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Intracranial Hemorrhage in Neonates with Erythroblastosis Fetalis: Sonographic and CT Findings

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Cranial sonography revealed cerebral hemorrhage in three of seven neonates with erythroblastosis fetalis. Among the three infants with hemorrhage, one was 28 weeks gestational age and experienced germinal matrix hemorrhage with ventricular extension, a finding typical of cerebroventricular hemorrhage in the premature population. The other two infants with intracranial hemorrhage were more gestationally mature, and extensive intraparenchymal cerebral hemorrhages were found at sonography. These hematomas were peripheral in location and one was multifocal. Computed tomography (CT) further revealed hemorrhages in both neonates to be multifocal and in close proximity to the pia-arachnoid. In one case, the hemorrhage appeared to extend centripetally and rupture into the ventricular system. The high incidence, severity, and unusual appearance of intracranial hemorrhages in neonates with erythroblastosis fetalis has not been previously emphasized in the radiologic literature. In severe cases, children with erythroblastosis fetalis should be closely observed for intracranial hemorrhage by either sonography or CT, regardless of gestational age.

The high incidence of cerebroventricular hemorrhage in premature neonates less than 32 weeks gestational age has been well documented [1-3]. Most investigators would agree that its etiology is unique, residing in the germinal matrix in the vast majority of intracranial hemorrhages in such infants. Although intracranial hemorrhage does occur in more gestationally mature neonates, it is relatively unusual [4, 5]. Because the germinal matrix is no longer present in such infants, hemorrhage has a different etiology and appearance [6].

We examined a group of seven neonates, all of whom were the result of pregnancies complicated by Rh incompatibility resulting in hemolytic disease of the newborn. Among these seven, three had sonographic evidence of intracranial hemorrhage. Of the three, one was very premature and demonstrated a hematoma confined to the germinal matrix and ventricles, typical of the type of hemorrhage found at this age. The two more gestationally mature neonates, however, experienced unusual intracranial hemorrhages that were large, peripheral, and intraparenchymal. Details of these cases and their significance follow.

Materials and Methods

Four of the seven infants were 32 weeks gestational age or younger. Therefore, they were admitted to the neonatal intensive care unit, where they routinely underwent cranial sonography, regardless of clinical condition or history. As infants older than 32 weeks gestation are not routinely scanned at our institution, the three neonates in this group underwent cranial sonography due to extremely poor clinical conditions with severe bleeding diatheses.

The infants were examined with an ATL Mark III or Mark 500 real-time sector scanner with a 5 MHz medium-focus transducer system. The transfontanelle scanning approach was used exclusively [7]. Computed tomographic (CT) scans were obtained in two of the three cases in which the intracranial hemorrhage was detected sonographically. Follow-up sonograms were obtained at weekly intervals on the infants with intracranial hemorrhage, and at least two sonograms were obtained on each of the four normal infants.
Case Reports

Case 1

An Rh-positive female infant weighing 3020 g was delivered vaginally at 36 weeks gestational age by an Rh-negative mother. The child was cyanotic and had hepatosplenomegaly. Multiple petechiae were present on the skin and a large cephalhematoma was noted. Hematocrit at birth was 28% and total bilirubin was 8.3 mg/dl. Multiple exchange transfusions were required and profound thrombocytopenia was present. The respiratory status was relatively good and the infant was easily weaned from the respirator.

At 3 days of age, a cranial sonogram revealed focal areas of cerebral hemorrhage in both hemispheres. These were in peripheral locations (fig. 1A), and the largest involved much of the right temporal lobe (fig. 1B). A CT scan the next day also identified multiple focal hematomas in A. Another large hematoma occupies most of right temporal lobe (TL). Sylvian fissure bowed somewhat superiorly (arrows). C. CT scan. Large right parietal hematoma (H) extending to surface of brain. Similar but smaller hematoma in left posterior parietal area (arrows).

Fig. 1.—Case 1. A, Semiaxial sonogram. Two peripherally located areas of increased echogenicity representing hematoma are in right anterior and posterior parietal areas (H). Choroid plexus (arrows). B, Right parasagittal sonogram. Echogenic foci in anterior and posterior parietal areas (H) correspond to areas of hemorrhage, all of which were near the pia-arachnoid (fig. 1C). The infant was discharged at 3 weeks of age and did well during the ensuing 3 months.

Case 2

This 1470 g, 27-week-gestational age female infant was born to a 35-year-old gravida 4, para 2, previously sensitized Rh-negative mother. History included two stillbirths. An intraterine sonogram revealed a hydropic fetus, and intraterine transfusions were performed. The infant was delivered by cesarean section with initial Apgar scores of 1 and 3. Sonographic evaluation at 48 hr revealed germinal matrix hemorrhage with ventricular extension (fig. 2). CT was not performed. Multiple problems including worsening pulmonary status, severe hyperbilirubinemia, and diffuse hemorrhage led to the death of this neonate at 4 days of age.

Case 3

This 1940 g, Rh-positive, 33-week-gestational age neonate was born to a gravida 4, para 2, Rh-negative, previously sensitized 34-year-old mother. An earlier infant had died as the result of erythroblastosis fetalis. During this pregnancy one intraterine transfusion was necessary, and a final prenatal sonogram revealed fetal ascites. On the day of delivery, the mother noted decreasing fetal movement, and a cesarean delivery was performed. Apgar scores were 1 and 5 at 1 and 5 min, and 8 at 10 min. Hematocrit was 18% and bilirubin was 6.2 mg/dl. Intubation was necessary and a partial exchange transfusion was performed in the delivery room. Severe respiratory problems included hyaline membrane disease and a persistently patent ductus arteriosus. Marked hyperbilirubinemia required six full exchange transfusions; despite this, thrombocytopenia persisted to the point of requiring platelet transfusions. Clinically, motor activity was markedly decreased.

