Personal Practice

Use of Newer Imaging Modalities in the Neonate: A Rational Approach

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The amazing advances made in the science of imaging has revolutionized the art of diagnosis, especially in neonatology. The neonate cannot express its symptoms and there are very few specific clinical signs to go by. The array of new imaging modalities available today, especially for neuroimaging, have made what was imperceptible, truly visible.

This does not mean that conventional radiology is taking a backseat in the diagnostic armamentarium. In fact, the chest X-ray and the plain X-ray abdomen are the two most frequently done X-rays in the Neonatal Intensive Care Unit (NICU). These X-rays are usually done in emergency situations where no radiologist is available to interpret them and many therapeutic decisions are based on their correct interpretation by the Pediatrician. Ultrasonography has practically become a routine investigation in the NICU, especially since compact, portable ultrasound machines became available. *Table I* summarizes the indications for ultrasonography (USG) in the neonate.

Neuroimaging

The neonate responds to various neurological conditions with non-specific, stereotyped responses. Hence neuroimaging has assumed great importance in neonatology. However, the Pediatrician has to be aware of which modality to use to obtain the maximum information at that stage of the lesion or illness. For instance, all the initial studies on intraventricular hemorrhage (IVH) in the very preterm infants were done using computerized tomography (CT). But the easy availability of USG has made the use of CT scan redundant for the diagnosis of IVH. However, CT scan does have a role when you are doing a follow up for hydrocephalus. Most neurosurgeons will feel uncomfortable without CT evaluation of hydrocephalus, prior to shunt procedures, even in clearly post-hemorrhagic cases. Thus, a thorough and clear understanding of the advantages and limitations of each imaging modality will help in asking for the right investigation at the right time. The keyword should be maximum information, with least possible disturbance to the baby and with the least expense (only when possible) to the parents. The various neuroimaging techniques that are being currently used are shown in *Table II.*

Ultrasonography

Ultrasound scanning is a technique that capitalizes on the bone free anterior fontanelle to provide a kind of window into the neonatal brain. Real time ultrasound is a cheap, convenient, non-invasive technique for imaging the newborn brain. It has gained acceptance as a first line imaging investigation in the NICU since Pape first published his results in 1979(1). It is the easiest and the most ideal investigation for diagnosing; (z) germinal matrix-intraventricular hemorrhage in preterms;

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TABLE *I—Indications for Ulirasonography in a Neonate*

To confirm abnormalities detected in the fetus during antenatal USG.
Abdomen - to study masses, kidneys and bladder, internal organs in a baby with ambiguous genitalia.
Brain - intracranial bleeds, meningitis, cerebral edema, hydrocephalus and other congenital anomalies.
Echocardiography - congenital cardiac defects, pulmonary hypertension and persistent pulmonary fetal circulation.

TABLE *11—Neuroimaging Techniques*

Structural
Ultrasonography (USG) Computerized Tomography (CT) Magnetic Resonance Imaging (MRI)
Physiological
(to assess function of the brain)
Positron Emission Tomography (PET)
Single Photon Emission Computerized Tomography (SPECT)
Study of cerebral blood flows
Doppler studies
Magnetic Resonance Spectroscopy

(ii) cerebral edema in hypoxic-isehemic encephalopathy in term neonates; *(iii)* ventriculitis following meningitis; and *(iv)* some congenital defects of the brain. A 5MHZ or 7.5 MHZ sector transducer is used for transfontanellar USG. In very low birth weight babies, a 7.5 MHZ transducer gives the best results. We usually classify the USG findings in bleeds as germinal matrix bleed, intraventricular bleed with or without dilatation. A separate notation of the parenchymal lesion is done, as parenchymal flare (a mild lesion), parenchymal leukomalacia, parenchymal cystic lesions and parenchymal hemorrhage, as these have a more guarded prognosis.

Ultrasonography is also ideal for follow up in babies suspected to have enlarging heads, where repeated examinations are required. In an infant with IVH and suspected hydrocephalus, we determine the ventricular index(2) at each USG examination, to make the examination more objective. An actual value of the index is written down on the case paper. It is only when a shunt is being planned by the neurosurgeon, that we order a CT scan. However, this situation is getting more and more infrequent, as we have started realizing that most intraventricular hemorrhages with dilatation of the ventricles in the acute stage, resolve without any residues. In hypoxic ischemic encephalopathy, USG is of particular value in identification of necrosis of basal ganglia and thalamus, periventricular leukomalacia and to a certain degree focal and multifocal ischemic injury.

