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# The Encephalopathic Neonate: Choosing the Proper Imaging Technique

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The central nervous system (CNS) of the neonate may be injured by a number of different mechanisms, including birth trauma, hypoxia-ischemia, hypoglycemia, hyperbilirubinemia, inborn errors of metabolism, and neonatal infections. Neurologic assessment of affected neonates includes evaluation of alertness level, cranial nerve function, motor function (tone, posture, motility, power, and reflexes), presence of neonatal reflexes (Moro, palmar grasp, and tonic neck response), and gross sensory examination. However, because of the immaturity of the CNS, neonatal neurologic assessment tests only the function of the brain stem and basal ganglia. Abnormal findings will alert the clinician to the fact that the infant has suffered a CNS injury. The precise cause of injury and the severity, extent, and location of the injury to the cerebral cortex are difficult to establish on clinical grounds. Neuroimaging plays an essential role in the assessment of brain injury in these patients by helping to establish the cause of injury and the expected neurologic outcome.

Although the value of high-quality neuroimaging in the assessment of the neonate who has suffered an insult to the CNS has been generally well accepted, the choice of neuroimaging study has not. Some radiologists rely primarily on transfontanelle sonography while others advocate the use of computed tomography (CT) or magnetic resonance (MR) imaging techniques. The purpose of this report is to review briefly the literature on neonatal neuroimaging and to propose a logical approach.

## Techniques

### *Sonography*

Because the anterior fontanelle of the neonate is usually large, nearly the entire brain can be seen with transfontanelle sonography. The ultrasound machine is portable, so it can be used at the bedside in the neonatal intensive care unit and obviates transporting the sick infant. Sonography

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is particularly useful in the imaging of premature neonates, who have small brains and unstable circulatory systems. Moreover, the availability of Doppler sonography has added a new dimension to the arsenal of the sonographer, who can detect altered resistive indexes in neonates who have suffered hypoxic-ischemic injury (1–3).

*CT*

CT is more useful in older children than in neonates. The main reason for the limited utility in neonates is the high water content of the neonatal brain, which reduces contrast between normal and injured tissue. CT is least useful in premature neonates, in whom white matter injury is most common; it is more useful in term neonates, who are more likely to have suffered gray matter injury (4–6). In terms of the difficulty of examination, CT is intermediate between sonography and MR imaging. The patient must be moved to the CT suite, but is easily monitored during the examination and standard life-support equipment is easily accommodated in the modern CT suite.

*MR*

MR imaging and MR spectroscopy are probably the most sensitive and specific imaging techniques in the examination of neonates with suspected brain injury. White matter and gray matter injuries can be detected with MR imaging in both term and preterm neonates (5, 7–11). In addition, abnormalities detected on MR studies have predictive value for neurodevelopmental outcome (8, 12, 13). Proton MR spectroscopy (14, 15) and diffusion MR imaging (16) are useful adjuncts to routine MR imaging and can be acquired with only minimal additional imaging time. However, MR imaging requires transporting infants who are often hemodynamically unstable. Moreover, special life-support and monitoring equipment are needed to perform MR imaging safely on unstable neonates (17).

