Neurodevelopmental outcome of transient neonatal intracerebral echodensities

R E Appleton, R E J Lee, E N Hey

Abstract
The later neurodevelopmental progress of 15 babies who had neonatal periventricular echodensities or flares in the absence of any intraventricular bleeding or subsequent cystic degeneration was studied. At follow up four infants had neurological abnormalities, including spastic diplegia (n = 2). These findings suggest that transient flares may represent mild periventricular leucomalacia with consequent mild neurological dysfunction.

The findings on cranial ultrasound, and the neurodevelopmental outcome, of preterm infants with cystic periventricular leucomalacia are well known. Although the pattern of evolution of the cysts that characterise periventricular leucomalacia is not clear, it is likely that the large or persistent (or both) periventricular echodensities or 'flares' that have been seen on ultrasound scans represent ischaemic lesions that subsequently undergo cystic degeneration. Infants with these lesions usually have moderate or severe neurological consequences. Although the clinical importance of smaller or transient echodensities, or both, is less well established, limited data suggest that they may also be associated with neurological dysfunction.

We describe the neurodevelopmental outcome in a group of 15 infants in whom isolated and transient intracerebral flares were seen on cranial ultrasound scans during the neonatal period. Our findings support those of previous studies in suggesting that these flares may represent mild periventricular leucomalacia.

Patients and methods
The cranial ultrasound scans of all newborn infants admitted to our regional neonatal intensive care unit during the four year period May 1984 to May 1988 were reviewed to identify those showing transient intracerebral echodensities. In this unit routine and serial scans are carried out on any infant whose gestational age is less than 34 weeks, any infant who is given ventilatory support irrespective of gestational age, and any infant who shows abnormal behaviour or neurological signs, or both. The scans were carried out in both coronal and parasagittal planes through the anterior fontanelle, and interpreted by a paediatric radiologist (REJL). Scans were done with a Hewlett-Packard 77020AR real time phased array sector scanner with a short focus 5 MHz probe. Infants were usually scanned within 24 hours of birth, and thereafter twice or thrice weekly until they were discharged home or transferred back to their referring hospital.

In this four year period one or more scans were carried out on a total of 727 infants, of whom 15 had transient echodensities or flares within the cerebral parenchyma in a periventricular distribution. A 'flare' was defined as an echodensity which was present in both coronal and parasagittal planes and which, irrespective of duration, size, or location resolved without the subsequent development of cysts, irregularly shaped ventricles, or other abnormal findings seen on ultrasound scan. None of the 15 infants had ultrasonic evidence of germinal matrix or intraventricular haemorrhage. Review of the clinical records and follow up (neurological examination and Denver developmental assessment corrected for gestational age) were undertaken by a single observer (REA).

Results
Details of the demographic, cranial ultrasound, and neurodevelopmental findings of the 15 infants are shown in the table. Of the six twins in this series, five shared a single placenta (cases 2–6) but in only case 2 was the placenta monochorionic. All the flares appeared within the first week of life. In 14 the parietal lobe(s) superolateral to the lateral ventricles were affected (bilateral in seven, and right sided in five). In the remaining infant (case 15) both caudate nuclei were affected. In eight infants there was complete resolution within seven days, while in four resolution was noted between 15 and 36 days after the onset. In the remaining three patients, no follow up scans were available; in one (case 13) the flares were unchanged six days after onset. These three infants were included in the study as the initial scan findings were identical to those of the rest of the group.

All the infants survived. The neurological examination was normal in 11 infants (73%). Two infants had spastic diplegia (one of which was pronounced and accompanied by a bilateral sensorineural hearing loss of 60 decibels (case 11), and one of which was minimal). Two other infants had abnormal and variable muscle tone (dystonia) and in one of these (case 13) hypotonia was the predominant finding; this child also had frequent and spontaneous shuddering spells. Two other infants (cases 8 and 9) had required surgical correction of bilateral squints. No child had developed epilepsy at the time of writing. Ten children (67%) had developed normally. Centiles for head circumference (at birth and at follow up) remained unchanged in...
10 infants. In five the centile increased by between 5 and 10%, but in only one (case 8) did this reach the 97th centile. The weight and height of this infant lay above the 97th centile, the neurodevelopmental status was normal, and cranial ultrasonography at follow up showed normal ventricles.

