ABSTRACT

SUMMARY: Children who present with acute transient focal neurologic symptoms of stroke or transient ischemic attack. We present a series of 16 children who presented with transient focal neurologic symptoms that raised concern for acute stroke but who had no evidence of infarction and had unilateral, potentially reversible imaging features on vascular and perfusion-sensitive brain MR imaging. Patients were examined with routine brain MR imaging, MRA, perfusion-sensitive sequences, and DWI. Fourteen (88%) children had lateralized MRA evidence of arterial tree pruning without occlusion, all had negative DWI findings, and all showed evidence of hemispheric hypoperfusion by susceptibility-weighted imaging or arterial spin-labeling perfusion imaging at presentation. These findings normalized following resolution of symptoms in all children who had follow-up imaging (6/16, 38%). The use of MR imaging with perfusion-sensitive sequences, DWI, and MRA can help to rapidly distinguish children with conditions mimicking stroke from those with acute stroke.

CASE SERIES

Cases were collected retrospectively as part of a larger, institutional review board–approved review of children with transient neurologic symptoms presenting to a free-standing children’s hospital. A total of 16 children met both the clinical criteria of transient focal neurologic symptoms and the imaging criteria of focal hypoperfusion and/or focal vascular pruning. We collected clinical information on each of the children, including symptoms at presentation, time from presentation to imaging, headache at presentation, and history of migraines. All clinical information was reviewed by a pediatric neurologist.

Clinical Features

Our cohort of 16 children included 6 females (38%). The children ranged from 2 to 16 years of age. Among the 16 children, 13 (81%) had headache at presentation. Only 6 (38%) had a previous diagnosis of migraine (Table 1). Most patients (94%) did not meet the International Classification of Headache Disorders criteria for
hemiplegic migraine. All patients had complete resolution or marked improvement in symptoms by 24 hours after symptom onset. Only 6 (38%) had recurrence of transient neurologic symptoms since the initial presentation; none had stroke at the time of presentation or at follow-up. We had a median follow-up of 0.7 years with a range of 1 day to 3.4 years.

Imaging Approach and Features

MR imaging was performed at a median of 6.4 hours, with all patients imaged within 16.5 hours of presentation. All examinations were performed on a 3T Magnetom Skyra or Trio imaging system (Siemens, Erlangen, Germany) with a 32- or 64-channel head coil. All patients were examined with the standard institutional brain imaging sequences, including the following: sagittal T1 MPRAGE (TR = 1520–2530 ms, TE = 1.63–3.39 ms, section thickness = 0.90–1 mm, echo-train length = 1, matrix = 220–256/220–256, one or 4 excitations); axial fast spin-echo T2 (TR = 4400–14,143 ms, TE = 89–100 ms, section thickness = 2.5 mm, echo-train length = 13–19, matrix = 269–359/512, two-to-three excitations); axial T2 FLAIR (TR = 6800–9000 ms, TE = 135–137 ms, section thickness = 4 mm, echo-train length = 13–16, matrix = 250–320/320, one-to-two excitations); diffusion tensor imaging with 30 or 35 directions, b=1000 s/mm² (TR = 5300–13,800 ms, TE = 88–92 ms, section thickness = 2–4 mm, echo-train length = 1,48, or 51, matrix = 128/128, one excitation); and 3D time-of-flight angiography (TR = 21–22 ms, TE = 3.43–3.88 ms, section thickness = 0.60–0.80 mm, echo-train length = 1, matrix = 230–344/384–512, one excitation). Perfusion-sensitive sequences, including perfusion-weighted pulsed arterial spin-labeling (n = 11 patients: TR = 2500–5000 ms, TE = 11–35 ms, section thickness = 3–5 mm, echo-train length = 1–51, matrix = 64–96/64–84, one-to-sixty excitations, TI = 700 ms); velocity-selective arterial spin-labeling (n = 2 patients: TR = 3000 ms, TE = 13 ms, section thickness = 5 mm, matrix = 64/64, one excitation, TI1 = 700 ms, TI1,swap = 1400 ms, and TI2 = 2000 ms [to the center section]); and axial susceptibility-weighted imaging (n = 16 patients: TR = 28 ms, TE = 20 ms, section thickness = 1.25 mm, echo-train length = 1, matrix = 184–336/256–384, one excitation) were also performed.

Images were independently reviewed by 2 pediatric neuroradiologists. The final interpretation was reached by consensus in cases of disagreement between the reviewers. Each MR imaging examination was evaluated for the following imaging abnormalities: linear sulcal signal abnormality on FLAIR imaging, subcortical hypointensity on T2-weighted imaging, localized brain parenchymal signal or diffusion abnormalities, gyral swelling, venous prominence on susceptibility-weighted imaging, perfusion abnormality on arterial spin-labeling, abnormal leptomeningeal and parenchymal enhancement following the administration of intravenous contrast, and evidence of increased/decreased flow-related enhancement or vessel stenosis on 3D TOF MR angiography. Imaging abnormalities were further characterized according to vascular distribution for MRA and lobes of the brain involved in SWI and arterial spin-labeling.

