Cerebellar hemorrhage in the premature infant

Lesions of the central nervous system were reviewed in 144 premature neonates without anomalies or infections coming to autopsy from the Intermountain Regional Neonatal Intensive Care Unit. Twelve neonates were found to have had cerebellar hemorrhages. Eleven of the 12 with cerebellar hemorrhage also had germinal plate hemorrhages at postmortem examination. Some hemorrhages destroyed one or both cerebellar hemispheres. Three of 19 (16%) infants between 20 to 24 weeks' gestation, six of 26 (25%) infants between 26 to 28 weeks' gestation, two of 24 (8%) infants between 28 to 30 weeks' gestation, and one of 19 (5%) infants between 20 to 32 weeks' gestation had cerebellar hemorrhage. No premature neonate after 32 weeks' gestation had cerebellar hemorrhage. It is probable that trauma does not play a role in the pathogenesis of the cerebellar hemorrhage.

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Cerebellar hemorrhage in the neonatal period is a rare disease. It has been reported primarily in term infants. In the past four years, however, among 144 premature infants evaluated at postmortem examination we noted 12 (8%) with cerebellar hemorrhage. We have, therefore, reviewed our autopsy specimens and the clinical histories in a retrospective study of cerebellar hemorrhage in premature infants cared for in the Intermountain Newborn Intensive Care Center.

MATERIAL AND METHODS

One hundred forty-four gross and microscopic brain specimens from consecutive autopsies on infants dying between January, 1970, and December, 1974, were examined. Gestational age was estimated by the expected date of confinement, the Dubowitz score as determined by the admitting pediatrician, and the brain convolutional pattern. Infants having brain malformation, trauma, infectious disease, or metabolic disease were eliminated from the study.

Brains were removed at autopsy and placed in 50% formalin for at least three weeks. Brains were then sectioned coronally, and sections from medulla, pons, midbrain, cerebellum, calcarine cortex, cingulate gyrus, hippocampus, thalamus, caudate, putamen, globus pallidus, orbital frontal cortex, and areas of gross lesions were taken for microscopic examination. Microscopic sections were processed through the ultra-autotechnicon, embedded in paraffin, sectioned at 5-10μ, and stained with hematoxylin and eosin. Specimens were grouped by gestational age (Table I). The groups were compared by percentages.

The hospital charts of the patients with cerebellar hemorrhage were reviewed. Possible contributing factors which were evaluated included the age and parity of the mother, prenatal intrapartum complications, birth presentation, one- and five-minute Apgar scores, birth weight, gestational age, and the clinical course. These were compared with similar data obtained from the charts of infants who had no evidence of cerebellar hemorrhage at postmortem examination and who were of similar gestational age.

RESULTS

Cerebellar hemorrhages, usually destroying a part of a cerebellar hemisphere, and in four cases destroying one or both cerebellar hemispheres, were seen in 12 of 87 (14%) premature infants under 32 weeks' gestation. It was seen in three of 19 (16%) premature infants of 24 to 26 weeks' gestation, six of 26 (25%) of 26 to 28 weeks' gestation, two of 24 (8%) of gestational age 28 to 30 weeks, and one of 19...
Fig. 1. Graph showing percentage of premature infants having cerebellar hemorrhage as related to gestational age.

Table I

<table>
<thead>
<tr>
<th>Gestational age (wk)</th>
<th>No. of infants</th>
<th>No. with cerebellar hemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td>24-26</td>
<td>19</td>
<td>3</td>
</tr>
<tr>
<td>26-28</td>
<td>26</td>
<td>6</td>
</tr>
<tr>
<td>28-30</td>
<td>24</td>
<td>2</td>
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<tr>
<td>30-32</td>
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<tr>
<td>32-34</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>34-36</td>
<td>23</td>
<td>0</td>
</tr>
<tr>
<td>36-38</td>
<td>16</td>
<td>0</td>
</tr>
<tr>
<td>38-40</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>144</strong></td>
<td><strong>12</strong></td>
</tr>
</tbody>
</table>

(5%) of gestational age 30 to 32 weeks (Fig. 1). Cerebellar hemorrhage was not seen in infants of more than 32 weeks' gestation. Older infants, however, occasionally had petechiae in the cerebellum. Ten of the 12 patients with cerebellar hemorrhage had hemorrhages into the cerebral germinal plate that appeared to have occurred at about the same time as the cerebellar hemorrhage. In one infant the cerebral germinal plate hemorrhage was several days older than the cerebellar hemorrhage, and in one infant there was no germinal plate hemorrhage.

The distribution of the hemorrhage within the cerebellum was variable. No pattern seemed to predominate. In one case both cerebellar hemispheres were destroyed by hemorrhage. This was the most extensive hemorrhage noted. In three cases the hemorrhage essentially destroyed one hemisphere (Fig. 2). In most of the others the hemorrhage occurred in the peripheral half of a hemisphere. This was usually associated with subarachnoid hemorrhage. Hemorrhage was also seen in the cerebellar germinal plate in the roof of the fourth ventricle in eight of the infants (Fig. 3). Serial sections through the cerebellum were not available in any case, so it is possible that some hemisphere hemorrhages represented extension of vermian hemorrhage.

