8,13,14} Most perfusion abnormalities have been reported in the occipital cortex, corresponding with visual aura symptoms, whereas aphasic aura is likely a symptom of CSD in the parietal lobe.^{14,15} Subtle differences in disease mechanisms may, however, exist across the migraine spectrum.¹⁶

Hemiplegic migraine is a rare subtype of migraine with transient hemiplegia during the aura phase.¹⁷ Hemiplegic migraine is a very rare disease with prevalence of 0.01%,¹⁸ and therefore imaging studies in these patients are mostly single cases. Most observations of spontaneous aura have been carried

Table.—Neuroimaging in Patients With Hemiplegic Migraine or Suspected Hemiplegic Migraine

| Reference | Acute Imaging; Timing | Perfusion | Follow-Up; Timing | Perfusion | Comment |
|----------------------------------|---|---|-----------------------------------|--|--|
| Hsu et al ²⁰ | MR perfusion; day 1 | Hyperperfusion | CT perfusion; days 6 and 14 | Hyperperfusion | Two clonic seizures during admission |
| Masuzaki et al ²¹ | MR perfusion; 47 hours | Hyperperfusion | MR perfusion; 1 month | Normal | Initial imaging carried out during headache phase |
| Jacob et al ²² | MR perfusion; 1 week | Hyperperfusion | 3 months | Almost complete resolution | — |
| Oberndorfer et al ²³ | MR perfusion; day 2 | Hyperperfusion | MR perfusion; days 9 and 24 | Hyperperfusion; day 9 Normal; day 24 | SPECT showed increased (day 2) and normal (day 24) tracer uptake |
| Lindahl et al ²⁴ | MR perfusion, DWI; 6 hours | Hyperperfusion DWI normal | MR perfusion; 4 days and 3 months | Hyperperfusion; day 4 Normal follow-up at 3 months | — |
| Friberg et al ¹⁹ | SPECT; during the attack; ND | Hypoperfusion, preceded by focal hyperperfusion | ND | ND | Triggered by angiography |
| Cheng et al ²⁷ | SPECT; during the attack; ND | During aura: hypoperfusion During headache: hyperperfusion | SPECT; 10 days | Normal | — |
| Yilmaz et al ²⁸ | MR perfusion, DWI; day 2 | Hypoperfusion DWI normal | MR perfusion, DWI; 12 months | Near normal | Diagnosed with “headache with neurological deficits and CSF lymphocytosis (HaNDL)” |
| Alinok et al ²⁹ | MR perfusion, DWI; during the attack; ND | Hypoperfusion, small area of restricted diffusion DWI normal | MR perfusion; 3 days | Normal | — |
| Chen et al ³⁰ | MR; within the time limit for lytic therapy, timing not disclosed CT; on admission, ND | Normal | ND | ND | Evaluated for, but not given, thrombolysis |
| Mjaset and Russell ²⁶ | — | Normal | DWI; day 9 | DWI: ischemia without infarction SPECT: reduced perfusion | Readmitted on day 55: MRI normal SPECT: reduced perfusion |
| Petersen et al ³¹ | CT; within the time limit for lytic therapy, timing not disclosed | Reduced perfusion | SPECT; day 22 3 days | Normal DWI | DWI 3 days after onset was normal |

| | | | | | |
|--|--|---|---|---|--|
| Kraus et al ¹³ | MR perfusion, DWI; within the time limit for lytic therapy; timing not disclosed | Hypoperfusion DWI normal | ND | ND | Two cases evaluated for, but not given, thrombolysis |
| De Sanctis et al ³² | MRA, DWI; not disclosed | MRA, DWI were normal | Day 10; MRI | Normal DWI Diffuse cortical edema on FLAIR | SHM |
| Gutschalk et al ³³ | DWI; day 1 MR perfusion; day 2 PET; day 6 | DWI and MR perfusion: normal PET: reduced relative tracer uptake | DWI, MR perfusion; day 98 | Normal | — |
| Butteriss et al ³⁴ | Contrast CT (1st visit); ND DWI (2nd visit); 3 weeks | CT normal DWI high signal | MRI (1st visit); day 6 MRI (2nd visit); 6 months | Normal | Same patient examined on 2 episodes |
| Toldo et al ³⁵ | CTC; 1 hour DWI; 9 hours | CT normal DWI normal | MRI on days 4, 11 and 15; SPET on day 27; showed a marked left hemispheric hypoperfusion | Diffuse cortical edema on FLAIR that was reduced at day 15; SPET on day 27; showed a marked hemispheric hypoperfusion MRA showed increased flow SPET normal perfusion PET decrease cortical metabolic activity | SHM MRI and SPET at 6 months was normal — |
| Kumar et al ³⁶ | MRI, DWI; 48 hours | DWI normal | MRA; 5 days SPET; 13 days PET; 14 days | MRI, DWI; 5 days SPET; 6 days | — |
| Gonzalez-Alegre & Tippin ³⁷ | MRA; 2 days | MRA normal | MRI, DWI; 5 days SPET; 6 days | SPET on day 6 hypoperfusion of the left cerebral hemisphere compared with the right FLAIR; high signal throughout the cortex of the right cerebral hemisphere | Left-sided hemiparesis. Patient 38 weeks pregnant |
| Barbour et al ²⁵ | MRI and MRA; 2 days | Normal | MRI-FLAIR; day 8 SPET; 14 days | FLAIR; high signal throughout the cortex of the right cerebral hemisphere SPET; hyperperfusion of the right cerebral hemisphere | Left-sided hemiparesis. Patient 36 weeks pregnant |

