Congenital Measles in a Premature 25-week Gestation Infant

Erin Hanft, MD, Sandhya Brachio, MD,* Maria Messina, RN, CIC,† Philip Zachariah, MD MS,*† Desmond Sutton, MD,† Dena Goffman, MD,† Janett Pike, RN, CIC,† Lesley Covington, MSPH, CIC,† Krishika A. Graham, MD, MPH,‡ Bindy Crouch, MD, MPH,‡ Eleanor Adams, MD, MPH,§ Nina Ahmad, MD,§ Elizabeth Rausch-Phung, MD, MPH,§ Karen Southwick, MD, MSc,§ Patrick Bryant, PhD,¶ Meghan Fuschino, MS,¶ Anagha Khandekar, PhD,¶ Karen Kulas, BS,¶ and Lisa Saiman, MD, MPH*†*

Abstract: We describe a premature infant with congenital measles. Laboratory testing confirmed measles in the mother (polymerase chain reaction- and IgM-positive) and congenital measles in the infant (polymerase chain reaction-positive, culture-positive and IgM-positive). The infant never developed a rash, pneumonia, or neurologic complications. This case supports using compatible laboratory findings to diagnose congenital measles in infants without clinical manifestations of measles.

Key words: extremely low birth weight, measles, neonate, premature, congenital

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Measles is a highly infectious virus. Illness is characterized by fever, malaise, coryza, cough, conjunctivitis and morbilliform rash. In 2000, measles elimination was declared in the United States because of widespread vaccination.[1] However, low vaccine uptake, including refusals, has led to worldwide increases in measles, including reemergence in higher income countries.[1] From September 2018 to July 2019, a measles outbreak occurred in New York. The outbreak resulted in 649 cases, most of which occurred in patients living in Orthodox Jewish communities.[2] Our institution serves as a referral center for patients in this population.

Measles causes morbidity and mortality in nonimmune pregnant women and their fetuses including miscarriages, spontaneous abortion, intrauterine fetal demise, preterm labor and birth and congenital measles.[3,4] Pregnant women with measles have increased risk of hospitalization, pneumonia or death, and infants with congenital measles are at increased risk of mortality.[4,5]

Currently, congenital measles is described as a rash in a neonate at birth or within the first 10 days of life whose mother had measles around the time of delivery.[1,3] We present an extremely low birth weight infant with congenital measles born during the 2018–2019 measles outbreak in New York. We describe the infant's clinical presentation, infection prevention and control (IP&C) strategies implemented, measles diagnostic testing and potential long-term consequences of congenital measles.

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From the *Columbia University Irving Medical Center; †New York-Presbyterian Hospital; ‡New York City Department of Health and Mental Hygiene, New York; §New York State Department of Health, Albany; and ¶Wadsworth Center, New York State Department of Health, Albany, New York. Erin Hanft, MD is currently at New York University Langone Health, New York, New York.

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Address for correspondence: Lisa Saiman, MD, MPH, Columbia University Irving Medical Center 622, West 168th Street PH4West, Room 470, New York, NY 10032. E-mail: Ls5@cumc.columbia.edu.

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CASE PRESENTATIONS

Mother

The mother was a White 28-year-old multigravida, with no medical problems who lived in one of the communities affected by the measles outbreak in New York. She had no prior preterm births. She presented at 25 6/7 weeks gestation for preterm premature rupture of membranes with preterm labor to an outside hospital (OSH) in May 2019. Prenatal laboratory results were not available at the time of delivery; all laboratory results, including HIV and Hepatitis B, were later confirmed to be negative. She reported never receiving the measles vaccine. Eight days before delivery, the mother developed a morbilliform rash on her face that spread to her trunk. Two days before delivery, she developed cough and nonpurulent bilateral conjunctivitis. On the day of delivery, she was clinically diagnosed with measles when she presented in preterm labor. She received 1 dose of betamethasone and antibiotics for preterm premature rupture of membranes and arrangements were made for transfer to our hospital. To avoid exposures on arrival, the mother was masked in the ambulance bay and taken by commandeered elevator to a positive pressure obstetrical operating room. All other operating rooms were emptied. She delivered by cesarean section for breech presentation and was then transferred to a negative pressure Airborne Infection Isolation (AII) room. Maternal nasopharyngeal (NP) swab was positive by measles-specific real-time reverse-transcription polymerase chain reaction (rRT-PCR) assay and her serum was IgM-positive and IgG-negative for measles on the day of delivery. The mother never developed measles pneumonia but had a persistent cough. Out of an abundance of caution for the other patients in the neonatal intensive care unit (NICU), the mother was permitted to visit her infant when her symptoms resolved, 9 days after discharge. The father was positive for measles IgG and permitted to visit the infant.

