Hemorrhagic Periventricular Leukomalacia in the Neonate: A Real-Time Ultrasound Study

Malcolm I. Levene, MD, MRCP(UK), Jonathan S. Wigglesworth, MD, FRCPath, and Victor Dubowitz, MD, FRCP

From the Department of Paediatrics and Neonatal Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London

ABSTRACT. Periventricular leukomalacia is an important complication of hypoperfusion of the brain in immature newborn infants. In a real-time ultrasound study with frequent scanning of 120 infants of birth weight <1,501 g, hemorrhagic periventricular leukomalacia was observed in nine (7.5%), and in five of these infants subsequent development of cystic degeneration was noted. The overall incidence of intraventricular hemorrhage in the same population was 48%. Pediatrics 1983;71:794-797; periventricular leukomalacia, hypoperfusion, ultrasound, cerebral cysts.

The immature brain is especially vulnerable to variations in cerebral blood flow. Hyperperfusion may precipitate intraventricular hemorrhage (IVH) due to rupture of the fragile capillaries of the germinal matrix whereas hypoperfusion may cause infarction within the periventricular white matter. The latter condition, periventricular leukomalacia (PVL) may lead to the development of areas of cystic degeneration. The diagnosis of IVH is now readily made by computed tomography (CT) or real-time ultrasound, but PVL is not usually recognized by similar currently available imaging techniques. Hill et al1 have, however, recently described a single case report of the ultrasound diagnosis of hemorrhagic PVL. We have seen similar appearances in the neonatal brain and over the last year have observed the natural history and frequency of this condition in the early neonatal period.

METHODS AND PATIENTS

It is the policy at Hammersmith Hospital to scan all infants weighing ≤1,500 g admitted to a regional neonatal intensive care unit for the detection of intracranial hemorrhage. Over a 1-year period from May 1, 1981, the ultrasound scans of all infants weighing ≤1,500 g were analyzed for specific abnormalities described in detail below. All infants were scanned through the anterior fontanel2 using an ATL mechanical sector scanner fitted with a multifrequency scan head (3-, 5-, and 7.5-MHz crystals). The gestational age was determined from the maternal dates, if those were reliable, and by the Dubowitz score.3 If there was a discrepancy of more than 2 weeks between the dates and the assessment, then the latter was used as the actual gestational age.

Periventricular or intraventricular hemorrhage (PVH/IVH) arising from the germinal matrix was graded according to the 3-point system of Levene et al.4 Hemorrhagic periventricular leukomalacia was defined as an area of increased echodensity in the periventricular region distinct from the site of PVH/IVH seen both on coronal and parasagittal views (Fig 1). All infants were then further observed by regular scans in order to detect cystic PVL. This was defined as areas of reduced echodensity appearing from within the area of echodensity in the periventricular region; detection was again required in two planes (Fig 2). The lateral resolution of the sector scanner was limited to 2 mm; smaller lesions could not be detected.

RESULTS

The study included 120 infants with gestational age ranging from 25 to 35 weeks (median 29) and weight ranging from 625 to 1,500 g (median 1,095 g). Infants were scanned from 1 to 56 times (median 6) while on the neonatal unit. Of the 120 infants 28 (23%) died. Of the 120 infants 58 (48%) had IVH...
diagnosed on real-time ultrasound: 32 were grade I (55%), 14 were grade II (24%), and 12 were grade III (21%). Nine infants (7.5%) were found to have the ultrasound appearances of hemorrhagic PVL as described above (see Table). In two of these infants death occurred one day after the first detection of the periventricular echodensity. In five infants cystic PVL developed and in four the echo-free areas appeared within five to 19 days of the dense periventricular areas being noted. One infant was discharged to the referring hospital with the ultrasound appearance of mild hemorrhagic PVL, and when seen 31 days later multiple echo-free areas were present in both hemispheres, consistent with the diagnosis of cystic PVL (Fig 3).

The echo-free areas appeared to originate within the center of the most dense echoes and varied in diameter from 2 to 20 mm. In each case, cysts were detected using the 7.5-MHz transducer earlier than was possible with the 5-MHz transducer. Five of the nine infants with this condition also had IVH; one had grade I, three had grade II, and one had grade III. In four infants development of IVH preceded the periventricular echodensity. One infant was first scanned at 60 hours of age and both IVH and PVL were present; it is likely that these appearances predated delivery. Data for the nine children with ultrasound diagnosis of PVL are presented in the Table.

Four of the nine infants with hemorrhagic PVL died, permission for autopsy was obtained for only two. In Infant 9 who showed periventricular echodensity, autopsy revealed venous congestion in the periventricular region; in infant 6, ultrasound showed characteristic resolving hemorrhagic PVL with cyst formation and autopsy-confirmed periventricular infarction with cystic degeneration. The latter infant with ultrasound evidence of cystic PVL had a CT scan (Siemans Somatom 2) shortly after death and cysts were not identified (Fig 4). One other baby who had ultrasound evidence of extensive PVL with multiple areas of cystic degeneration involving the periventricular region from the frontal to occipital region (Fig 3) also had CT performed, and this showed extensive areas of low

Fig 1. First ultrasound examination (infant 7 at 27 days) showing areas of increased echodensity (arrows) in periventricular region on coronal (upper) and left parasagittal (lower) scans. Death occurred two days later before cystic degeneration. Abbreviations used are: L, left; R, right; P, posterior; A, anterior.

