Bone Lesions in an Infant With Congenital Parvovirus B19 Infection

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Parvovirus, neonatal infection, radiology

ABBREVIATIONS
Ig—immunoglobulin
PCR—polymerase chain reaction

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Bone lesions on radiographs of newborns often suggest congenital infections. Skeletal roentgenograms are recommended in the evaluation of suspected congenital syphilis, but bone lesions have been recognized in other congenital infections. We report the case of an infant with hydrops fetalis secondary to congenital parvovirus B19 infection who was found to have bone lesions in multiple long and axial bones on admission to the neonatal ICU. Both the infant and her mother were evaluated for other causes of congenital infection, but no other agents were identified. The bone lesions had nearly completely resolved by 10 weeks of age. Screening of neonates with congenital parvovirus B19 infection for bone lesions may provide additional insight into the incidence and pathophysiology of these lesions. Pediatrics 2013;131:e1659–e1663
Bone lesions on plain radiographs of neonates often initiate an evaluation for congenital infections. Abnormalities such as metaphyseal lucencies and periostitis initially were described with congenital syphilis, but subsequently have been recognized in an increasing number of congenital infections, including congenital rubella syndrome, congenital toxoplasmosis, congenital cytomegalovirus infection, and congenital herpes simplex infection. However, bone lesions have not been described with congenital parvovirus infection, and its occurrence in a preterm newborn forms the basis of this report.

**CASE REPORT**

A 1390-g female infant was born by cesarean delivery because of a prolapsed foot at 29 5/7 weeks’ gestation to a 27-year-old gravida 2, para 1 white female who lacked antibodies to HIV, had an reactive rapid plasma reagin test, and had immunoglobulin (Ig) G antibodies to rubella during the first trimester. The pregnancy was complicated at 24 weeks by the sonographic detection of profound fetal hydrops. Amniocentesis was performed at 25 weeks’ gestation; parvovirus B19 DNA was detected in amniotic fluid by qualitative polymerase-chain reaction (PCR) testing (Quest Diagnostics, San Juan Capistrano, CA). Fetal hemoglobin was 3.2 mg/dL and an intrauterine transfusion of packed red blood cells was performed at 30 days before delivery and repeated 4 and 14 days later. The third transfusion, performed 16 days before delivery, was complicated by elevated maternal blood pressure, raising concern for mirror syndrome (fetal and placental hydrops in the setting of maternal preeclampsia). However, the maternal blood pressures normalized, but spontaneous rupture of fetal membranes without labor occurred 13 days before delivery. The mother received betamethasone 19 and 18 days before delivery.

The infant was not vigorous at birth; Apgar scores were 2, 6, and 7 at 1, 5, and 10 minutes, respectively. She was intubated in the delivery room secondary to hypoventilation and bradycardia. Physical examination in the delivery room revealed marked abdominal distention and decreased breath sounds bilaterally. She was admitted to the NICU; her initial vital signs included a heart rate of 195 beats per minute and a respiratory rate of 59 breaths per minute. Her birth weight was 1390 g (55th percentile), and her length and head circumference were both 25th percentile for gestational age. Her extremities were mildly edematous, and the abdomen was distended. No hepatosplenomegaly was detected, and there were no petechiae or purpura. The infant’s first postnatal hemoglobin was 12.6 mg/dL. Initial chest radiograph showed diffuse haziness with bilateral pleural effusions; lucencies were visible in the proximal humeral heads bilaterally. Abdominal radiographs obtained for umbilical catheter placement revealed lucencies in the femoral heads and iliac wings bilaterally (Fig 1). Cranial ultrasound was normal. Abdominal sonogram showed moderate ascites without hepatosplenomegaly. Parvovirus PCR test performed on serum at the same reference laboratory was positive on the first day of age.

The infant received 48 hours of ampicillin and gentamicin; blood cultures obtained on admission were sterile. Total parenteral nutrition was initiated at birth and continued through 32 days of age. Fentanyl was provided as needed for sedation. The infant did not receive any additional medication until 15 days of age, when intermittent doses of furosemide for evolving chronic lung disease of prematurity was provided. She received daily chlorothiazide starting on the 29th day of age, and lansoprazole was started at 30 days of age due to concerns.