We did our first small study on IVH in 86 neonates(3) in 1985. Here we screened only those neonates who were thought to be at high risk for hemorrhage. The incidence of IVH was found to be 39%. In 1991, we did a much larger study where 216 preterm neonates were routinely screened for IVH(4). Serial USGs were done on third, seventh and fourteenth day of life. In this study, the incidence of IVH was 26%. Ninety per cent of the hemorrhages were detected on the third day of life, while no new hemorrhages were detected on the fourteenth day. USG at term (40 weeks

postconceptual age) has been used as a predictor of neurodevelopmental outcome in preterm infants(5,6). Our study(4) showed that a normal USG at term was a very good predictor of normal neurodevelopmental outcome at one year (negative predictive value of 90%), in preterm infants. It must however be underscored that USG is a very operator dependent modality; the yield of positive findings on USG being directly proportional to the expertise of the ultrasonologist.

CT Scan

CT scan is a very good modality to study congenital anatomical defects in the brain like agenesis of the corpus callosum. Infarcts seen in hypoxic ischaemic encephalopathy (HIE), are sometimes missed on USG, but easily diagnosed on CT *(Fig. 1)*. It is also a good investigation to study the topography of the lesions in the later period following HIE. CT scan findings were proposed as a prognostic indicator for neurodevelopmental outcome following perinatal asphyxia(7). In a follow up study of 40 full term neonates with HIE(8), we found CT scan to be a poor predictor of neurodevelopmental outcome at one year.

CT scan can give more definitive diagnosis of hemorrhagic fluid collections in the subdural space or subarachnoid hemorrhage compared to USG. In neonates suspected to have intrauterine infections like cytomegalovirus or toxoplasmosis, CT is the best modality to visualize calcifications in the brain.

The disadvantages of CT scan are that it needs transport of a sick neonate to the scan unit, where management of life support systems may be difficult. It is a much longer procedure than doing an USG, it is much more expensive (approximate cost Rs 1,500) and it also gives ionizing radiation. Contrast studies are usually not required in neonates, and should never be done if you are suspecting hemorrhage.

Magnetic Resonance Imaging

Magnetic resonance imaging is a recent technique that is being increasingly used

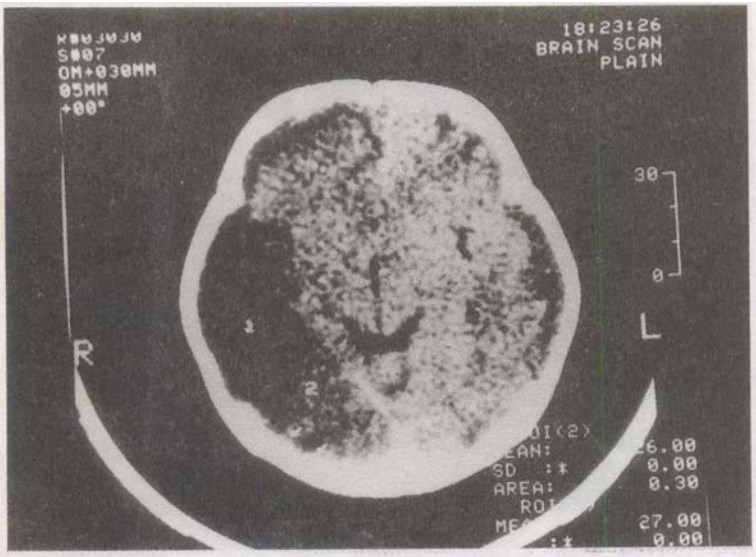

Fig. 1. CT scan of the brain showing a large infarct in hypoxic ischemic encephalopathy.

for neuroimaging. The value of this technique in neonates lies in its ability to define developmental disorders, especially those of myelination. In general, the deposition of myelin is accompanied on Tl weighted images by an increase in signal (which means that myelin appears white) and on T2 weighted images by a decrease in signal (myelinated regions appear black). Although there is disagreement about the choice of Tl weighted versus T2 weighted images for delineation of myelin development, importance on Tl weighted images in the neonate appears to be better. The areas that show myelination on MRI in the first month of life are dorsal midbrain, cerebellar peduncles, posterior limb of the internal capsule, lateral thalamus, subcortical white matter of the paracentral gyrus.