**Discussion**

Limited data have suggested that some periventricular echodensities is a common and transient finding, and therefore of no clinical importance. However, there is no information, however, on the duration of 'transient', and therefore what constitutes 'normal' echodensity. Trounce et al arbitrarily defined prolonged, and presumably therefore clinically important, echodensities as lasting for two weeks or more and not becoming cystic. De Vries et al observed that persistence of densities for more than 10 days was particularly associated with subsequent neurological problems. In our study we included all infants with parenchymal echodensities or 'flares' of any duration, but excluded any infant who had evidence of germinal matrix or intraventricular haemorrhage in addition to flaring. Our reason for doing so was to try and correlate neurodevelopmental outcome with the duration of the flare alone. All our infants developed flares within the first week of life, a finding in agreement with that of Trounce et al.

Several follow up studies have been reported that associate neurodevelopmental outcome with the presence of cystic periventricular leukomalacia. The outcome of infants with flares or intracerebral echodensities that have not undergone cystic degeneration has been reported less frequently. Of the 15 patients in our study (73%) have a normal neurological examination; however, one of these 11 (case 3) is developmentally delayed. One infant, although normal at the time of this assessment, had shown abnormal muscle tone in the first year of life (transient dystonia). In two cases (2 and 5), flaring persisted for over three weeks; as their ages were only 9 and 10 months, respectively, however, these infants may yet develop neurological dysfunction. Four infants (all boys) had neurological abnormalities; in two the flares had persisted for over two weeks. In a further patient who had dystonia (case 13), flaring was unchanged six days after onset. It is therefore likely that the flares may have persisted for some considerable time.

McMenamin et al, in reporting 22 survivors of 32 infants with small intraparenchymal echodensities, found that complete resolution occurred in 19 while the remaining three developed small cysts. Fourteen of the 22 infants (64%) were normal neurologically, and six demonstrated mild, and two moderate, deficits. All but one of their surviving patients, however, also had germinal matrix or intraventricular haemorrhages, and there were no data on the duration of the echodensities. Data from the Hammer smith Hospital that identified periventricular echodensities in 59 infants, showed that there was a normal outcome in about half. Four infants developed spastic diplegia and 24 transient dystonia. Infants with periventricular densities in association with germinal matrix or intraventricular haemorrhages, or both, were also excluded from their study. The neurodevelopmental outcome of the infants with prolonged flares initially reported by Trounce et al indicated that such infants had a higher risk of neurological dysfunction, but that the presence of prolonged flares was less accurate in predicting adverse outcome than for cystic periventricular leukomalacia. The results of a further study also showed that persistent echodensities (lasting between two and four weeks) were associated with severe neurological handicap.

Frequent and unprovoked episodes of shuddering were observed in one of the dystonic infants (case 13). Shuddering attacks are considered to be benign, unrelated to epilepsy, and a possible early clinical manifestation of essential tremor. There is no evidence that they are

