AJNR

MR and CT Evaluation of Profound Neonatal and Infantile Asphyxia

Elke H. Roland and Alan Hill

AJNR Am J Neuroradiol 1992, 13 (3) 973-975
http://www.ajnr.org/content/13/3/973.citation

Commentary

MR and CT Evaluation of Profound Neonatal and Infantile Asphyxia

Elke H. Roland[1] and Alan Hill[2]

Despite recent advances in obstetrics and neonatal intensive care, perinatal asphyxia remains a major cause of long-term neurologic sequelae in childhood (1, 2). Improvements in the resolution of computed tomography (CT) and magnetic resonance imaging (MR) that have occurred in recent years permit more accurate localization and quantification of hypoxic-ischemic cerebral injury, which, in turn, allow more reliable prediction of outcome. The thought-provoking article by Dr Barkovich in this issue of AJNR documents the topography of profound hypoxic-ischemic cerebral injury in the newborn and young infant on MR and CT and correlates neuroradiologic abnormalities with recent theories of pathogenesis.

In this article, Dr Barkovich, an eminent neuroradiologist with extensive experience in imaging of the newborn brain (1), describes the topography of neuroradiologic abnormalities in 16 infants who had sustained severe hypoxic-ischemic insult (12 newborns and four infants under 2 years of age). The CT scans, performed without contrast enhancement in six infants (two newborns and four older infants), demonstrated decreased attenuation of cerebral tissue in central regions of the brain, ie, basal ganglia, thalamus. The detailed observations on MR scans in this study are of particular interest in view of the increasing evidence that this mode of imaging is becoming the technique of choice for precise anatomical localization of hypoxic-ischemic cerebral injury. Furthermore, because normative data on MR concerning stages of myelination in the immature brain have been established recently (3–6), it has become possible to follow the evolution of cerebral lesions more accurately using this technique.

In the study by Barkovich, MR scans of the 12 newborns demonstrated abnormalities that were located predominantly in lentiform nuclei, thalamic, and hippocampal regions. In contrast, in the four older infants who sustained hypoxic-ischemic insult after the newborn period, there was extensive injury of corpus striatum and cerebral cortex, with relative sparing of perirolandic regions. MR scans obtained at a later age, eg, months to years following the original insult, demonstrated atrophy in the regions outlined above as well as in the lateral geniculate nuclei and hippocampus. Based on these observations, Dr Barkovich suggests that the anatomical pattern of hypoxic-ischemic cerebral injury in newborns may be different from that in older infants. However, in view of the small number of older infants (ie, four) in this study, these conclusions must be regarded with caution.

It is relevant to consider the neuroradiologic observations in the context of existing neuropathologic data in experimental animals and in human newborns. It has been demonstrated that the neuropathologic pattern of hypoxic-ischemic cerebral injury correlates closely with the nature and duration of the insult and with the level of maturation of the immature brain at the time of injury. Thus, two distinct neuropathologic patterns have been documented which correlate closely with the nature of the hypoxic-ischemic insult (1, 2, 7–9). *Acute, total* asphyxia in rhesus monkey fetuses near term results in extensive destruction of brain stem and thalamus, with relative preservation of cortex and subcortical structures. In contrast, following *prolonged, partial* asphyxia, there is disproportionate involvement of the cortex and subcortical regions, either diffusely, or in parasagittal watershed zones between the vascular territories of anterior, middle, and posterior cerebral arteries (7). The MR abnormalities that were documented most commonly in the study by Dr Barkovich correspond more closely to the neuropathologic pattern observed following acute, total hypoxic-ischemic insult. On the basis

[1] Assistant Professor, Division of Neurology, Department of Pediatrics, University of British Columbia.

[2] Professor and Head, Division of Neurology, Department of Pediatrics, University of British Columbia, British Columbia's Children's Hospital, Vancouver, British Columbia, Canada V6H 3V4

Index terms: Asphyxia, in infants and children; Commentaries

AJNR 13:973–975, May/June 1992 0195-6108/92/1303-0973

of these observations, it is suggested that injury affecting predominantly brain stem and basal ganglia may occur more commonly than has been documented previously.

However, the suggestion that this pattern of injury may be the most common is at variance with existing data from CT studies in which the most common radiologic appearance of neonatal hypoxic-ischemic cerebral injury is one of diffuse or multifocal low attenuation affecting predominantly cortex and subcortical regions (10, 11). It is possible that the uncommon observation of brain stem injury on CT scans (8) may relate more to poor visualization of these regions as opposed to an actual low incidence of such injury. In fact, clinical assessments of newborns with severe hypoxic-ischemic encephalopathy often demonstrate brain stem dysfunction, eg, abnormal extraocular eye movements, apnea, disturbances of sucking and swallowing (1, 12). Unfortunately, in the study by Dr Barkovich, the relatively small study population and paucity of clinical information makes it difficult to determine whether or not there is clinical brain stem dysfunction that corresponds to MR abnormalities.