In a review of affected infants' charts and a group of matched infants without cerebellar hemorrhage no significant differences in age of mother, parity, prenatal and intrapartum complications, birth presentation, one- and five-minute Apgar scores or birth weight compared to gestational age were noted.

The clinical course of each infant was reviewed. There was no consistent event or sequence of events that indicated a cerebellar hemorrhage had occurred. Most of the cases (eight of 12 or 68%) were associated with an episode of sudden deterioration hours or days prior to death. This was manifested always by bradycardia and occasionally by apnea and/or seizures. The neurologic picture was not recorded in the chart in most infants, but in one case the infant was noted to be "rigid" and another infant was "floppy," in the interim between the acute episode and death. A drop in the hematocrit value was noted in most cases within 24 hours of deterioration. There was no evidence of mechanical deformation of the occiput in any infant, and none had had a face mask held in place by an occipital band. The clinical picture is essentially the same as in infants who have had a cerebral germinal plate hemorrhage. The one infant in whom cerebellar hemorrhage occurred without hemorrhage into the cerebral germinal plate was born at 27 weeks' gestation with an Apgar score of 1 after a double footling breech delivery complicated by compression of the umbilical cord and fetal distress for at least ten minutes. Resuscitative efforts failed, and the infant was pronounced dead ten minutes after birth. One infant had a sudden deterioration of clinical status leading to death several days after surviving a similar episode of clinical deterioration. This infant had an acute cerebellar hemorrhage and a cerebral germinal plate hemorrhage with intraventricular rupture which appeared to have occurred several days prior to death. An infant not in this series who died at another hospital but had been treated in our Intermountain Regional Neonatal Intensive Care Unit had evidence of an old cerebellar hemorrhage with rupture into the fourth ventricle and subarachnoid space. No germinal plate hemorrhage was present, but the patient had severe hydrocephalus.

**DISCUSSION**

Cerebellar hemorrhage in adults is a well-described disease in hypertensive individuals, but there have been...
Fig. 2. Microscopic section through pons and cerebellum of a 26 week gestation infant, showing hemorrhage destroying one cerebellar hemisphere (arrow). (H & E; ×20.)

relatively few reports of cerebellar hemorrhage in neonates. Michael reported one case in 1932 of an infant who developed signs of increasing intracranial pressure at ten days of life and died at one month. A large clot in the right cerebellar hemisphere and hydrocephalus were found at postmortem examination. Towbin, in a review of spinal cord and brainstem injuries in neonates, describes a term infant who died shortly after birth with hemorrhage in the cerebellar hemisphere. This was ascribed to the trauma of a difficult delivery. There are several other case reports of cerebellar hemorrhage in term newborn infants. Hemeseth, in 1933, reported on fractures of the posterior intraoccipital synchondrosis and demonstrated injury to the cerebellum in cases of separation and depression of this synchondrosis. This is presumably the mechanism of injury in some cases. Potter reports one infant with hemorrhage, apparently arising from the choroid plexus of the fourth ventricle, causing destruction of the interior of the cerebellum. Gestational age of this infant is not stated. One case of cerebellar hemorrhage in a premature infant of 34 weeks' gestation is reported, but the hemorrhage was secondary to an arterial-venous aneurysm. In the early case reports the diagnosis cerebellar hemorrhage was made at postmortem examination. More recently, infants have been diagnosed during life, and surgical removal of cerebellar blood clots has been carried out. Some of the patients survived, but some required surgical shunting procedures to relieve hydrocephalus.

The etiology of cerebellar hemorrhage in the premature infant is unclear. Extreme prematurity is certainly a factor, since 75% of our cases occurred in infants of less than 28 weeks' gestation, and no cerebellar hemorrhages were seen in infants whose gestation was more than 32 weeks. Eleven of the 12 infants had the respiratory distress syndrome. Eighty-five percent of our cases were associated with an apparent concurrent hemorrhage into the cerebral germinal plate. The cause of hemorrhage into the cerebral germinal plate has not been firmly established. Towbin ascribes it to congestion and thrombosis of the striate veins that cause infarction of the germinal plate with secondary hemorrhage. A cerebellar germinal zone in the roof of the fourth ventricle has been identified in human beings from Day 60 to Day 80 of gestation. We believe that a cerebellar germinal plate can be identified in the roof of the fourth ventricle in premature infants up to 28 to 30 weeks' gestational age. It is possible that the etiology of cerebellar hemorrhage in the premature infant may be similar to cerebral germinal plate hemorrhage. We have not seen evidence, however, of large, thin-walled veins in the cerebellar germinal plate. Since these hemorrhages are seen only in young premature infants, maturation of vessel walls, clotting factors, or other factors may be involved.

Recently Pape and associates have reported nine cases of cerebellar hemorrhage in small premature infants of less than 1,500 gm. They have attributed the hemorrhages
to mechanical deformation of the infants' occiputs by a Velcro band used to attach a face mask for positive pressure breathing. The extreme prematurity of the infants they report is similar to ours. All of our cases occurred in premature infants of less than 32 weeks' gestation. In none of our 12 cases was a facemask held onto the infant by a Velcro band.

It is possible that some factor related to treatment, such as rapid changes in osmotic pressure, as suggested by Simmons and associates, may play a role. Whatever the cause, the incidence of cerebellar hemorrhage is increasing in our center as younger premature infants, previously thought to be nonviable, are given intensive care and survive for a longer time.

REFERENCES