### Demographic, ultrasound, and neurodevelopmental findings in the 15 infants

<table>
<thead>
<tr>
<th>Case No</th>
<th>Sex</th>
<th>Gestation (weeks)</th>
<th>Birth weight (g)</th>
<th>Singleton/ twin</th>
<th>Ventilatory support (days)</th>
<th>Onset to resolution of flares (days of life)</th>
<th>Age (months)</th>
<th>Neurological examination</th>
<th>Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>29</td>
<td>890</td>
<td>Twin 2</td>
<td>33</td>
<td>2-9</td>
<td>16</td>
<td>Normal (but showed transient dystonia until 14 months old)</td>
<td>Normal</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>29</td>
<td>1600</td>
<td>Twin 2</td>
<td>7</td>
<td>4-40</td>
<td>10</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>3</td>
<td>Female</td>
<td>31</td>
<td>1160</td>
<td>Twin 2</td>
<td>2</td>
<td>4-8</td>
<td>17</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>4</td>
<td>Male</td>
<td>31</td>
<td>1550</td>
<td>Twin 2</td>
<td>5</td>
<td>6-21</td>
<td>23</td>
<td>Spastic diplegia</td>
<td>Gross motor delay</td>
</tr>
<tr>
<td>5</td>
<td>Female</td>
<td>32</td>
<td>1840</td>
<td>Twin 2</td>
<td>7</td>
<td>5-28</td>
<td>9</td>
<td>Normal</td>
<td>Neurological delay</td>
</tr>
<tr>
<td>6</td>
<td>Male</td>
<td>33</td>
<td>1875</td>
<td>Twin 1</td>
<td>0</td>
<td>1-6</td>
<td>35</td>
<td>Normal</td>
<td>Neurological delay</td>
</tr>
<tr>
<td>7</td>
<td>Female</td>
<td>27</td>
<td>1180</td>
<td>Singleton 0</td>
<td>2-not recorded</td>
<td>26</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>8</td>
<td>Male</td>
<td>29</td>
<td>1510</td>
<td>Singleton 1</td>
<td>1</td>
<td>1-7</td>
<td>16</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>9</td>
<td>Female</td>
<td>30</td>
<td>1340</td>
<td>Singleton 0</td>
<td>2</td>
<td>2-6</td>
<td>17</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>10</td>
<td>Female</td>
<td>31</td>
<td>1620</td>
<td>Singleton 2</td>
<td>4</td>
<td>4-7</td>
<td>14</td>
<td>Normal</td>
<td>Neurological delay</td>
</tr>
<tr>
<td>11</td>
<td>Male</td>
<td>33</td>
<td>1200</td>
<td>Singleton 10</td>
<td>10</td>
<td>4-35</td>
<td>14</td>
<td>Spastic diplegia</td>
<td>Gross motor delay</td>
</tr>
<tr>
<td>12</td>
<td>Female</td>
<td>33</td>
<td>2020</td>
<td>Singleton 0</td>
<td>2-8</td>
<td>28</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>13</td>
<td>Male</td>
<td>34</td>
<td>1560</td>
<td>Singleton 5</td>
<td>4-&gt;10</td>
<td>16</td>
<td>Dystonia</td>
<td>Neurological delay</td>
<td>Neurological delay</td>
</tr>
<tr>
<td>14</td>
<td>Male</td>
<td>34</td>
<td>2200</td>
<td>Singleton 2</td>
<td>1</td>
<td>5-5</td>
<td>41</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>15</td>
<td>Female</td>
<td>40</td>
<td>4115</td>
<td>Singleton 0</td>
<td>3-not recorded</td>
<td>16</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
</tbody>
</table>
Neurodevelopmental outcome of transient neonatal intracerebral echodensities

associated with cerebral injury. The small number of patients in this study precludes a definitive conclusion about neurodevelopmental outcome with respect to the laterality of the flares. Thus those infants who had bilateral echodensities fared no better or worse than those with unilateral flares.

One third of the infants in this study were the second of twins (one of the six having a monochorionic placenta)—a relatively high proportion of the entire group. This is not necessarily unexpected, given that twin pregnancies (and particularly the second twin) are at increased risk of adverse peripartum events that may predispose to hypoxic or ischaemic brain damage, or both. It has also been suggested that a monochorionic placenta increases this risk even further. 13

Our results show that neonatal transient intracerebral echodensities are not always benign. Thus all infants showing such echodensities should be carefully followed up and parents should be given a guarded prognosis about their neurological development.

The authors express their appreciation to the paediatricians of the Northern region for permission to study their patients.

1 Grant EG, Schelling D, Richardson JD, Coffey ML, Smirniotopoulos JG. Echogenic periventricular halo: normal sonographic finding or neonatal cerebral haemorrhage. AJR 1983;140:793-6.