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ADVANCES IN PEDIATRIC RESEARCH

Congenital cytomegalovirus infection presenting with intrapulmonary calcifications on prenatal sonogram

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Abstract

Cytomegalovirus (CMV) is the most common congenital viral infection in developed countries. Although pneumonitis has been reported in infants with congenital CMV infection, involvement of the lung parenchyma is less common in congenital than in perinatal CMV infections. We report an infant with congenital cytomegalovirus (CMV) infection and multiple intrapulmonary calcifications on prenatal sonogram that had congenital pneumonia and persistent oxygen requirement after birth. To our knowledge, this is the first case report of a live-born infant with pulmonary calcifications due to CMV noted on prenatal sonograms.

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Introduction

Cytomegalovirus (CMV) is the most common congenital viral infection in developed countries [1-3]. Sonographic features that raise suspicion of congenital CMV infection include ventriculomegaly, microcephaly, increased periventricular echogenicity, calcifications, periventricular pseudocysts, intraventricular synechia (a lesion of the iris), malformations of cortical brain development, cerebellar lesions, and intrauterine growth retardation [4]. Although pneumonitis has been reported in infants with congenital CMV infection, involvement of lung is less common in congenital than in perinatal CMV infections [5].

We report a neonate with congenital CMV infection associated with multiple intrapulmonary calcifications noted on prenatal sonograms.

Case report

A 19-year-old G1P0 African American woman was referred to our center at 31 weeks' gestation for a specialized scan because of a left club foot and a prominent stomach. The club foot was confirmed but mild intracranial ventriculomegaly (10.5 mm) and both intracranial (Figure 1) and pulmonary (Figure 2) calcifications were identified also. The estimated fetal weight was 1682 grams (22nd percentile). She had undergone mid-trimester multiple-marker serologic screening for fetal aneuploidy which was negative. She was counseled that the sonographic findings were consistent with a congenital infection but declined amniocentesis. Serologic screening at this time were: CMV IgG positive, CMV IgM negative, toxoplasmosis IgG and IgM negative, HSV I IgG positive, and HSV II IgG negative. Prenatal records indicated that VDRL was nonreactive and hepatitis B antigen was negative.

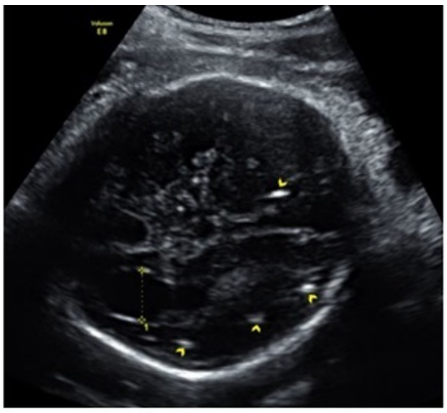

Figure 1. Image of fetal brain showing dilated lateral ventricle (calipers) and scattered calcifications (echogenic areas-arrow heads).

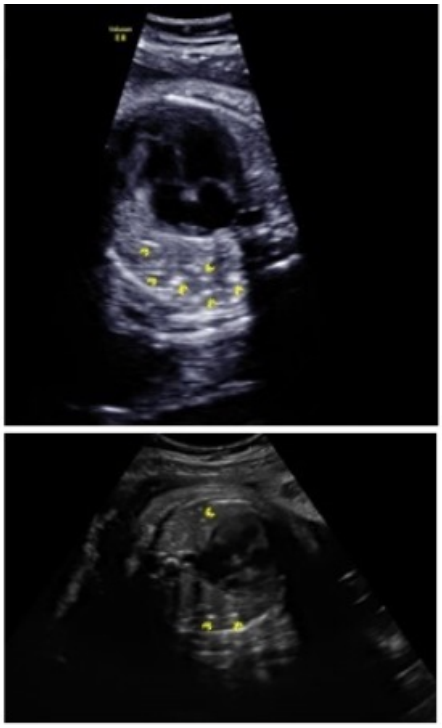

Figure 2. Fetal thorax at four chamber level showing scattered calcifications (echogenic areas-arrow heads) in both lungs.

A follow-up scan at 36 weeks confirmed poor interval growth with an estimated fetal weight of 2061 grams (<5th percentile) but normal amniotic fluid and umbilical cord arterial Doppler assessment. In addition to ventriculomegaly and enlarged liver and spleen, there was a midline posterior fossa cyst with an enlarged third ventricle.

