

ACASE Report of Congenital Rubella Syndrome (CRS) With Blueberry Muffin Lesion

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Abstract: Congenital rubella syndrome (CRS) is a consequence of rubella infection that can occur when the virus is transmitted in utero during maternal primary infection. It still affects 110,000 children around the world.⁵ It has a wide spectrum of presentation which ranges from silent viremia to spontaneous abortions, blindness, deafness, congenital heart disease, and mental retardation.⁶ Congenital rubella syndrome (CRS) is an important cause of severe birth defects. When a woman is infected with the rubella virus early in pregnancy, she has a 90% chance of passing the virus on to her fetus. This can cause the death of the foetus, or it may cause CRS. Deafness is the most common, but CRS can also cause defects in the eyes, heart, and brain. Rubella is spread in airborne droplets when infected people sneeze or cough. Once a person is infected, the virus spreads throughout the body in about 5 to 7 days. During this time, pregnant women may pass the virus on to their foetuses. Our case was a live born VLBW preterm, normally delivered by vaginal delivery at preterm by a 27-year-old primi gravida of lower socioeconomic status. Physical examination of the baby revealed caput, micrognathia, cloudy cornea, multiple blue purpuric spots (blueberry muffin lesions) all over the body including the face. We report this case though its rare in developed country, its still common in developing country and the existence of congenital rubella syndrome in the community, prompt the clinicians to make a diagnosis of CRS in children with suggestive clinical signs, and to create awareness against this vaccine- preventable disease and consideration to include MMR vaccination in nation immunization schedule and preterm live birth.

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I. Introduction

Congenital rubella syndrome (CRS) is a consequence of rubella infection that can occur when the virus is transmitted in utero during maternal primary infection. Infection occurring within 12 weeks of gestation causes CRS in 90% with 100% risk of congenital defects. If the infection occurs 13–26 weeks after conception, the risk is 23% of the infant being affected by the disease. Infants are not generally affected if rubella is contracted during the third trimester, or 26–40 weeks after conception. Problems rarely occur when rubella is contracted by the mother after 20 weeks of gestation and continues to disseminate the virus after birth. It has a wide range of presentation from silent viremia to spontaneous abortion and multiple congenital anomalies with devastating consequences. Classically CRS is a constellation of deafness (SNHL), cataract, congenital heart disease. Some cases are commonly associated with IUGR, retinopathy, microcephaly, hepatosplenomegaly, blue purpuric rash (blueberry muffin lesions) and intracranial calcifications. Less common complications include glaucoma, encephalitis, myocarditis, thyroid abnormalities.

II. Case Report

A 27-year-old with an unbooked pregnancy at 34 weeks 6 days' gestation was admitted in Regional Institute of Medical Sciences, Imphal, Manipur with complaints of abdominal pain and leaking PV for 8 hours. On past history patient told that she had mild fever 3-4 months back for which she took medication. She had no previous history of prior antenatal care or antenatal USG. There was no history of any rash, arthralgia, lymphadenopathy, bleeding diathesis, vaccination received during the pregnancy. HIV and VDRL were non-reactive. She belonged to a meitei community of Manipur with lower socioeconomic status. There was no declared history of exposure to other drugs. She did not recall a history of rubella infection or of rubella vaccination. She was otherwise healthy with no known history of genetic or congenital anomaly in her family. Ultrasonography at the time of presentation revealed a live foetus, in cephalic position, oligohydramnios and reduced end diastolic velocity flow of umbilical artery. The USG film is not included in this case. A very low birth weight (1100g) male baby was delivered by preterm vaginal delivery at 34 wks 6 days by an unbooked,

27yrs old primigravida in RIMS, Imphal. Baby cried after initial steps of resuscitation with A/S -7/10 at 5 minutes with multiple blue purpuric rash (blueberry muffin lesion) all over the body including face [picture 1]. Finding on the initial physical examination, the child had no pallor, icterus, cyanosis, and edema, no dysmorphic features, the infant had Cold stress, feeble cry, caput, micrognathia, cloudy cornea. Skin had multiple well defined violaceous, blue purpura (blueberry muffin lesion), non blanchable macules and barely palpable plaques to nodules ranging in size from $0.2 \times 0.2 \text{ cm}^2$ to $0.3 \times 0.3 \text{ cm}^2$, present all over the body including palms and soles, predominantly over face. HR- 136/min, RR- 34/min. Anthropometry showed BW < 10th percentile for the gestation, HC- 27cm, CC- 23 cm, Length-39cm, Ponderal Index -1.85(Picture 1 and picture 2). On systemic examination- pan systolic murmur of grade IV on left intercostal space was present, liver was 7cm palpable below the right costal margin, with firm consistency and sharp margin, Spleen: 3 cm palpable below the left costal margin and undescended testis with hypospadias. Intrapartum and the postpartum period of mother was uneventful.

Baby was admitted in NICU and though investigation was done. Further workup for the diagnosis showed Rubella serology of baby reveals Rubella IgM titre was >400AU/mL highly positive (>25 AU/mL is considered Positive by Method: Chemiluminescence Immunoassay, CLIA) and the rubella Avidity was 55% (>40% high avidity IgG). Ultrasonography of skull on Day 2 showed B/L basal ganglia calcification, plain CT scan of brain was normal. Echocardiography showed atrial septal defect with patent ductus arteriosus and tricuspid regurgitation. The ophthalmologic exam revealed the presence of a mature cataract. The ear, nose, throat (ENT) examination showed a hearing impairment that needed further evaluation for sensorineural hearing defect. Hence, CRS was confirmed in this case. There is no specific treatment for CRS. Symptomatic and supportive treatment was given.