MRI remains the imaging modality of choice for diagnosing disorders of myelination like leukodystrophies and all disorders of neuronal migration like pachygyria, polymicrogyria and schizence-phaly *(Figs. 2 and 3).*

The advantages of MRI in detecting certain lesions of the neonatal brain as enumerated by Volpe are shown in *Table 111(9).* Although, it is clear that MRI is superior to CT in the diagnosis of many neurological developmental lesions(10), it does not pick up calcification easily. CT is far superior for delineating intracranial calcifications. One of the main disadvantages of MRI is that the neonate cannot be monitored while it is in the bore of clinical magnets and hence it is not a suitable imaging modality in criti-

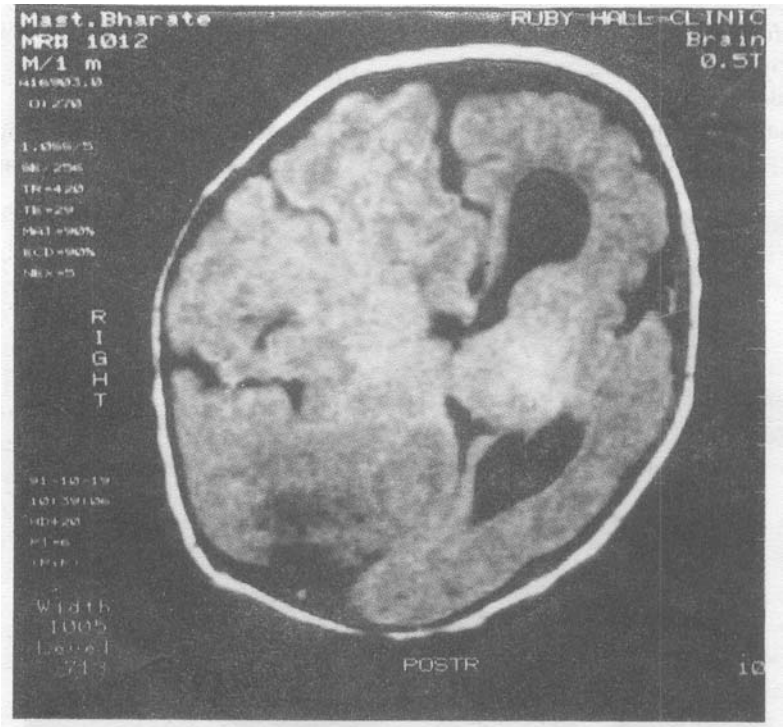

Fig. 2. T1WSE axial section of neonate brain showing pachygyria with 'closed-up' schizencephalic defect in post-central gyrus on right side.

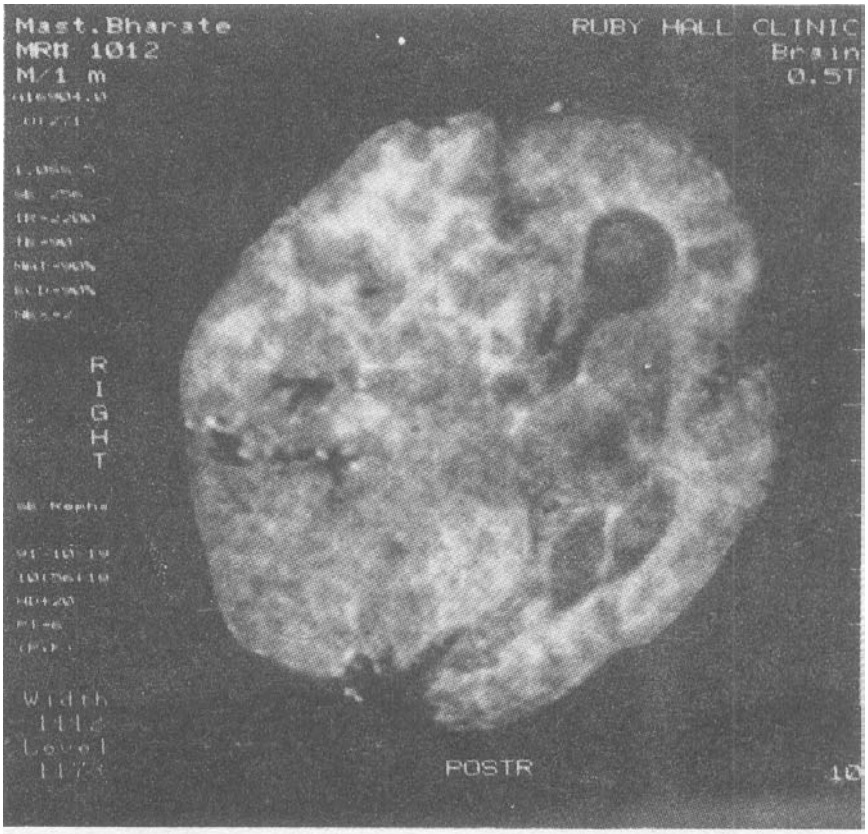

Fig. 3. T2WSE axial section of same neonate showing abnormal myelination pattern with markedly hypoplastic right lateral ventricle.

