

Maternal and Fetal Morbidities in Perinatal Measles Infection: A Case Report

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Measles during pregnancy has been associated with deleterious effects on the perinatal outcomes. We encountered a case of perinatal measles infection during the 2013 measles outbreak in South Korea. The mother experienced severe gestational measles associated with the lack of vaccination. She had a preterm delivery and the neonate developed congenital measles, which was diagnosed based on the results of serological tests for the mother and neonate. Herein, we described the case, first reported with confirmed transplacental transmission in Korea to our best knowledge, and also reviewed relevant literature regarding measles during pregnancy, which suggested that perinatal measles and the outcomes are markedly influenced by the status of maternal immunity during prenatal period.

Key Words: Measles, Pregnancy, Maternal-fetal infection transmission

Measles is one of the most contagious viral infections in humans, and it often results in explosive epidemics.¹⁻³ The measles monovalent vaccine and the measles, mumps, and rubella (MMR) vaccine were introduced in 1965 and 1980, respectively. After a nationwide outbreak in 2000–2001 in South Korea, the Five-Year Measles Elimination Program was established, which introduced the 2-dose measles vaccination. Measles was declared to have been eliminated in South Korea since 2006.⁴

Measles during pregnancy has been reported to be associated with deleterious effects on the perinatal

outcomes as well as severe complications in the mother and fetus.³

We report a case of perinatal measles infection during a measles endemic outbreak in the northern Gyeonggi province between July and October 2013,⁵ which is documented for the first time in Korea to our best knowledge. We also reviewed the literature regarding measles during pregnancy.

Case report

A previously healthy 37-year-old Korean woman (gravida 3 and para 2) at 36 weeks of gestation was referred to us because of a persistent fever that had lasted for 5 days. Physical examination revealed a body temperature of 38.9°C, blood pressure of 140/80 mm Hg, pulse rate of 100 beats/min, respiratory rate of 20 breaths/min, cough, coryza, pharyngeal injection, and tonsillar enlargement. Laboratory evaluation demonstrated a WBC count of $6.54 \times 10^3/\mu\text{L}$ (89% neutrophils, 7.8% lymphocytes, and 2.8% monocytes)

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and an elevated C-reactive protein level of 1.74 mg/dL. A chest radiograph revealed bilateral pneumonic infiltrations. An empirical antibiotic with cefuroxime (2,250 mg/day) was started, and 3 days after, the antibiotic was changed to ceftriaxone (2,000 mg/day) and clarithromycin (1,000 mg/day) which were maintained for 5 days. No microorganisms were noted on the culture of the blood, sputum and urine. The stool culture for salmonella and shigella was negative. Real-time polymerase chain reaction tests of the nasal swab were all negative for influenza, respiratory syncytial A/B virus, parainfluenza 1/2/3, metapneumovirus, rhinovirus A/B/C, bocavirus, coronavirus, and adenovirus.

Abdominal sonogram and electronic fetal monitoring showed normal fetal growth and intrauterine conditions without abnormalities.

On the 3rd day of admission, dyspnea with hypoxia (oxygen saturation of 87%) developed and elevated liver enzyme levels (AST/ALT: 86/61 IU/L) were noted. Chest radiograph revealed the development of bilateral pleural effusions (Fig. 1). Additionally, bilateral conjunctivitis with diarrhea and maculopapular rashes around the face and neck were noted.

On the 4th day of admission, she developed spontaneous labor pain and gave birth to a living male

(2,900 g) at 36 weeks and 3/7 days of gestation via normal vaginal delivery. The Apgar score of the newborn was 5 at 1 minute and 7 at 5 minutes. Maculopapular rashes that were spreading cephalocaudally and centrifugally were noted (Fig. 2). The patient had no history of measles vaccination because she had lived in a low vaccination coverage area, which had had a low vaccination rate due to a low socioeconomic status and lack of resource, during her childhood.

The results of maternal serologic tests performed on the delivery day, including ELISA (Platelia Measles IgM, Platelia IgG, Bio-Rad, USA) were positive for measles V IgM (2.89; the reference value: negative ≤ 0.80 , equivocal 0.80–1.20, positive ≥ 1.20) and negative for measles V IgG (0.67; the reference value: negative ≤ 0.80 , equivocal 0.80–1.20, positive ≥ 1.20).

The newborn showed good activity and oral feed-



Fig. 1. Bilateral pneumonic infiltration with pleural effusion of both lung fields in the mother on the 3rd hospital day.