Infant

The infant emerged with no respiratory effort and a low heart rate. Her birth weight was 840 g (66th percentile), length 36.5 cm (96th percentile) and head circumferences 24 cm (76th percentile). APGAR scores were 1, 6 and 9 at 1, 5 and 10 minutes of life. She received positive pressure ventilation before transitioning to bubble continuous positive airway pressure (bCPAP), was transported by isolette to the NICU and placed on AII in a negative pressure room. All staff were required to wear N95 respirators when entering her room.

Within 6 hours of life, she was intubated and given surfactant for respiratory failure. On day of life (DOL) 1, she was extubated to bCPAP which continued until DOL 42 (32 weeks postmenstrual age).

She received 48 hours of broad-spectrum antibiotics for rule-out sepsis evaluation. She received 2 doses of intravenous immunoglobulin (400 mg/kg) on DOL 0 and DOL 2 for measles

postexposure prophylaxis, out of concern that a single dose would be diluted by the numerous blood draws performed during the first few days of life. Table 1 provides results from multiple specimens sent for testing during her NICU stay. At birth, serum IgM and IgG, oropharyngeal (OP)/NP specimen (PCR and culture), urine (PCR and culture) and placenta (culture) were positive for measles.

On DOL 14, the infant developed a fever of 38 °C, tachycardia and increased secretions. She had no increased oxygen requirement and chest radiograph was negative for pneumonia. Oral vitamin A (50,000 IU daily × 2 doses) was given to treat presumed symptomatic congenital measles because test results confirming measles infection at birth returned at this time. Evaluation for sepsis was negative and antibiotics were discontinued after 36 hours.

On DOL 36, urine PCR was positive for measles virus. On DOL 60, she was removed from AII in consultation with the New York City Department of Health and Mental Hygiene and the New York State Department of Health (NYSDOH) having had negative tests at DOL 46 and 60 (Table 1).

On DOL 68 (35 weeks postmenstrual age), the infant was discharged home. She weighed 2590 g (50th percentile), length 44 cm (10th percentile) and head circumference 30 cm (22nd percentile). She was feeding orally, passed her hearing screen, and had mild retinopathy of prematurity. Serial head ultrasounds were normal. Brain magnetic resonance imaging, obtained at discharge to establish a baseline in the setting of congenital measles, showed symmetric undersulcation of bilateral cerebral hemispheres consistent with prematurity and a myelination pattern that was appropriate for age.

IP&C STRATEGIES

In Quarter 4 2018, in response to the measles outbreak,[2] our institution's Workforce Health & Safety verified measles immunity via documentation of 2 doses of measles-containing vaccine or positive measles IgG, in all obstetric, pediatric and NICU staff. As NICU staff are generally unaccustomed to AII, IP&C reviewed appropriate personal protective equipment. IP&C recommended determining measles immune status of all pregnant women before delivery via documentation of 2 vaccinations or serum testing for measles IgG. Those who were IgG-negative or had fewer than 2 doses of vaccination, received a measles-mumps-rubella (MMR) vaccine immediately after birth.

An interdisciplinary team, including IP&C, nursing, physician and operations leadership, developed NICU visitor restrictions which were implemented in May 2019. Only 3 visitors, including parents, were permitted for each infant. All visitors, regardless of epidemiologic risk factors, had to demonstrate measles immunity based on 2 documented measles-containing vaccinations, positive IgG, or birth before 1957. MMR vaccine was administered to designated visitors who were nonimmune or had received only 1 MMR vaccine at our hospital-affiliated urgent care centers or by the visitor's primary care provider.

LABORATORY METHODS

The New York City Department of Health and Mental Hygiene performed testing for IgM and IgG antibodies by measles capture ELISA (Microimmune, Inc., Guildford, UK) which utilizes a recombinant measles nucleoprotein antigen. The test was performed according to the manufacturer's instructions.[6] Measles virus-specific nucleic acid was detected using a rRT-PCR assay targeting the viral nucleoprotein gene, designed by the Centers for Disease Control and Prevention (CDC).[7] Nucleic acid was extracted from nasopharyngeal/oropharyngeal swabs, urine and placenta specimens at the NYSDOH Wadsworth Center with an automated easyMAG instrument (bioMérieux, Durham, NC) and the rRT-PCR assay was performed on an ABI 7500 Fast Dx Instrument (Thermo Fisher, Waltham, MA).