**FIGURE 1**

Chest and abdominal radiograph of infant on first day of age demonstrating lucencies in long bones (thick arrows), vertebral bodies (thin arrows), scapula (arrowhead), and iliac wing (bracketed arrowheads).
for gastroesophageal reflux disease. The infant’s hemoglobin decreased to a nadir of 11.7 mg/dL at 2 weeks of age, and she did not require any postnatal blood transfusions.

Review of all radiographs by the pediatric radiologist (MP) noted marked metaphyseal lucencies involving all visualized long bones, including the humeri, femurs, and clavicles, as well as the peripheral aspects of the vertebral bodies and iliac wings (Figs 1 and 2). Because syphilis was a possible cause, the mother had another rapid plasma reagin test that was nonreactive on the infant’s 10th day of age. Urine viral culture performed on the 11th day of age did not yield cytomegalovirus. Maternal serum lacked IgG antibodies to *Toxoplasma gondii*. Newborn screening and consultation by the genetics service did not identify any associated or inherited conditions or syndrome. The metaphyseal lucencies remained visualized on radiographs obtained for other indications through 5 weeks of age but were nearly completely resolved at 10 weeks of age (Figs 3, 4, and 5). Overall, the hospital stay was complicated by bronchopulmonary dysplasia and feeding difficulty, and at 96 days of age, the infant was transferred to a level 2 nursery at a hospital that was closer to the parent’s home.

**DISCUSSION**

Bone lesions in infants with congenital infections have been observed for more than a century. These findings include periostitis and cortical demineralization, usually in the metaphyseal or diaphyseal portions of long bones, but the axial bones also can be affected. These findings are variable and nonspecific, and an increasing number of pathogens have been associated with radiographic bone lesions (Table 1). Congenital infection with *Treponema pallidum*, rubella, *Toxoplasma gondii*, cytomegalovirus, and herpes simplex virus have all been associated with osseous lesions on radiographs. However, such lesions have not been associated with hydrops fetalis due to noninfectious causes. To our knowledge, this is the first report associating congenital parvovirus infection with radiographic bone lesions.
Our infant had classic manifestations of intrauterine parvovirus infection, including nonimmune hydrops fetalis secondary to severe anemia. The virus was identified both prenatally in the amniotic fluid and postnatally in the infant’s blood by PCR testing. Other causes of congenital infection were excluded by using a combination of maternal and neonatal screening and absence of other clinical signs. The infant was not tested for the presence of rubella IgM antibody; although the mother was immune to rubella, reinfection has been reported. Diuretic use has been associated with osteopenia, but this infant had visible lesions well before the start of diuretic therapy, and these lesions improved while on diuretics. Although it is possible that a separate agent or process could be responsible for the metaphyseal lucencies seen in our patient, it is most likely that parvovirus B19 was the inciting agent.

The near resolution of the metaphyseal lucencies between the fifth and 10th week of age in our patient is notable. The exact timing is unclear as the infant was extubated at 5 weeks of age and did not have additional radiographic imaging performed until long bone films were obtained at 10 weeks of age to evaluate the bone lesions. The dramatic improvement of our patient’s radiographic findings is consistent with that seen in other congenital infections. The bony lesions of syphilis resolve in infancy with treatment, and those associated with congenital rubella infection and congenital cytomegalovirus infection resolve in the first few months of age without specific therapy. Whether these changes are due to the presence of the infectious agent or the host’s inflammatory response is not known, although studies of other congenital infections involving the middle and inner ear suggest that lesions may be due to a combination of both factors.

**CONCLUSION**

This case report adds parvovirus B19 as a likely cause of metaphyseal bone lesions present at birth. Because such bone lesions can occur with other congenital infections, we speculate that the fetal inflammatory response to infection with certain agents may be an important determinant for its occurrence. Screening of neonates with congenital parvovirus B19 infection for bone lesions may provide additional insight into the incidence and pathophysiology of these lesions.

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