DWI revealed no areas of decreased diffusivity in any patient. None had evidence of gyral swelling. Linear sulcal signal abnormality in the hemodynamically affected region was seen on FLAIR imaging in 2 patients (2/16, 13%). One patient had subcortical hypointensity on T2-weighted imaging (1/16, 6%). All 16 patients had unilateral increased prominence of the cortical or medullary veins in ≥1 cerebral lobe on SWI, suggesting elevated venous deoxyhemoglobin, indicative of hypoperfusion. Of the 11 patients evaluated with arterial spin-labeling, decreased perfusion to ≥1 lobe of the brain was evident in all. Diminished flow-related enhancement due to decreased hemispheric flow in at least 1 branch vessel of the circle of Willis was evident in 14 patients (14/16, 88%). Multivessel unilateral vascular pruning was present in 9 patients. None of the patients demonstrated hemodynamic change in the posterior fossa structures. Arterial beading on MRA was not demonstrated in any patient. Intravenous contrast was administered in 3 patients (3/16, 19%) with increased leptomeningeal prominence seen in the regions corresponding to those with arterial spin-labeling, SWI, and MRA changes in all 3. No parenchymal enhancement was observed in any of the 3 patients administered contrast. The Figure represents an example of the imaging findings observed in our cohort. Follow-up imaging was performed in 6 patients (6/16, 38%). Resolution of MR imaging changes, including normalization of arterial spin-labeling, SWI, and MRA findings, was observed in all 6 patients who had follow-up imaging (Table 2).

Table 1: Clinical details of the presentation of the children

| Patient No. | Age (yr) | Sex | Headache | History of Migraine | Headache | Time from Presentation to Imaging | Clinical Symptoms |
|-------------|---------|-----|----------|---------------------|----------|----------------------------------|------------------|
| 1           | 15      | Female | Yes | Yes | Right face and arm weakness, hypoesthesia, hemianopia, aphasia |
| 2           | 13      | Male | Yes | No | Left face and hand paresthesia |
| 3           | 16      | Female | Yes | No | Left hand and foot paresthesia and weakness |
| 4           | 14      | Male | Yes | Yes | Aphasia, right hemianopia |
| 5           | 2       | Male | No | Yes | Right hemiparesis and hemianopia |
| 6           | 12      | Female | Yes | Yes | Aphasia |
| 7           | 13      | Male | Yes | No | Aphasia and right face and arm weakness |
| 8           | 8       | Male | Yes | No | Aphasia, bilateral blurry vision, left hand paresthesia |
| 9           | 10      | Male | Yes | No | Right hand paresthesia, confusion |
| 10          | 11      | Female | No | Yes | Right hand paresthesia |
| 11          | 5       | Male | No | No | Right hemiparesis, dysarthria, and confusion |
| 12          | 13      | Female | Yes | No | Left hand weakness and paresthesia, aphasia |
| 13          | 8       | Male | Yes | Yes | Left facial weakness, hemiparesis |
| 14          | 15      | Male | Yes | Yes | Aphasia |
| 15          | 10      | Male | Yes | No | Aphasia and blurry vision |
| 16          | 4       | Female | Yes | No | Left facial weakness, dysarthria |
We describe a cohort of children with a specific radiologic presentation that included negative diffusion-weighted imaging findings, evidence of lobar or hemispheric hypoperfusion by susceptibility-weighted imaging, and/or arterial spin-labeled perfusion imaging associated with transient focal neurologic symptoms. MRA evidence of arterial pruning without occlusion was usually present. In all children who had repeat imaging, the vascular and perfusion findings had normalized and there was no evidence of infarction. Most children had headache at presentation, and only

**FIGURE.** A 5-year-old boy presenting with right-sided weakness. Symptoms were improving at the time of the initial MR imaging performed 3 hours after presentation (A–D). A, Susceptibility-weighted imaging shows increased prominence of the cortical veins throughout the left cerebral hemisphere, indicating increased deoxyhemoglobin on the left. B, Collapsed maximum intensity projection from time-of-flight MR angiography shows reduced flow-related enhancement in the left anterior, middle, and posterior cerebral arteries. C, The average trace of the diffusion tensor image shows no abnormality of diffusion. D, Pulsed arterial spin-labeled perfusion-weighted imaging relative CBF map shows a marked decrease in perfusion throughout the left cerebral hemisphere. Follow-up imaging at 4 days after presentation (E–H). E, SWI shows resolution of venous asymmetry. F, MRA shows normal flow-related enhancement in the left anterior, middle, and posterior cerebral arteries. G, Findings of the average trace image continue to be negative. H, Pulsed arterial spin-labeling relative CBF map shows resolution of perfusion asymmetry.