Further difficulties arise if attempts are made to correlate the MR findings in this study with the nature of the preceding hypoxic-ischemic insult. For example, some infants had prolonged periods of cardiorespiratory arrest which were well-documented, (and which may approximate acute, total insult) eg, patients 1, 2, 4, 8, 11, and 12, while, in other instances, the nature, severity, and duration of the hypoxic-ischemic insult are not known, eg, patients 3, 5, and 7 or are documented less precisely, eg, "large placental abruption." In the majority of clinical situations, it is probable that the hypoxic-ischemic insult that affects the human term newborn is a *combination* of both *acute, total* and *prolonged, partial* asphyxia with predominance of one or the other variety (often the latter). This would correlate with published observations that the most common pattern of injury on CT scans involves predominantly cortex and subcortical white matter with relative sparing of deep central structures.

It appears probable that more widespread use of MR in the future will result in improved documentation of these patterns of cerebral injury in the newborn infant. Thus, a fruitful direction for research would be the correlation of patterns of cerebral injury observed on MR with the nature and severity of the hypoxic-ischemic insult, as established by detailed assessment of antenatal and postnatal clinical parameters, eg, fetal heart-rate, cord pH, Apgar scores, and the severity of early neonatal encephalopathy.

Another issue that merits consideration is the optimal timing of neuroradiologic investigations following hypoxic-ischemic brain injury. It has been established by CT studies that there is evolution of the radiologic appearance of hypoxic-ischemic cerebral injury during the days immediately following the insult and that this corresponds to neuropathologic changes that occur at a cellular level. Based on this, it appears that the optimal timing of CT scanning to demonstrate the maximum extent of acute cerebral edema or necrosis is between 2 and 4 days following the original insult (11). This study does not address the particular issue of optimal timing of MR scanning for the demonstration of acute hypoxic-ischemic injury. Clearly, this would be another important area for future study.

The most interesting aspect of the manuscript by Dr Barkovich relates to his correlation of the detailed anatomical abnormalities observed by neuroimaging techniques with recent theories of pathogenesis of hypoxic-ischemic cerebral injury. Thus, possible explanations for the selective vulnerability of neurons in specific locations within the brain may relate to a combination of 1) circulatory factors, ie, ischemic injury in watershed zones of arterial supply; 2) metabolic factors, particularly regional metabolic rates and the distribution of synapses involving excitatory neurotransmitters (glutamate); and 3) stages of maturation of myelination in the immature brain. These theories of pathogenesis are being used increasingly as a theoretical basis for experimental interventional strategies following hypoxic-ischemic cerebral insult. For example, treatment with glutamate receptor antagonists, eg, ketamine, MK-801, have been associated with encouraging neuronal protective effects following such injury (2).

The study by Barkovich provides an indication of the potential major role for MR scanning in the assessment of hypoxic-ischemic cerebral injury, especially in the newborn infant. Clearly, this technique permits detailed localization of such injury which, in turn enables more accurate prediction of outcome and evaluation of the beneficial effects of interventional strategies. In this context, consideration should be given to the potential usefulness of contrast agents, eg, gadolinium DTPA, for earlier documentation of cerebral edema and disruption of the blood-brain

barrier associated with severe, acute hypoxic-ischemic encephalopathy.

References

1. Volpe JJ. *Neurology of the newborn.* 2nd ed. Philadelphia: Saunders 1987;159–280
2. Hill A. Current concepts of hypoxic-ischemic cerebral injury in the term newborn. *Pediatr Neurol* 1991;7:317–325
3. Barkovich AJ, Kjos BO, Jackson DE, Norman D. Normal maturation of the neonatal and infant brain: MR imaging at 1.5 T. *Radiology* 1988;166:173–180
4. Johnson MA, Pennock JM, Bydder GM, et al. Clinical NMR imaging of the brain in children: normal and neurologic disease. *AJR* 1983; 141:1005–1018
5. Holland BA, Haas DK, Norman D, Brant-Zawadski M, Newton TH. MRI of normal brain maturation. *AJNR* 1986;7:201–208
6. McArdle CB, Richardson CJ, Nicholas DA, Mirfakhraee M, Hayden CK, Amparo EG. Developmental features of the neonatal brain: MR imaging. I. Gray-while matter differentiation and myelination. *Radiology* 1987;162:223–229
7. Myers RE. Experimental models of perinatal brain damage: relevance to human pathology. In: Gluck L, ed. *Intrauterine asphyxia and the developing fetal brain.* Chicago: Year Book, 1977;37–97
8. Roland EH, Hill A, Norman MG, Flodmark O, MacNab AJ. Selective brainstem injury in an asphyxiated newborn: correlation of clinical, radiological and neuropathological features. *Ann Neurol* 1988;23: 89–92
9. Pasternak JF, Predey TA, Mikhael MA. Neonatal asphyxia: vulnerability of basal ganglia, thalamus, and brainstem. *Pediatr Neurol* 1991; 7:147–149
10. Adsett DB, Fitz CR, Hill A. Hypoxic-ischemic cerebral injury in the term newborn: correlation of computerized tomographic findings with neurological outcome. *Dev Med Child Neurol* 1985;27:155–160
11. Lupton BA, Hill A, Roland EH, Whitfield MF, Flodmark O. Brain swelling in the asphyxiated term newborn: pathogenesis and outcome. *Pediatrics* 1988;82:139–146
12. Hill A. Clinical assessment of perinatal asphyxia in the newborn. *Can Med Assoc J* 1988;(suppl):53–58