At 37 weeks, a biophysical profile scored 4/10 and labor was induced. The mother received 3 doses of ampicillin during labor because of a positive Group B streptococcus culture. Delivery was by vaginal birth, and Apgar scores were 4 and 8. The female infant was initially hypotonic with minimal spontaneous respiratory drive. She required bag-mask ventilation for approximately one minute and was transferred to the neonatal intensive care unit. The birth weight was 2.46 kg (12th percentile), head circumference was 29.5 cm (1st percentile) and the length was 44 cm (3rd percentile). The physical examination was pertinent for mild respiratory distress, palpable liver edge, and mildly decreased tone.

Initial laboratory findings included, a cord arterial gas with low pH: 7.17, increased PCO2: 63 mmHg normal bicarbonate of 23 mmol/L; hemoglobin 14.4 g/dl, hematocrit 43%, white blood cell count 12,000/mm^3 (normal differential), platelet count 271,000/mm^3, all within normal limits; increased AST 58 IU/L; normal ALT 17 IU/L; and increased alkaline phosphatase 104 IU/L. The chest radiograph revealed low lung volumes with interstitial densities. The infant received ampicillin and gentamicin.

Congenital CMV infection was confirmed with a positive saliva rapid culture. The cranial ultrasound revealed immature gyral and sulcal pattern with calcifications, prominent third and lateral ventricles, and prominent cystic space in the posterior fossa. The magnetic resonance imaging of the brain revealed microcephaly, simplified gyral pattern, cerebral calcifications, and dilatation of third and lateral ventricles with a small posterior fossa arachnoid cyst. There was no evidence of CMV retinitis. The auditory brainstem response test was normal bilaterally. The placenta weighed 336g and had signs of chronic cytomegalovirus placentitis (low placental weight for period of gestation, lymphoplasmacytic villitis, villous sclerosis and hemosiderin with scattered dystrophic mineralization). Valgancyclovir was started on day 3.

The infant had persistent respiratory distress requiring oxygen since birth to maintain saturations above 90%, consistent with CMV pneumonia. The infant was sent home on day 17 after birth on valgancyclovir 16 mg/kg PO q12h and a nasal cannula with 0.1 liter per minute flow and 100%

inspired oxygen concentration to keep oxygen saturations in the 90-95% range. On her one-month follow up visit, she continued to require oxygen support. The valgancyclovir dose was adjusted for her weight. Three months after discharge, during her follow up visit, she was noted to have normal growth and development. Oxygen was also discontinued during this visit, as oxygen saturation was 100% on room air.

Discussion

CMV is the most common cause of congenital viral infection in the world, occurring in 0.2–2.2% of infants born alive [1,2]. Between 20% and 60% of pregnant women are CMV seronegative at conception. Of these, between 1% and 4% will acquire CMV during pregnancy, and on average between 40% and 50% of infected women will transmit the virus to the fetus [6]. After primary maternal infection, it may take weeks to months for transplacental transmission of CMV to occur [7]. In this case, the mother was IgG positive and IgM negative which can represent either reactivation of previously acquired virus or reinfection with a new virus strain that led to fetal infection during early gestation. As pre-conceptional serum specimens from the mother were unavailable, it was not possible to confirm whether the mother had acquired a primary infection during early gestation or if an intrauterine infection occurred even though the mother had preexisting immunity (non-primary maternal infection). Although pre-conceptional immunity has been associated with decreased rates of intrauterine transmission, it has been estimated that three-quarters of all congenital CMV infections in the United States were attributable to non-primary maternal infection [6].

Currently, universal screening for CMV in mothers or newborns is not recommended [8]. Thus, at least in some cases, prenatal sonographic evaluation may be the only tool available to identify an affected fetus [9]. Obstetricians will most likely be presented with the possibility of a CMV diagnosis when confronted with sonographic findings characteristics of such a disease [10].

Ethical approval

The authors contacted the University of Alabama at Birmingham (UAB) Institutional Review Board (IRB) before we submitted this manuscript. The IRB does not require a submission for a case report of less than 3 patients.

Author contribution

Prem Fort; Millie R. Chang: Design the study, acquisition of data, drafting and revising the manuscript, approval of the final manuscript

Waldemar A. Carlo: Design the study, acquisition of data, review and editing the manuscript, approval of the final manuscript

Suresh Boppana, Richard Davis: Review and editing the manuscript, approval of the final manuscript

John Owen: Acquisition of images, review and editing the manuscript, approval of the final manuscript

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