Frequency of Linear Hyperechogenicity Over the Basal Ganglia in Young Infants with Congenital Rubella Syndrome

Ying-Chao Chang, Chao-Ching Huang, and Ching-Chuan Liu
From the Department of Pediatrics, National Cheng Kung University Hospital, Tainan, Taiwan

Five young infants with congenital rubella syndrome (CRS) underwent cranial ultrasonographic examinations and/or computed tomographic examinations. Only two of these infants were small for their gestational age, and none of them were microcephalic at birth. Deafness and ocular lesions were found in four patients, and congenital heart disease was found in three. All had abnormal ultrasonographic findings: linear-shaped hyperechogenicity over the basal ganglia was noted for five patients, periventricular punctate hyperechogenicity was noted for three, and subependymal cysts were observed in two. Follow-up ultrasonograms for two of the patients showed progressively enlarging hyperechogenic lesions. Calcification was found in both patients examined by means of computed tomography. All patients became microcephalic, with profound global developmental delay. Intracranial calcifications are common findings in patients with CRS. Ultrasonography should be performed for high-risk neonates, regardless of their symptoms. The finding of linear hyperechogenicity over the basal ganglia should prompt a search for all congenital infections, including CRS.

Most patients with congenital rubella syndrome (CRS) have CNS involvement [1–3]. Since most maternal rubella infection is subclinical and most of the infants with CRS are asymptomatic at birth [1, 4], timely diagnosis of CRS is difficult. Vascular lesions within the striatum are a frequent pathological finding in infants with CRS [5, 6]. Branching hyperechogenicity over the thalamus and basal ganglia region has been reported mainly for patients with congenital cytomegalovirus (CMV) infection and in only a few cases of CRS [7–10]. Cranial ultrasonography was performed for five infants with CRS to determine if a hyperechogenic lesion in the basal ganglia can be a sensitive, early sign of cerebral involvement.

Patients and Methods

Cranial ultrasonograms (Aloka SSD-630 unit with 5.0-MHz transducers, Japan) were obtained for five infants whose ages ranged from 1 day to 2 months and who later proved to have CRS. Congenital infection was suspected on the basis of physical stigmata and ultrasonographic findings. All of the patients underwent serological screening for congenital infections, including rubella, CMV infection, herpes simplex (Behringwerke AG, Marburg, Germany), toxoplasmosis (Abbott, North Chicago, IL), and syphilis. CRS was confirmed by detection of the rubella-specific IgM antibody [1]. None of the infants had other concomitant congenital infections. CT scans and follow-up ultrasonograms were available for two patients. The CT scan was performed with use of a General Electric CT9800 scanner (General Electric) in standard 10-mm axial sections.

The clinical manifestations and neuroimaging findings are summarized in table 1. The infants’ gestational ages ranged from 35 weeks to 38 weeks, and only two of them were small for their gestational age. Rubella was not suspected prenatally in any of the mothers, and none of the infants were microcephalic at birth. The initial neurological manifestations included poor feeding, irritability, hypotonia, and bulging fontanelles. CSF from two of the patients was analyzed, and all findings were within normal limits. All of the infants became microcephalic, with profound global developmental delay, at an average age of 27 months.

All of the patients had abnormal ultrasonographic findings: five had linear-shaped hyperechogenicity over the basal ganglia, three had punctate hyperechogenicity over the periventricular area, and two had subependymal cysts. Follow-up ultrasonograms were available for two patients; both ultrasonograms showed progressive hyperechogenicity over the basal ganglia and periventricular areas (figure 1). Calcifications over the periventricular areas and the basal ganglia were found in both of the patients examined by CT scanning (figure 2).

Although their neurological manifestations were subtle, all of our patients had abnormal cranial ultrasonographic findings that were clearly evident in early infancy. Linear-shaped hyperechogenicity over the basal ganglia is a rare finding in infants and has been associated with a variety of etiologies such as congenital CMV infection, chromosomal abnormalities, meningitis, and asphyxia [8–12]. Only a few reports have related the ultrasonographic findings with CRS [7–10]. Our findings suggest that linear hyperechogenic basal ganglia lesions are common in patients with CRS. Although nonspecific for CRS [12], this finding is sensitive and should alert the clinician to the possibility of a congenital infection, including CRS.

It has been suggested that linear hyperechogenicity over the basal ganglia represents vasculopathy in the thalamus and basal...
Table 1. Clinical manifestations in five patients with congenital rubella syndrome and findings of neuroimaging studies.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Sex/age</th>
<th>Gestational age (w)</th>
<th>Birth weight (kg)</th>
<th>Congenital heart disease</th>
<th>Eye lesion</th>
<th>Deafness</th>
<th>Neuroimaging study findings</th>
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<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>periventricular area on US</td>
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<tr>
<td>1</td>
<td>F/2 d</td>
<td>35</td>
<td>1.7</td>
<td>Patent ductus arteriosus</td>
<td>Retinopathy</td>
<td>Yes</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>M/1 mo</td>
<td>38</td>
<td>2.9</td>
<td>None</td>
<td>None</td>
<td>Yes</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>M/1 mo</td>
<td>37</td>
<td>2.7</td>
<td>Patent ductus</td>
<td>Cataract, glaucoma,</td>
<td>Yes</td>
<td>+</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>arteriosus, peripheral</td>
<td>retinopathy</td>
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<tr>
<td>4*</td>
<td>M/3 d,</td>
<td>36</td>
<td>1.6</td>
<td>None</td>
<td>Cataract</td>
<td>No</td>
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<tr>
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<tr>
<td>5*</td>
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NOTE. ND = not done; US = ultrasonography; + = present; - = absent; ++ = progressive.

* Progressive hyperechogenicity noted on follow-up ultrasonography.

ganglia vessels [8, 10, 12]. Rorke [5, 6] reported that all infants with CRS had vasculopathy, with destruction of the vessel walls by deposits of amorphous material; this vasculopathy especially involved the small penetrating vessels within the basal ganglia [5, 6]. The hyperechogenic lesions in these patients appeared to be progressively enlarging on subsequent ultrasonograms; this finding corresponds to the progressive clinical manifestations seen in cases of CRS [1–3] and might be due to chronic persistence of the rubella virus or to vascular damage caused by the viral infection [2]. Intracranial calcifica-

Figure 1. Progressive hyperechogenic lesions in a patient with congenital rubella syndrome. A, Coronal view at 3 days of age; hyperechogenic lesions are located bilaterally in basal ganglia area (arrows). B and C, Coronal views at 10 months of age; the hyperechogenic lesions have increased both in number and size in the basal ganglia (arrows) and periventricular areas (arrowheads).
Figure 2. CT scan of patient in figure 1. A and B, intracranial calcifications located in the basal ganglia (arrow) and periventricular areas (arrowheads).

ation is common in congenital CMV and toxoplasmosis but rare in CRS [1, 4, 5, 13]. With the use of CT, however, the findings in our cases and in all those reported in the literature demonstrated that the incidence of intracranial calcification in patients with CRS is 60%, even during infancy [7–9, 14–16].

The frequent findings of linear hyperechogenicity over the basal ganglia and intracranial calcification in early infancy are helpful in diagnosing CRS and the associated cerebral involvement. Ultrasonography should be performed for every neonate at high risk for CRS, regardless of symptoms. The findings of linear hyperechogenicity over the basal ganglia should prompt an intensive search for any congenital infection, including CRS. Even when symptoms are not present, neurodevelopmental follow-up should be carried out for all infants with basal ganglia lesions.

References