Fig. 2. Diffuse multiple maculopapular rashes on the right arm and shoulder, and the upper trunk of the mother on the 4th hospital day.

ing, except for a laboratory finding of leucopenia ($3.31 \times 10^3/\mu\text{L}$; 46% neutrophils, 32% lymphocytes, and 16% monocytes) at birth. Before the results of the maternal serological tests were obtained, an intramuscular polyvalent immunoglobulin injection (γ -globulin, 0.3 mL/kg) was administered on the day of birth as post-exposure prophylaxis. However, after 3 days, mild maculopapular rashes, without fever or other symptoms, developed around the face and neck and spread slightly to the trunk; these observations were noted for 2 days, and then they disappeared. Any oral mucosal lesions encompassing Koplik spots had not been observed since birth until the cutaneous erythematous eruptions developed. Magnetic resonance imaging examination of the brain and cerebrospinal fluid study were not performed. Results of serological tests for measles on the day of birth showed that the newborn was negative for IgM and IgG; however, the follow-up serological test on the 14th day of life revealed positive results for IgM (2.27) and IgG (1.45), which indicated mother-to-child transmission of the virus.

The mother was discharged on day 8. The newborn had shown normal growth and development, and did not develop any neurological or other complications during the 9-month follow-up period; His head circumference, weight, and height were 45.0 cm (50-75 percentile), 9.8 kg (75-90 percentile), and 73.0 cm (50-75 percentile), respectively, at 8 months of corrected age. His Korean ages and stages questionnaires (K-ASQ) score at 8 months of corrected age was as follows; communication score was 20 (cut-off value, 14.2), gross motor 50 (cut-off value, 23.5), fine motor 45 (cut-off value, 12.4), problem solving 45 (cut-off value, 27.0), and personal/social 40 (cut-off value, 25.6).

Discussion

Measles during pregnancy usually manifests severe clinical features in the mother; further, serious complications of the respiratory and digestive systems are common.³ It is associated with adverse obstetric outcomes including fetal loss, prematurity, and fetal/neonatal infection.^{3,6} In utero transmission of the measles virus to the fetus can cause congenital measles that exhibits highly variable clinical outcomes such as asymptomatic cases, maculopapular rash, pneumonia, and sub-acute sclerosing pan-encephalitis with fulminant course,⁷ which may be likely related to the lack of maternal immunity against measles, as noted in our case.

We have reviewed and provided a summary of the findings of medical literature in the past decade regarding measles during pregnancy (Table 1). Despite the fewer fatality cases than those noted in older publications, recently reported measles infection cases were still associated with a high maternal, fetal, and neonatal mortality rate in undeveloped countries; these may be due to the absence of or incomplete maternal vaccination, and the status of prenatal and postnatal care, including immunoglobulin prophylaxis.

In this case, the severe clinical features exhibited by the mother, including pneumonitis, hepatitis, and enteritis, were thought to be related to the lack of vaccination. In the newborn, post-exposure prophylaxis with polyvalent immunoglobulin may be helpful to avoid potential fulminant infections in the absence of maternal transplacental immunity, needed based on the fact that the duration between the development of maternal rash and delivery was 1 day. The develop-

Table 1. Data from the literature regarding cases of measles during pregnancy in the past decade

Year	References	Number of cases	Pregnancy and neonatal outcomes	Maternal outcomes	Comments
2009	Ohij, et al. ⁸	1	Prematurity, congenital measles with skin rash	Preterm delivery	Japan; time between rash and delivery, 4 days; prophylactic immunoglobulin administered to the neonate
2010	Bar-on, et al. ⁹	1	Abortion due to premature rupture of membranes at 16 weeks' gestation		Israel; identification of the virus in the placental tissue
2010	Go, et al. ¹⁰	1	Prematurity, no evidence of congenital measles	Preterm delivery	Japan; time between rash and delivery, 1 day; prophylactic immunoglobulin administered to the neonate
2012	Huoi et al. ¹	13	1 preterm delivery	6 (46%) cases requiring hospitalization, 4 (31%) pneumonia cases	French; 2010-2011 outbreak in Lyon
2012	Peruzzo, et al. ¹¹	1	Congenital measles with skin rash		Switzerland; time between rash and delivery, 0 day; prophylactic immunoglobulin administered to the neonate
2014	Ali, et al. ⁶	61	Of total 53 deliveries, 40 (75.5%) term deliveries, 6 (11.3%) abortions, 4 (7.5%) preterm births, 3 (5.7%) stillbirths	11 maternal deaths (18.0%; pneumonia (n=9), encephalitis (n=1), and intracranial hemorrhage (n=1); including 8 during the prenatal period), 35 (57.4%) illiteracy	Sudan; 46 (75.4%), no prenatal care; 12 (19.7%), vaccinated; 32 (52.5%), not vaccinated; 17 (27.8%), vaccine status not known
2013	Giusti, et al. ⁷	2	2 cases of prematurity, 2 asymptomatic congenital measles cases	Preterm delivery	France; time between rash and delivery, 14 and 3 days, respectively; prophylactic immunoglobulin administered to 1 neonate
2014	Ogbuanu, et al. ¹²	55	Of a total of 42 known fetal or neonatal outcomes, 7 (16.7%) spontaneous abortions, 4 (9.5%) IUFD, 9 (21.4%) cases of prematurity; Of the 31 live births, 3 (9.7%) neonatal mortalities; Of 18 with known birth weight, 7 (38.9%) newborns with low birth weights	33 (60%) diarrhea, 22 (40%) pneumonia, 3 (5%) encephalitis, 5 (9.3%) maternal mortality; Of 42 with available data of hemorrhage, 3 (7.1%) excessive hemorrhage cases	Namibia; 2009-2010; retrospective case-control study
2014	Casalegno, et al. ¹³	13	1 (7.7%) prematurity	11 (84.6%) fever cases, 4 (30.8%) pneumonia cases	French; 2011 outbreak in Lyon
Present case		1	Prematurity, congenital measles with skin rash	Preterm delivery, pneumonia, enteritis, hepatitis	South Korea; time between rash and delivery, 1 day; prophylactic immunoglobulin administered to the neonate