## Recommendations

*Premature Infants*

Premature infants are often hemodynamically unstable; therefore, transporting them is somewhat risky. Transfontanelle sonography can be performed in the neonatal intensive care unit without moving the neonate and is therefore the initial imaging study of choice in all premature neonates with definite or suspected neurologic impairment. Such techniques as color Doppler sonography and quantitative sonographic feature analysis (18) may ultimately result in improved detection of parenchymal injury and make the use of other techniques unnecessary. However, sonography is not very sensitive to the detection of nonhemorrhagic parenchymal injury. Periventricular leukomalacia (PVL) has been shown pathologically in 85% of infants with birth weights between 900 and 2200 g who survived beyond 6 days (19). The periventricular lesions show a characteristic evolution, with the injured regions undergoing necrosis followed by cavitation and then shrinkage of the cavity with resultant focal enlargement of the adjacent ventricle (20, 21). PVL should be suspected when increased echogenicity is present in the periventricular regions on sonographic studies; however, edema also causes increased echogenicity and it can resolve without any subsequent brain damage (22). Moreover, increased echogenicity can be seen in this region in the absence of PVL or edema (23) and normal sonograms have been reported in infants subsequently proved to have PVL at autopsy (24, 25). Therefore, *the appearance of hyperechogenicity in itself is not enough to make a diagnosis of PVL.* The best early sonographic sign of periventricular white matter injury is the periventricular “flare,” a globular area that has echogenicity equal to or greater than that of the choroid plexus. If prolonged periventricular flares are seen, the prevalence of spastic diplegia or tetraplegia can be as high as 50% (26). A definitive diagnosis of periventricular leukomalacia by sonography requires demonstration of cavitation and the subsequent formation of periventricular cysts (27–31). Cavitation occurs 2 to 6 weeks (usually less than 3 weeks) after injury (31). Although it has been reported that patients with large periventricular cysts (more than 5 mm in diameter) have a poorer motor outcome than those with smaller cysts (26), it is wise to remember that the size of the cysts varies over time; they enlarge as cavitation develops, and then rapidly shrink (21). As a result of the rapid and continuous change in cyst size, it is probably unwise to rely too heavily on this measurement in predicting outcome. Moreover, it is important to remember that mildly or moderately injured tissue may not cavitate yet can still cause neurologic deficit (32).

Other causes of neurologic impairment in premature neonates, such as infection, infarction, and malformation, may be diagnosed with variable confidence at sonography. Congenital infections are suggested by the presence of lenticulostriate vasculopathy (33, 34); however, this finding is nonspecific (33). Large cortical infarctions are easily diagnosed as triangular regions of hyperechogenicity; smaller, more posterior infarctions are more difficult to detect. Midline malformations are more easily diagnosed than those occurring more laterally. In spite of its limitations, the bedside availability of sonography makes it an invaluable tool in the diagnosis of conditions requiring rapid intervention, such as hydrocephalus and hematomas.

Owing to the low sensitivity of sonography in the detection of nonhemorrhagic, noncavitary parenchymal injury, another imaging study is usually necessary if the neurologic status of a child is worse than can be explained by sonographic findings. In our experience, CT is not significantly more sensitive than sonography for the detection of nonhemorrhagic brain injury in premature neonates. The relatively low contrast sensitivity of CT is exacerbated by the high water content of the premature brain, making white matter injury (the most common brain injury in premature neonates) very difficult to identify. Because of the limitations of CT, *MR imaging is recommended as the neuroimaging study of choice after sonography*. Standard

MR imaging has much higher contrast resolution and can unequivocally detect brain injury (manifested as T1 and T2 shortening of affected brain parenchyma) within 2 to 3 days of injury (11, 12), before cavitation develops, and, therefore, significantly earlier than sonography. MR imaging can be performed safely if chemical blankets are used to keep the neonate warm and nonparamagnetic or properly shielded equipment is used. MR imaging is likely to become more sensitive to early injury as diffusion imaging and spectroscopy become more widely available.

In summary, the initial imaging study in premature neonates should be sonography because it is portable and shows most injuries that require immediate intervention. In those patients in whom sonographic findings are inconsistent with the clinical neurologic examination, MR studies should be obtained.