Picture: 1



Picture: 2





Picture: 3

III. Discussion

Congenital rubella syndrome (CRS) is a consequence of rubella infection that can occur when the virus is transmitted in utero during maternal primary infection. Infection occurring within 12 weeks of gestation causes CRS in 90% with 100% risk of congenital defects. If the infection occurs 13th –26th weeks after conception, the risk is 23% of the infant being affected by the disease. Though rubella may be a mild viral infection spread by droplet infection, the effect it has on the growing fetus can be catastrophic. CRS results from infection of fetus with rubella virus through the infected placenta, the virus enters the fetal circulation by embolic transport. Classically CRS consist of cataract, sensoneural hearing loss and congenital heart disease. IUGR and prematurity were frequently manifested. The onset of some other abnormalities may be delayed for months to years and the consequences can be devastating. The first description of CRS belongs to Gregg in 1941 but it was completely described in 1944.¹¹ Webster showed, on a series of pathology examinations performed on abortion fetuses due to rubella syndrome, that the majority of the functional and structural defects had a disruptive pattern, resulting actually from the destruction of the normal tissues.^{9,10}

A study of Miller et al⁸ showed that the risk of congenital infection was 81% and the risk of malformation was of 69% if the mother had rubella in the first pregnancy trimester. The risk fall to 33% after 12 weeks of gestation and no defects were encountered after week 16. Infants who are moderately or severely affected by CRS are recognizable at birth, but mild CRS might be recognized only month or years after birth or even not at all.⁷ The mother of our newborn had in the first trimester of pregnancy a viral exanthema with previous fever for a couple of days. As soon as the suspicion of congenital rubella syndrome was raised we have performed the mother's antibodies towards rubella. These were positive for recent infection. Efforts should be still done to vaccinate all women of childbearing age especially high risk groups like hispanic population or refugees^{12,13}. However, the only prophylactic measure for congenital rubella syndrome remains the correct vaccination of mothers at childbearing age.

WHO has published guidelines that recommend identifying all children with congenital birth defects that are associated with CRS and follow up of all risk pregnancies. Serologic screening for rubella is not necessary if the person has an acceptable evidence of immunity against the disease. Women who are known to be pregnant but can not show any evidence of acceptable immunity should receive the vaccine. During outbreaks screening for rubella is not a recommended practice due to the time that is lost and it is considered that vaccination is the most important aspects in regard of ending the outbreak.¹³ In the prenatal period, ultrasound examination may fail to diagnose CRS but molecular analysis performed on amniotic fluid (collected at least 6 weeks after maternal infection and after 21 weeks of gestation) will confirm or infirm congenital infection. Diagnostic criteria have been established by World Health Organization. In the postnatal period, CRS

may be diagnosed by its classic triad of clinical signs: cataract, heart disease, and deafness. To date, no treatment for rubella or CRS is available. In order to prevent CRS, vaccination of adolescent girls and women of childbearing age is recommended.¹⁴

According to the study by P. Vijayalakshmi et al¹⁵ 238,000 children are born world over with CRS each year, majority of cases being in the developing countries. The report of overall incidence of rubella immunity in mother during the first three months of pregnancy is 55%, and nearly 45% of women were susceptible to CRS. Maternal infection can transfer the infection trans-placentally and cause congenital defects in the fetus. Rubella virus enters the cell via endocytic pathway.¹⁶ During the period of maternal viremia the placenta may become infected causing necrosis and desquamation of the epithelium of the chorionic villi and the endothelium, which causes, placental hypoplasia, placentitis and thus giving viral entry into the fetal circulation by embolic transport. The RA27/3 vaccine for rubella is considered as highly efficacious and the immunity after a single dose is supposed to be life long, however, following administration of any vaccine, there may be few cases of primary vaccine failure and some of the responders may lose their protective immunity over time (secondary vaccine failure). This may be a logical explanation for the second dose of rubella vaccine to serve the susceptible individuals.

IV. Conclusion

Congenital rubella syndrome (CRS) is a debilitating disease with serious outcome and is easily preventable by effective vaccination. This case highlights the need for MMR vaccination and for carrying out adequately powered studies for effective MMR vaccination policies. Though the case is presented on account of its rarity in developed country while it is still common in India (0.4-4.3 per 1000 livebirth) and to emphasize on the fact that it can be easily prevented by vaccination. Prognosis of rubella congenital infection mainly depends on the term at maternal infection. Infected children surviving the neonatal period may face serious developmental disabilities (for example, visual and hearing impairments) and have an increased risk for developmental delay, including autism, type I diabetes mellitus and thyroiditis. Vaccination at high risk groups is necessary in order to avoid the appearance of the congenital rubella syndrome. We should adopt measures to ensure high vaccination rates among children. Checking rubella antibody status should be made a part of preconception counseling and antenatal care, and to initiate health education measures to create awareness among women regarding the effects of Rubella infection in pregnancy and CRS.

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