Abbreviation: IUFD, intrauterine fetal death

ment of mild illness despite the prophylaxis may have been due to attenuation of the disease by prophylaxis or insufficient dosage of the immunoglobulin administered.

nistered.

In fact, the effectiveness of passive immunoglobulin for preventing congenial measles remains unknown.

The incubation period from the development of skin eruptions in the mother to the onset of illness in the newborn was 4 days (1 day in utero and 3 days postpartum), which is markedly shortened due to direct transplacental transmission of the virus in utero and bypassing of the respiratory and replication phases.⁸

The establishment of the nationwide measles vaccination program resulted in a dramatic decrease in the number of measles cases. However, there have been several measles outbreaks in South Korea, possibly due to the relatively lower immunity acquired by vaccination than the naturally achieved immunity.¹⁴ This is supported by the findings of another study on maternal measles antibody levels that demonstrated lower immunity levels in vaccinated women than in naturally immune women; further, maternal antibody titers were highly correlated with those of the neonate.¹⁵ In the measles outbreak that occurred in the northern Gyeonggi province in 2013, out of 25 confirmed cases, 22 had no vaccination history, and of these, 15 were infants aged less than 12 months, including our case.⁵ The status of immunity against measles may play an important role in cases of maternal infection during pregnancy and perinatal infection among their newborns.

We did not performed RT-PCR tests for the diagnosis of perinatal measles infection because the case was the second identified patients with measles infection encountered in the early period of a 2013 measles endemic outbreak, and the clinicians did not primarily suspect the disease due to the domestic low prevalence of measles infection. Of total confirmed 25 cases (including the present case) of the diagnosis of measles infection during the 2-month outbreak, 17 cases (not involving the present case), which were subject to RT-PCR tests for measles, revealed to caused by the strain detected to belong to

genotype B3.⁵

In conclusion, we suggest that the perinatal measles infection, although rare, should be considered in the diagnosis of the perinatal infection of the mother and newborn presenting with cutaneous manifestations, and regarding the morbidity and mortality of gestational measles in mothers and their children, women of childbearing age should be screened for immunity against measles and, if needed, vaccinated.

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주산기 홍역감염으로 인한 모체와 태아측 이환에 대한 증례보고

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임신 중 홍역은 산모와 신생아 건강의 예후에 해로운 영향을 주는 것으로 알려져 왔다. 저자들은 2013년 국내 경기북부 지역에서 홍역이 유행한 기간 초기에 열, 피부발진, 그리고 폐렴 증상들을 동반하고 홍역예방접종을 받았던 과거력이 없는 한 산모에서 홍역을 진단하였고 이 산모에게서 조기 분만한 신생아에서도 피부 증상과 함께 산모로부터 홍역의 전파가 확인된 선천성 홍역을 진단하여 문헌 고찰과 함께 국내 처음으로 보고한다. 본 증례를 통해서 드물지만 임신 기간 중 홍역은 피부증상을 동반한 출산 전후 감염으로서 고려되어야 할 것으로 생각되며, 홍역의 태반경유감염은 산모의 홍역에 대한 면역력 여부가 가장 중요하고 이는 산모와 신생아 건강의 예후와 직결된다. 따라서 가임기 여성들은 홍역에 대한 선별 검사와 함께 필요하다면 예방접종을 시행 받아야 할 것으로 생각된다.

중심 단어: 홍역, 임신, 태반경유감염