Utility of Neurovascular Imaging in Acute Neonatal Arterial Ischemic Stroke

Ishita Siddiq, MSc, MD[1], Derek Armstrong, MB, BS[2], Ann-Marie Surmava, MBA[1], Nomazulu Dlamini, MD, PhD, MHSc[1], Daune MacGregor, MD, MBA[1], Mahendranath Moharir, MD, MSc[1], and Rand Askalan, PhD, MD, EMBA[1]

Objective To evaluate the prevalence of magnetic resonance angiography (MRA) findings and clinically characterize neonates with arterial ischemic stroke (AIS) who have abnormal or variable vasculature.

Study design This was a single-center, retrospective study of patients with neonatal stroke from 1991 to 2012. We reviewed charts and neuroimaging, including MRA, in neonates with AIS. Clinical data of patients with MRA findings were compared with the control group of neonates with AIS and a normal MRA.

Results We identified 142 cases of neonatal AIS, of which 81 patients had magnetic resonance imaging and MRA. Among the neonates with arterial neuroimaging, 29 had arterial findings (for a prevalence rate of 20%-35%). The majority of the findings were stenotic or hypoplastic branches. Two patients had presumed carotid artery dissection. Low Apgar scores and the presence of sepsis were significantly ($P < .05$) more common in neonates with MRA findings.

Conclusion The prevalence of arterial abnormalities or variations in neonatal AIS has been underestimated because neurovascular imaging is often not performed. We recommend an MRA for neonates with AIS, particularly those who have low Apgar scores and/or sepsis, to rule out a vasculopathy that may warrant therapeutic intervention. *(J Pediatr 2017;188:110-4).*

Neonatal arterial ischemic stroke (AIS) has been defined as a cerebral vascular injury resulting in neurologic deficits occurring between 20 weeks' gestation and 28 days of life, with focal seizures being the most common presentation.[1] In most cases, the etiology of neonatal stroke remains unknown. Infections, cardiac disorders, hyperhomocysteinemia, hyperviscosity syndromes, and birth asphyxia have been identified as potential causes of neonatal stroke.[1-3] Primary maternal causes also have been evaluated and include maternal autoimmune disorders, coagulation disorders, infection, diabetes, trauma, and cocaine use.[4-7]

To date, arterial abnormalities have not been identified as a cause. This may be because investigation for possible arteriopathy via magnetic resonance angiography (MRA) is not completed commonly in neonates. Neonates require special care while in the magnet, such as monitoring their vital signs and preventing heat loss with minimal disturbance to the infant, and this can discourage use of MRA. Furthermore, a wide range of neonatal hematocrit values[8] and prevalence of anatomical variations,[9] such as hypoplastic branches, make MRA difficult to interpret in the neonatal population.

The presence of an arteriopathy is associated with a high risk of recurrence in childhood stroke.[10] However, studies characterizing or evaluating the risk of recurrence in neonatal stroke with MRA findings are lacking. We therefore sought to characterize the subgroup of neonates with AIS who have MRA findings and identify their risk factors that would predict the need for further evaluation with MRAs. Diagnosing an arteriopathy in a neonate with AIS may change clinical management in childhood stroke.

Methods

This is a single-center, retrospective study of patients with neonatal stroke enrolled in the International Pediatric Stroke Study (IPSS) group from 1991 to 2015. IPSS is a prospective and retrospective international series of children with AIS and cerebral sinus venous thrombosis that has been described previously.[11] Patients in this study were enrolled in the IPSS group registry at the Hospital for Sick Children site in Toronto, Canada, and their parents or caregivers provided consent to participate in research studies. The study included neonates born at term with acute AIS who had neuroimaging that included vascular

AIS	Arterial ischemic stroke
ICA	Internal carotid artery
IPSS	International Pediatric Stroke Study
MRA	Magnetic resonance angiography
MRI	Magnetic resonance imaging

From the [1]Division of Neurology; and [2]Department of Diagnostic Imaging, Hospital for Sick Children, Toronto, Ontario, Canada

The authors declare no conflicts of interest.

0022-3476/$ - see front matter.
http://dx.doi.org10.1016/j.jpeds.2017.05.046

imaging (magnetic resonance imaging [MRI]/MRA). Neonates with hemorrhagic or venous strokes were excluded from the study.

MRI and MRA studies were acquired with 1.5T at median of 24 hours after clinical presentation (range, 15 minutes to 2.5 days) and reviewed by the study neuroradiologist, who was blinded to the original report that was written by a different neuroradiologist in our center. The neurovasculature of each participant was assessed and any vascular abnormality or anatomical variation documented. The stroke laterality and vascular territories affected by the stroke also were evaluated with diffusion-weighted imaging and apparent diffusion coefficient mapping.

Clinical data collected included gestational age, maternal age, birth weight, Apgar scores at 1 and 5 minutes, complications of pregnancy, resuscitation, sepsis, and cardiac defects. Data entered into the central database of the IPSS registry were reviewed and cross-referenced to information from the hospital's electronic patient chart. Demographic information and clinical history also were collected.