TABLE III *Abnormalities Detectable by MRI and Readily Missed by CT*

Disorders of myehnation
Disorders of neuronal migration
Arteno-venous malformations
Focal cerebral ischemic lesions (Infarcts)
Venous thrombosis
Parasagittal cerebral injury
Hemorrhagic lesions
Virtually all lesions in posterior fossa and most lesions of spinal cord

cally ill neonates. The neonate has to be sedated and the procedure takes a long time, besides being very expensive (approximate cost Rs 3,500). Hence CT is used much more widely for infants in the NICU.

Position Emission Tomography (PET)

Despite the relatively restricted availability of PET scanning facilities, a considerable amount of data on physiological and biochemical measurements has been generated. The PET scan can determine regional cerebral blood flow, metabolism and blood volume. It is available only in few selected centers in India, but has not been used in neonates.

Single Photon Emission Tomography (SPECT)

This is a radionuclear technique analogous to PET scan, but much less expensive (approximate cost Rs. 1500). However, the intrinsic sensitivity is much less than the PET scan. It is primarily used to define

relative regional cerebral blood flow. There is no Indian data on the use of SPECT in neonates, although it is routinely done in adults in many nuclear scan centers.

Doppler Ultrasound

Doppler ultrasound has been used to measure cerebral blood flow velocity through the anterior cerebral artery. The clinical applications of this measurement are: (z) Cessation of cerebral blood flow (brain death and cerebrovascular occlusion); *(ii)* Alterations in cerebrovascular resistance, (hypoxic ischemic encephalopathy, arteriovenous malformation); and *(Hi)* "Ductal steal" in patent ductus arteriosus.

MR Spectroscopy

MR spectroscopy is another method of non-invasive monitoring, which can give frequent assessment of cerebral metabolism. Normal developmental changes in phosphorus metabolites have been defined using this method. This modality may be of use in determining brain death, before life support systems are discontinued.

As more and more centers start ventilating babies, discontinuance of life support systems after confirming "brain death" will become an important issue. Newer investigations like MR spectroscopy and near infrared spectroscopy, which are currently research tools, in the future will become a valuable tool for the clinician.

Radionuclide Scintigraphy

Although USG, CT and MRI are being used extensively, radioisotope scans are very rarely used for diagnosis in neonates. Pediatricians are probably wary about using this modality in the neonate, out of fear of radiation risk. The radiation received through a CT scan of the brain is far more than that received through a radionuclide scan. For instance, the dose of a radioisotope tracer used for a bone scan is less than 5 microcuries.

Risk *vs* Benefit

If radionuclide scintigraphy is to be of value in the investigation of neonatal disease, it must accomplish one of the following:

(i) It must make earlier diagnosis of the disease.

(ii) It must pinpoint an area of abnormality so that further action can be taken immediately.

(Hi) It must substitute for other more invasive procedures.

(iv) It must give information about the function of an organ, which would not have been otherwise possible.

In certain situations, the radionuclide scan may give vital information which is not gained by any other modality. While asking for a radionuclide scan in a neonate, one must weigh the risk involved in moving the neonate to another hospital with a nuclear medicine department, against the benefit derived from this procedure. Radionuclide scintigraphy is now available in most big cities. The cost ranges between Rs. 1,000 - Rs. 1,200 in Pune city. Some of our experiences with renal, bone and hepatobiliary scans are outlined below.

Renal Scan

Assessment of renal function is very important in neonates with hydronephrosis and vesicoureteral reflux. It is essential to assess the function of both kidneys before planning any surgery. It is useful in differentiating ureteropelvic junction obstruction, severe enough to need surgery, as opposed to the mild and moderate variety where a more conservative approach can be used. In unilateral hydronephrosis, this

scan may be used to determine the correct timing of the surgery by assessing the function of the normal kidney(ll).