*Term Infants*

Sonography may be useful as the initial neuroimaging study in the examination of term infants with suspected brain injury. As in preterm infants, sonography detects large space-occupying masses and hemorrhages that require immediate intervention. The presence of a "featureless brain" (poor gray–white differentiation and effaced sulci) and increased parenchymal echogenicity is evidence of diffuse cerebral edema and probable brain injury (35). In perinatal hypoxia-ischemia, the presence of hyperechogenic basal ganglia or cystic degeneration of the white matter is predictive of poor outcome (8, 36). However, as many as 50% of neurosonograms in neonates with hypoxic-ischemic encephalopathy are normal (3); this percentage is almost certainly higher in neonates with brain injury resulting from causes other than asphyxia, such as trauma, kernicterus, and meningitis. The use of Doppler increases the sensitivity and specificity of sonography in asphyxiated neonates, as low resistive indexes in the anterior and middle cerebral arteries are strong evidence of hypoxic-ischemic injury and are predictive of poor outcome (1–3). However, Doppler sonographic studies have not proved to be as sensitive for other causes of neonatal brain injury. In addition, sonography and Doppler sonography both lack the specificity afforded by recognition of patterns of injury on MR images. Moreover, sonography has low sensitivity to cortical injuries over the cerebral convexities, as it is difficult to angle the transducer sufficiently to see those areas; focal infarctions, watershed injuries, and parietooccipital injury consequent to hypoglycemia are, therefore, difficult to detect. Furthermore, sonography suffers from being highly operator dependent, a situation compounded by the fact that the operator is often a technologist who may not be familiar with the pathophysiology of neonatal brain injury. Finally, if the scan is not performed properly, deliberation with a more experienced consultant may not be fruitful.

CT has the disadvantage of requiring transportation of the sick neonate. However, sedation is not required for CT, especially if modern scanners with 1- and 2-second scan time are available. In addition, adequate monitoring and access to the neonate is maintained during a CT scan. CT may show low attenuation in affected gray matter, such as the thalami, basal ganglia, or cerebral cortex in asphyxiated neonates. Unfortunately, no studies showing a good correlation of CT appearance during the acute phase of injury with neurodevelopmental outcome have been published; correlations in published studies have not been precise, indicating only a gross relationship between the amount of brain damage and patient outcome (37–40). In these studies, CT suffered from poor detection of both subtle damage and developmental malformations. Therefore, *CT is often not helpful in assessing the term neonate.* It may be of some use if high-quality MR imaging is not available and if sonographic findings do not explain the neurologic status of the affected child.

MR imaging has the disadvantage of requiring extensive mobilization of the neonatal intensive care unit and radiology personnel in order to image a sick neonate safely. Special MR-compatible equipment must be acquired and used both for monitoring and for delivering medication to the infant (17). However, if the departments of neonatology and radiology are willing to make the necessary effort, *high-quality MR images give the most information about the severity of brain damage in the asphyxiated neonate in the early postnatal period.* On day 1, edema can be seen on diffusion-weighted images (16) and on the first echo of T2-weighted images; these findings are predictive of poor outcome (12). Increased levels of lactate, which are predictive of poor outcome as well (14, 41), can be identified with proton MR spectroscopy within the first few hours of life (15). T1 shortening develops in injured structures within 2 to 3 days and T2 shortening within 6 to 7 days (11). Other than areas of subtle T1 shortening in the basal ganglia, which are of uncertain long-term prognostic value (8), these MR abnormalities show excellent correlation with neurodevelopmental outcome (12, 13). Finally, the evolution of changes on T1- and T2-weighted images are well enough established to allow determination of the time of injury from an MR study obtained in the first few days of life; this timing can have important medicolegal implications.

In addition to its utility in the assessment of hypoxic-ischemic injury, MR imaging allows evaluation of the entire brain, extraparenchymal spaces, and spine, so that patterns of injury can be identified and used to establish a diagnosis. The entirety of the cerebral cortex is well seen with by MR imaging, so focal infarctions, watershed infarctions, and parietooccipital cortical injury consequent to hypoglycemia can be easily identified. In addition, the cerebellum and brain stem, which are difficult to evaluate by sonography because of their distance from the anterior fontanelle, are well seen by MR imaging. The many available MR sequences and the exquisite contrast sensitivity of MR imaging add to specificity. For example, gradient-echo imaging allows precise identification of specific parenchymal substances, such as blood. T1-weighted images can show the high-intensity signal of bilirubin in the globi palladi in patients with kernicterus. Finally, MR angiography allows the identification of vascular lesions that may have led to bleeding or stroke and may obviate catheter angiography (42).

In summary, it is always prudent to obtain a sonogram as the initial study in a sick neonate. However, if a lack of concordance is discovered between the clinical course or the neurologic examination and the sonogram, an MR study should be obtained if possible, even in the acute phase. In the subacute or chronic phase, MR imaging is the study of choice to determine the full extent of neurologic malformation or injury.

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