**Table 2: Radiology findings of children with ASL and SWI reported in lobes and MRA in vessels involved**

| Patient No. | Side | pASL (Decrease) | vASL (Decrease) | SWI (Increase) | MRA (Decrease) | Resolution |
|------------|------|-----------------|-----------------|---------------|---------------|------------|
| 1          | Left | P/T/O           | ND              | F/P/T/O       | MCA/PCA       | ND         |
| 2          | Left | P/T             | ND              | P/T           | MCA           | Yes        |
| 3          | Right| P               | ND              | P             | MCA           | ND         |
| 4          | Left | P/T/O           | ND              | P/T/O         | None          | Yes        |
| 5          | Left | F/P/T/O         | ND              | F/P/T/O       | ACA/MCA/PCA   | Yes        |
| 6          | Left | F/P/T/O         | Left F/P/O/T    | F/P/T/O       | ACA/MCA/PCA   | ND         |
| 7          | Left | F/T             | ND              | F/T           | MCA           | ND         |
| 8          | Left | P/T             | ND              | P/T           | None          | ND         |
| 9          | Left | F/P/T/O         | ND              | F/P/T/O       | ACA/MCA/PCA   | ND         |
| 10         | Left | ND              | ND              | P/T/O         | MCA/PCA       | ND         |
| 11         | Left | F/P/T/O         | ND              | F/P/T/O       | ACA/MCA/PCA   | Yes        |
| 12         | Right| F/P/T/O         | ND              | F/P/T/O       | ACA/MCA/PCA   | Yes        |
| 13         | Right| ND              | Right P/O/T     | P/T/O         | MCA/PCA       | Yes        |
| 14         | Left | ND              | ND              | F/P/T/O       | MCA/PCA       | ND         |
| 15         | Left | ND              | ND              | F/P            | MCA           | ND         |
| 16         | Left | ND              | ND              | P/T/O         | MCA           | ND         |

Note:—pASL indicates pseudocontinuous arterial spin-labeling; vASL, velocity-selective arterial spin-labeling; ND, study not done; F, frontal; P, parietal; T, temporal; O, occipital; ACA, anterior cerebral artery; PCA, posterior cerebral artery.
one-third had recurrence of symptoms. Most interesting, only 1 of the children met the International Classification of Headache Disorders criteria for hemiplegic migraine.5,6

The literature describing the neuroimaging findings in children with transient focal neurologic symptoms is limited. Imaging findings of focal hypoperfusion and vascular pruning have been reported previously in pediatric and adult patients with hemiplegic migraine (genetically proved or clinically diagnosed) in case reports and small case series.7-9 Perfusion findings have been reported and are temporally variable in children with acute onset of migraine with an aura. In a case-control study, 10 patients with migraine with an aura were acutely imaged with arterial spin-labeled perfusion imaging and found to have a change in perfusion compared with controls. The children had decreased perfusion if scanned <14 hours from the onset of symptoms, while evidence of increased perfusion was found if imaging was performed at >17 hours from symptom onset.10 In addition, Saﬁer et al11 reported a series of 8 children with hemiplegic migraine who demonstrated vascular narrowing by MRA. However, in their case series, only the middle cerebral artery was examined.11 The study by Saﬁer et al did not report on the other branch vessels of the circle of Willis. Consequently, it is not certain whether the vascular changes occurred in only the middle cerebral artery in their patients or if other vessels were similarly affected but not evaluated as part of the study. In our patient cohort, several branch vessels were usually affected.

Children who present with the acute onset of focal neurologic symptoms raise concern for stroke. Rapid neuroimaging of these children is extremely important, given the availability of treatment with thrombolysis or endovascular thrombectomy for acute stroke. DWI permits differentiation of a stroke from a stroke mimic.5 While negative DWI excludes an infarction requiring acute stroke therapy, the addition of perfusion-sensitive imaging in patients with diffusion-negative transient neurologic deﬁcits can provide additional information regarding the etiology of the neurologic symptoms. Our ﬁndings indicate that a subset of children with symptoms mimicking acute stroke lack the anatomic or diagnostic diffusion-related changes of infarction but exhibit perfusion and flow-related vascular changes indicating reduced regional perfusion as a cause of symptoms. All children in our cohort with anatomic- and DWI-negative but perfusion-positive imaging ﬁndings demonstrated decreased rather than increased regional perfusion. The decreased perfusion ﬁndings in these children help to differentiate symptoms due to an ischemic cause from other conditions that may mimic stroke, such as a postictal state that typically shows increased regional blood ﬂow.12-14

We recognize limitations in our study. Our series is retrospective in nature and small in number. Furthermore, only a portion of the children we report had repeat imaging following resolution of symptoms. Finally, we have only limited outcome information.