Statistical Analyses

Clinical data of neonatal patients with AIS with an abnormal MRA were compared with the group of neonates with AIS with a normal MRA. Wilcoxon rank sum test was used for continuous data and χ^2 test for categorical data. P values $< .05$ were considered significant. Statistical analysis was performed with SAS v9.4 (SAS Institute, Cary, North Carolina).

Results

We identified 142 cases of neonatal stroke from the Toronto site's IPSS registry. All strokes were identified within 7 days of birth. A chart review identified that, within this sample size, 81 cases underwent MRA (57%) and 61 did not (43%); we excluded the latter from the study. Within the 81 patients with a MRA, radiologic review identified 52 with normal vasculature and 29 with a vascular abnormality or normal variation. Because the status of the vasculature for the 61 babies who did not have an MRA was unknown, we report a 20%-35% prevalence rate of MRA abnormalities and/or anatomical variants in neonatal stroke (**Figure 1**).

The main abnormalities and anatomical variations identified (**Figure 2**) included smaller or narrowed branches, hypoplastic branches, absent branches, fetal origins, and presumed internal carotid artery (ICA) dissection. The majority of vascular findings were stenotic (**Figure 3**, A) or hypoplastic (**Figure 3**, B) branches. Two patients (2.5%) were found to have a presumed ICA dissection (**Figure 3**, C). We observed other findings, such as vein of Galen malformations, duplications, and increased arterial caliber.

In the normal MRA group, 13 strokes were right-sided, 28 left-sided, and 7 bilateral. In the group with MRA findings, 7 strokes were right-sided, 17 left-sided, and 5 bilateral. There was no significant difference between the 2 groups in regard to the hemispheric involvement of the stroke ($P = .93$). The MRA findings were in the same distribution of the stroke in 28 of the 29 patients with changes on MRA. Similarly, the territories were evaluated to examine the involvement of the anterior, posterior, and middle cerebral arteries and their combinations. Again, there was no significant difference between the territorial involvements between the 2 groups ($P = .73$).

Apgar scores ranged from 0 to 10 with a median of 8 at 1 minute and 9 at 5 minutes for the normal MRA group, whereas

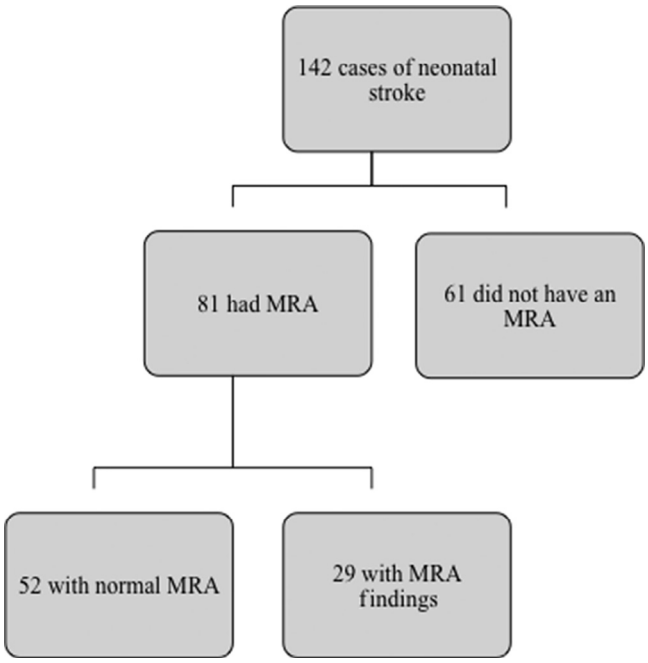

Figure 1. Study sample. The IPSS Toronto site registry had 142 neonates with AIS, of whom 81 had an MRA. MRA findings were reported in 29 infants. The prevalence of MRA findings in in this group of patients was 20% (29/142) to 35% (29/81).

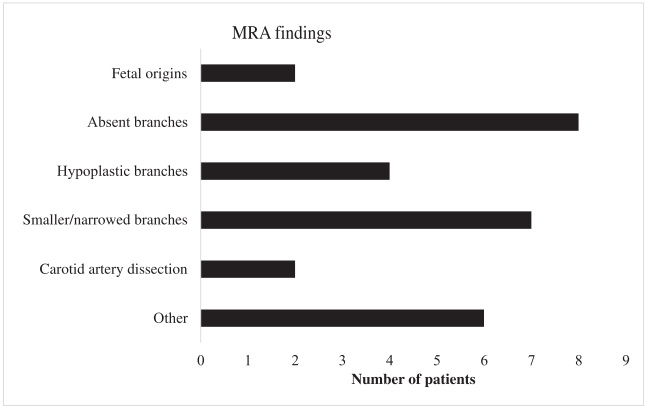

Figure 2. MRA abnormalities and variations found in the study patient sample. MRA findings were reported in 29 of 81 neonates. Vascular stenosis and absent branches were the most common MRA findings.