Fig 2. Area of reduced echodensity consistent with cystic degeneration in left periventricular region (arrows) in both coronal and left parasagittal planes (infant 3). This occurs within center of area of increased echodensity consistent with hemorrhagic periventricular leukomalacia (PVL). Abbreviations are defined in Fig 1 legend.
Fig 4. Axial computed tomographic (CT) scan of infant 6 at midthalamic level. Scan is relatively featureless and does not show multiple small cysts detected on ultrasound. Abbreviations are defined in Fig 1 legend.

**TABLE.** Infants with Ultrasound Findings of Congestive and/or Cystic Periventricular Leukomalacia*

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>GA (wk)</th>
<th>Birth Weight (g)</th>
<th>Grade of IVH</th>
<th>Age at IVH</th>
<th>Age at Onset of Congestive PVL</th>
<th>Age at Diagnosis of Cystic PVL</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>35</td>
<td>1,370</td>
<td>III</td>
<td>60 h†</td>
<td>60 h†</td>
<td>5 d</td>
<td>Alive</td>
</tr>
<tr>
<td>2</td>
<td>28</td>
<td>1,250</td>
<td>II</td>
<td>36 h</td>
<td>1 d</td>
<td>5 d</td>
<td>Alive</td>
</tr>
<tr>
<td>3</td>
<td>28</td>
<td>880</td>
<td>I</td>
<td>12 d</td>
<td>10 d</td>
<td>19 d</td>
<td>Died</td>
</tr>
<tr>
<td>4</td>
<td>31</td>
<td>1,460</td>
<td>No IVH</td>
<td>1 d</td>
<td>No cysts</td>
<td>Alive</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>31</td>
<td>1,420</td>
<td>No IVH</td>
<td>42 d</td>
<td>73 d‡</td>
<td>Alive</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>29</td>
<td>800</td>
<td>II</td>
<td>48 h†</td>
<td>5 d</td>
<td>14 d</td>
<td>Died</td>
</tr>
<tr>
<td>7</td>
<td>30</td>
<td>1,100</td>
<td>No IVH</td>
<td>27 d†</td>
<td>No cysts</td>
<td>Died</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>30</td>
<td>920</td>
<td>I</td>
<td>48 h</td>
<td>4 d</td>
<td>No follow-up</td>
<td>Alive</td>
</tr>
<tr>
<td>9</td>
<td>30</td>
<td>1,280</td>
<td>No IVH</td>
<td>1 d†</td>
<td>No cysts</td>
<td>Died</td>
<td></td>
</tr>
</tbody>
</table>

*Abbreviations used are: GA, gestational age; IVH, intraventricular hemorrhage.
† Abnormality present at first scan.
‡ Not scanned between 42 and 73 days.

DISCUSSION

Periventricular leukomalacia, a lesion characteristic of the preterm infant’s brain, is attributed to underperfusion of the boundary zones between different arterial territories within the periventricular white matter. Small areas of PVL are recognized on pathologic examination as white spots due to accumulation of lipid-laden macrophages within areas of gliosis in the periventricular white matter of the centrum semiovale as well as the auditory and optic radiations. More extensive lesions appear as ischemic or attenuation in the periventricular areas (Fig 5), a finding consistent with cystic PVL.
hemorrhagic infarcts which may undergo central liquefaction and cyst formation. Congestion or proliferation of small vessels may be recognized at the margin of the infarcted zones.\(^7\)

The location of areas of increased echodensity seen on ultrasound is the same as that involved in PVL in cases examined post mortem. The sequence of infarction followed by cavitation that can be established in pathologic material corresponds to the sequence of increased density followed by cyst formation as seen in sequential ultrasound scans. The identity of the ultrasound and pathologic changes has been established in a single case report.\(^1\) Either congestion or hemorrhagic infarction could cause the increased echoes seen on ultrasound examination. Ischemia and gliosis without cavitation would not be detectable on ultrasound. We believe that real-time ultrasound allows us to recognize a proportion of cases of PVL involving congestion, hemorrhagic infarction, and eventual cavitation.

The clinical significance of PVL is obvious from the anatomic position that the lesions occupy. The pyramidal tracts pass from the motor cortex through the internal capsule and then descend through the brainstem. The leg distribution is closer to the ventricles and is more likely to be damaged, thereby causing the clinical pattern of spastic diplegia.\(^8\) The incidence of handicap at follow-up is inevitably related to the extent of documented IVH and the possible contribution of PVL is often ignored.

Methods of diagnosis of this condition up to now have been of very limited use. Computed tomography appears to be of little value unless the cystic lesions reach a relatively large size; in one case reported here a third generation CT scanner did not detect cysts of 3-mm diameter. One case report describes the diagnosis of hemorrhagic PVL in an infant of 33 weeks of gestation who weighed 1,630 g.\(^1\) Ultrasound scan revealed a densely echogenic area in the periventricular region on one side and an area of slightly increased echogenicity on the other side. Hemorrhagic infarction of the periventricular region, particularly in the right hemisphere, was found at autopsy. With the recent availability of high-frequency 7.5-MHz transducers it is possible to recognize less severe degrees of this condition and to detect early cystic degeneration long before it is seen with a standard 5-MHz transducer. Further longitudinal studies of this condition with the high-resolution real-time ultrasound scanners currently available should increase our understanding of its pathogenesis and eventually elucidate its relative importance as a precursor of long-term handicap.

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