CONCLUSIONS
The use of combined MR imaging to include perfusion-sensitive, diffusion-weighted, and angiographic imaging can help to rapidly distinguish children who present with stroke mimics whose symptoms are likely to be transient and who do not require stroke treatment from those with an acute stroke. In our series, the imaging findings of unilateral, often multilobar, hypoperfusion and arterial vascular pruning without evidence of diffusion restriction in a child presenting with focal neurologic symptoms reﬂect a benign stroke mimic and conﬁrm a vasococonstrictive basis for the patient’s symptoms. Our observations support the routine use of perfusion-sensitive sequences as part of the neuroimaging evaluation of any child presenting with stroke or stroke-like symptoms.

Disclosures: Richard L. Robertson—UNRELATED: Other: GE Healthcare*. *Money paid to the institution.

REFERENCES
1. Schellinger PD, Bryan RN, Caplan LR, et al; Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Evidence-based guideline: the role of diffusion and perfusion MRI for the diagnosis of acute ischemic stroke—report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2010;75:177–85 CrossRef Medline
2. Haakke EM, Mittal S, Wu Z, et al. Susceptibility-weighted imaging: technical aspects and clinical applications, part 1. AJNR Am J Neuroradiol 2009;30:19–30 Medline
3. Wintermark M, Sanelli PC, Albers GW, et al; American Society of Neuroradiology, American College of Radiology, Society of Neuro-Interventional Surgery. Imaging recommendations for acute stroke and transient ischemic attack patients: a joint statement by the American Society of Neuroradiology, the American College of Radiology and the Society of NeuroInterventional Surgery. J Am Coll Radiol 2013;10:828–32 CrossRef Medline
4. Zaharchuk G, Olivot JM, Fischbein NJ, et al. Arterial spin labeling imaging findings in transient ischemic attack patients: comparison with diffusion- and bolus perfusion-weighted imaging. Cerebrovasc Dis 2012;34:221–28 CrossRef Medline
5. Rivkin MJ, deVeber G, Ichord RN, et al. Thrombolysis in pediatric stroke study. Stroke 2015;46:880–85 CrossRef Medline
6. Headache Classiﬁcation Committee of the International Headache Society (IHS). The International Classiﬁcation of Headache Disorders, 3rd edition (beta version). Cephalalgia 2013:33:629–808 CrossRef Medline
7. Boseman T, Burton VJ, Felling RI, et al. Pediatric hemiplegic migraine: role of multiple MRI techniques in evaluation of reversible hypoperfusion. Cephalalgia 2014;34:311–15 CrossRef Medline
8. Kim S, Kang M, Choi S. A case report of sporadic hemiplegic migraine associated cerebral hypoperfusion: comparison of arterial spin labeling and dynamic susceptibility contrast perfusion MR imaging. Eur J Pediatr 2016;175:295–98 CrossRef Medline
9. Fedak EM, Zumberge NA, Heyer GL. The diagnostic role for susceptibility-weighted MRI during sporadic hemiplegic migraine. Cephalalgia 2013;33:1258–63 CrossReff Medline
10. Boulouis G, Shotor E, Dangoullof-Ros V, et al. Magnetic resonance imaging arterial-spin-labeling perfusion alterations in childhood migraine with atypical aura: a case-control study. Dev Med Child Neurol 2016;58:965–69 CrossRef Medline
11. Saﬁer R, Cleves-Bayon C, Vaidele I, et al. Magnetic resonance angiography evidence of vasospasm in children with suspected acute hemiplegic migraine. J Child Neurol 2014;29:789–92 CrossRef Medline
12. Kim BS, Lee ST, Yun TJ, et al. Capability of arterial spin labeling MR imaging in localizing seizure focus in clinical seizure activity. Eur J Radiol 2016;85:1295–303 CrossRef Medline
13. Matsuura K, Maeda M, Okamoto K, et al. Usefulness of arterial spin-labeling images in perictal state diagnosis of epilepsy. J Neurol Sci 2015;359:424–29 CrossRef Medline
14. Verma RK, Abela E, Schindler K, et al. Focal and generalized patterns of cerebral cortical veins due to non-convulsive status epilepticus or prolonged seizure episode after convulsive status epilepticus: A MRI study using susceptibility-weighted imaging. PLoS One 2016;11:e0160495 CrossRef Medline