The NYSDOH Wadsworth Center performed conventional virus culture for measles on Vero/hSLAM cells, provided by the World Health Organization and CDC. Cultures were examined for cytopathic effect 3 times a week for 2 weeks and if positive, confirmed by indirect immunofluorescent staining with measles-specific monoclonal antibody (LIGHT DIAGNOSTICS, Temecula, CA).

DISCUSSION

To our knowledge, this is the first published report of congenital measles in an extremely preterm infant; previous reports have described congenital measles in full term or late preterm infants with rash.[8,9] This report provides an additional evidence of the adverse impact of low vaccination rates.

In 2013, the American College of Obstetricians and Gynecologist recommended review of vaccination history as part of women's preventive healthcare.[10] Presumptive evidence of immunity is considered written documentation of at least 1 dose of measles-containing vaccine for adults not considered to be at high risk or a detectable titer via serologic testing.[11] MMR vaccination is recommended for all nonimmune postpartum women and is compatible with breast-feeding.[10] Although rubella and measles vaccines are combined in the United States, immunity to one does not imply immunity to the other.[12]

Historically, newborns are diagnosed with congenital measles if a rash is present at birth or within the first 10 days of life and their mother had measles before delivery.[3] While this infant never developed a rash, diagnostic serologic and viral testing performed at birth were consistent with congenital measles (positive IgM and positive urine PCR and culture) and not with contamination of specimens by maternal virus.

Based on her clinical presentation, this mother was infected prior to delivery. In utero infection might have occurred during maternal viremia that occurs within 1 week after infection. The infant may not have developed a rash postnatally due to prematurity and immunologic immaturity or had in utero rash that resolved before birth. This case provides support to diagnose congenital measles in a newborn when laboratory findings are compatible with congenital measles, even in the absence of rash or other clinical presentations of measles.

TABLE 1. Measles Diagnostic Testing in Infant with Congenital Measles

DOL	Serum IgM	Serum IgG	NP/OP PCR	NP/OP Culture	Urine PCR	Urine Culture	Placenta Culture
0	Positive	Positive	Positive	Positive	Positive	Positive	Positive
6	NA	Positive	NA	NA	NA	NA	NA
36	NA	NA	NA	NA	Positive	Negative	NA
46	Negative	NA	Negative	NA	NA	NA	NA
60	NA	NA	Negative	NA	Negative	NA	NA

NA indicates sample not available.

Intravenous immunoglobulin was given as postexposure prophylaxis to this infant based on maternal symptoms before delivery.[13] Laboratory results confirming congenital measles infection were not available until DOL 14, at the same time as a rule-out sepsis evaluation was initiated due to fever and increased secretions. Thus, while Vitamin A is typically given as early treatment for measles,[13] Vitamin A was administered at the time of fever and increased secretions.

Individuals with measles infection can develop subacute sclerosing panencephalitis (SSPE), a fatal complication characterized by cognitive decline, myoclonus, vision loss, gait abnormalities and ultimately a vegetative state, which usually occurs 2.5–34 years after acute measles.[14] Infants with congenital measles are at increased risk of SSPE and may have a shorter incubation period for SSPE.[15] Thus, monitoring such infants for signs of SSPE as well as for the long-term effects of prematurity on neurodevelopment are prudent.

The IP&C strategies implemented in the NICU during this measles outbreak were time-consuming and costly. By confirming measles immunity for everyone, we hoped to minimize family concerns that a nonimmune individual was visiting the NICU and to reduce the risk of exposures to nonimmune infants. Although no data are available for the recommended duration of isolation, the infant remained in an AII room for most of her hospitalization, as the duration of viral shedding is unknown. The positive urine PCR at DOL 36 suggests that the infant may have been contagious for this duration and that prolonged AII was indicated. There were no secondary cases of measles.

Congenital measles, and possibly prematurity, occurred in this patient because of maternal measles, which could have been prevented by vaccination. The measles vaccine has proven to be safe and effective, and vaccine hesitancy and refusal led to a sustained outbreak in New York in 2018–2019. Notably, during the COVID-19 pandemic, vaccination rates have declined,[16] which could lead to the risk of future outbreaks of measles unless catch-up vaccination occurs expeditiously.

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