On the third day of life, a sonogram revealed massive intracranial hemorrhage (fig. 3A). A CT scan shortly thereafter confirmed these findings. More precisely, it showed multiple isolated intraparenchymal...
hemorrhages in the cerebral hemispheres and the cerebellum. All hematomas were close to the surface of the brain. In addition, a large component of subarachnoid hemorrhage was present (figs. 3B and 3C). The baby developed dilated fixed pupils, and autopsy confirmed the findings of subarachnoid, intraparenchymal, and intraventricular hemorrhage.

Cases 4–7

No evidence of intracranial hemorrhage was seen on any of at least two sonograms obtained on each neonate, although each had an early hospital course complicated by factors similar to those described in cases 1–3. Clinical data on these neonates are summarized in table 1.

Discussion

Erythroblastosis fetalis results from the transplacental passage of antibodies formed by the mother into the fetus. These antibodies are active against red-cell antigens of the baby and may result in massive red-cell destruction [8]. Fortunately, advancements in prenatal therapy including anti-Rh gamma globulin to prevent maternal sensitization and intratuterine transfusions, have drastically reduced the number of infants affected by this once common disease [9].

The intrauterine findings in erythroblastosis fetalis, manifested sonographically as hydrops fetalis, were well described by Fleisher et al. [10] and include an edematous fetus and placenta, ascites, and pleural effusions. Less attention has been directed in the radiology literature, however, toward the postnatal problems of the infant affected by this disease.

Clinically, all manifestations of erythroblastosis fetalis are the result of red-cell destruction in the fetus and neonate. They generally include jaundice, anemia, edema, hepatosplenomegaly, hypoproteinemia, thrombocytopenic purpura, and hemorrhage [8]. Recent studies seem to indicate that the hemorrhagic diathesis may be more complicated than previously suspected and may be the result of disseminated intravascular coagulation [11]. Among long-term effects of erythroblastosis fetalis, kernicterus is the most important. Kernicterus relates to the yellow staining of the basal ganglia and cerebellum by bile pigments. Clinically, it is associated with sometimes severe and permanent central nervous system deficits [12].

In our group of neonates, all of whom were severely affected by their hemolytic disease, three of seven experienced intracranial hemorrhage. One of the three patients was less than 32 weeks gestational age, and the type of hemorrhage was typical of hemorrhages in preterm neonates without erythroblastosis fetalis. It consisted of germinal matrix bleeding with ventricular extension [2]. In contrast, the hemor-

### TABLE 1: Summary of Clinical Data on Cases 4–7

<table>
<thead>
<tr>
<th>Case No. (gestational age in weeks)</th>
<th>Birth Weight (g)</th>
<th>No Sonograms*</th>
<th>Bilirubin (mg/dl)</th>
<th>Hematocrit (%)</th>
<th>No Exchange Transfusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>4(32)</td>
<td>2560</td>
<td>2</td>
<td>12</td>
<td>38</td>
<td>1</td>
</tr>
<tr>
<td>5(34)</td>
<td>2100</td>
<td>4</td>
<td>8.8</td>
<td>34</td>
<td>5</td>
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<tr>
<td>6(32)</td>
<td>1800</td>
<td>4</td>
<td>7.8</td>
<td>21.1</td>
<td>16</td>
</tr>
<tr>
<td>7(30)</td>
<td>2140</td>
<td>2</td>
<td>6.2</td>
<td>32</td>
<td>2</td>
</tr>
</tbody>
</table>

Note—Outcomes were good in cases 4, 5, and 7 and death in case 6.

* No evidence of intracranial hemorrhage was seen on any of the sonograms.
hemorrhages seen in cases 1 and 2 were unique in that they were multifocal and originated close to the pia-arachnoid. In case 3, one of these hematomas extended centripetally and ruptured into the ventricular system. This pattern is not typical of intracranial hemorrhages originating in the germinal matrix [2-4, 13], and other etiologies are therefore suggested.

Pape and Wigglesworth [6] reported cerebellar hemorrhage close to the pia-arachnoid as the result of a bleeding diathesis in a patient with severe Rh isoimmunization. Chessels and Wigglesworth [14] described the pathologic findings in two other cases of intracranial hemorrhage in Rh-sensitized neonates and suggested that it constitutes a distinct form of intracranial bleeding. The hemorrhage is in the form of a thick subarachnoid clot associated with destruction and infiltration of the underlying cerebral tissue. It is not merely an extension of an intraventricular or germinal layer hemorrhage, though they may coexist [14]. At autopsy, case 3 showed disseminated sites of purpura and hemorrhage throughout the body secondary to thrombocytopenia and intravascular coagulation. This suggests a similar etiology for hemorrhage in the brain of this infant. The relatively high rate of cerebral hemorrhage in Rh-sensitized babies, though reported before [15, 16], has not been emphasized recently. A larger group of such neonates will have to be evaluated to determine the current prevalence in light of the improved methods of diagnosis and prenatal and postnatal treatment available today. The late neurologic sequelae of hemolytic disease of the newborn have generally been attributed solely to kernicterus [12]. The high rate of intracranial hemorrhage in this particular group of neonates suggests that late neurologic deficits may in part be secondary to the types of hemorrhage described in this report rather than on the basis of kernicterus alone.

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REFERENCES