An intravenous pyelogram, which is traditionally used to determine function of the kidneys, is not a suitable investigation due to the renal physiology of a neonate. Glomerular filtration rate is only 44% of the adult, at the age of two weeks. As the opacification of the urogram depends directly on the glomerular filtration rate, the reason for failure of intravenous pyelography in many cases is quite obvious. The neonate's clinical condition, like presence of vomiting, may further aggravate the situation. The hyperosmolar load of the dye, poor visualization due to gas shadows, radiation hazard, are some of the other disadvantages of IVP.

Diuretic renography with Tc99m DTPA (Dimethyl triamine pentaaceticacid) or MAG3 (Mercaptoacetyltriglycine) can be used to study the urinary tract in the neonate after giving frusemide. The neonate has a very large extravascular space. The DTPA is a small molecule, which is not bound to plasma protein. It crosses the capillary membrane and easily moves from the intravascular to the extravascular space. It is also excreted by the glomerulus and as already mentioned, GFR is low in neonates. So MAG3, which is a large molecule and is bound to plasma protein, stays in the intravascular compartment and is excreted by the proximal tubules, is the tracer of choice in neonates. However, its exorbitant cost precludes its use in most neonates.

Bone Scan

When a neonate has a soft tissue swelling and tenderness over a long bone, it is very difficult to distinguish between cellulitis or abscess formation and osteomyelitis. Early diagnosis of a bone infection is very important, so that prompt treatment can be started before it spreads to the joint. X-ray changes take several days to appear, by which time it is too late. A diagnosis of osteomyelitis can be made by ultrasonography provided there is detectable amount of fluid. A radionuclide scan with Dimethylene Phosponate Tc99m shows a well-defined focus of radioactivity. This "hot spot" *(Fig.* 4) appears within 24 hours and definitely within 72 hours of the beginning of the infection(12).

Hepatobiliary Scan

In a neonate with persistent cholestatic jaundice, it is important to rule out biliary atresia. Surgery done before 60 days gives good drainage of bile in 80%, while surgery done after 3 months provides drainage of bile in only 20% of neonates(13). Hence it is essential to make a diagnosis of biliary atresia as early as possible(14). Ultrasonography may not give a definite answer. Since hepatobiliary scan is a non-invasive procedure, in our department scintigraphy is done before planning an invasive procedure like liver biopsy(15).

Derivatives of immudoacetic acid (IDA) are used to study the hepatobiliary system. Mebrofenin, which is the latest IDA agent, has a low renal excretion, high hepatic uptake and rapid biliary excretion. Imaging can start within a short time and delayed excretion studies do not take longer than 24 hours. A high hepatic index (above 2) signifies a good uptake. Visualization of the tracer within 4 hours in intestinal tract practically rules out biliary atresia. However, the reverse is not always true. In the severe cholestatic phase of neonatal hepatitis, tracer can be absent in the intestinal tract. IDA scanning has a specificity of 82% and sensitivity of 97% in diagnosing biliary atresia(16). Phenobarbitone (5 mg/kg) given for 5 days prior to the test, enhances the uptake of the dye, thereby improving the accuracy of the test.

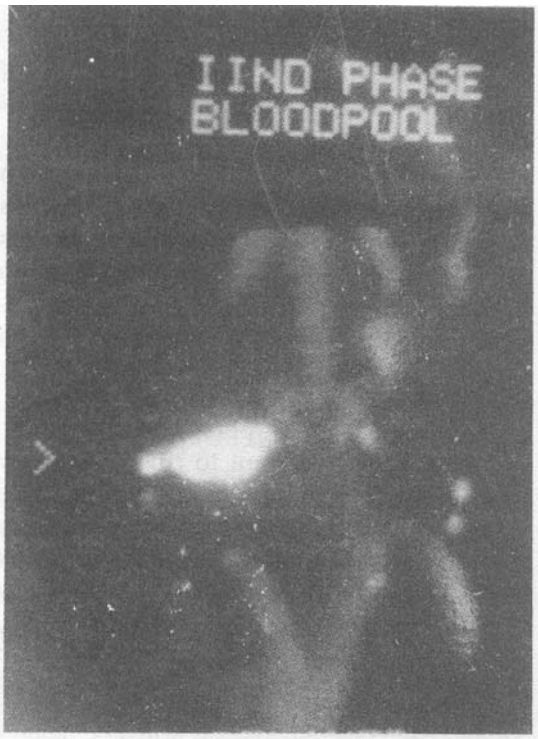

Fig. 4. Bone scan showing increased uptake of radiotracer in the femur.

The burgeoning knowledge and technical advances in the science of imaging will surely unravel a lot of the complexities and mysteries of neonatal medicine, in the forthcoming third millennium.

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