CSF = cerebrospinal fluid; CTC = computed tomography colonography; DWI = diffusion-weighted imaging; FLAIR = fluid-attenuated inversion recovery; MRA = magnetic resonance angiography; MRI = magnetic resonance imaging; ND = not described; PET = positron emission tomography; SHM = spontaneous hemiplegic migraine; SPET = single-photon emission computed tomography; SPET = single-photon emission tomography; — = inconclusive results.

out over a large time span with respect to onset of symptoms.

Cerebral blood flow studies during a hemiplegic aura provoked by angiography showed a spreading cortical hypoperfusion,¹⁹ similar to migraine with aura,¹⁰ which suggest that CSD is the most likely mechanism of hemiplegic aura.^{7,11} Most reports of *spontaneous* hemiplegic migraine aura, however, report cortical hyperperfusion,²⁰⁻²⁵ possibly because imaging in these patients has been carried out late in the aura phase, where blood flow is abnormally high (see also the Table). Reduced perfusion long after onset of symptoms²⁶ and even hypoperfusion in the right thalamus during the aura phase with SPECT²⁷ have been reported. In a case of headache and neurological deficits with cerebrospinal fluid lymphocytosis (HaNDL) with left-sided deficits, MRI was performed 30 minutes after onset of symptoms and showed focal hypoperfusion in the brain regions corresponding to the focal neurological deficits.²⁸ A recent paper reported cerebral hypoperfusion contralateral to the side of hemiplegic aura on perfusion MRI performed during the aura phase (timing, however, not disclosed).²⁹ Concomitant susceptibility-weighted MRI showed prominent vessels in the left cerebral hemisphere, likely caused by venous stasis raising the possibility of stroke or vasculitis.

In these 2 cases of spontaneous hemiplegic migraine attacks, the location of the perfusion defects in the relevant cortical areas may explain the clinical presentation with hemiplegia and aphasia (Figs. 1 and 2). Apart from the location, it seems that the cerebrovascular changes in hemiplegic migraine aura are similar to the aura of typical migraine.

Both patients were evaluated for acute systemic thrombolysis treatment. Migraine aura is a well-known differential diagnosis to stroke and because of the march of symptoms and taking into account the patient's family and headache history, thrombolysis treatment was not indicated.

CONCLUSION

The 2 cases underscore the importance of an accurate headache history, especially in younger patients. In a streamlined set-up for admission and evaluation of stroke patients for thrombolysis, some

patients who actually suffer from migraine with aura will be referred. Given an efficient cooperation between headache and stroke neurologists, this offers unique opportunities to study the early aura phase.

STATEMENT OF AUTHORSHIP

Category 1

(a) Conception and Design

Jakob M. Hansen; Henrik W. Schytz; Vibeke A. Larsen; Helle K. Iversen; Messoud Ashina

(b) Acquisition of Data

Jakob M. Hansen; Vibeke A. Larsen

(c) Analysis and Interpretation of Data

Jakob M. Hansen; Henrik W. Schytz; Vibeke A. Larsen; Helle K. Iversen; Messoud Ashina

Category 2

(a) Drafting the Article

Jakob M. Hansen; Henrik W. Schytz; Messoud Ashina

(b) Revising It for Intellectual Content

Jakob M. Hansen; Henrik W. Schytz; Vibeke A. Larsen; Helle K. Iversen; Messoud Ashina

Category 3

(a) Final Approval of the Completed Article

Jakob M. Hansen; Henrik W. Schytz; Vibeke A. Larsen; Helle K. Iversen; Messoud Ashina

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