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Case Report

Paediatrics Section

Congenital Rubella Syndrome with Blueberry Muffin Lesions and Extensive Metaphysitis

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ABSTRACT

We report a case of Congenital Rubella Syndrome (CRS) in a newborn. The baby had blueberry muffin skin lesions, long bone metaphysitis and congenital heart defects. With this case report we would like to highlight 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.

Keywords: Congenital infection, MMR, Microcephaly

CASE REPORT

A 37-week-term male child, born to a 23-year-old gravida$_2$ mother by Emergency Caesarean section in view of prolonged premature rupture of membranes with meconium stained amniotic fluid. The baby had Low Birth weight (2015 grams), was small for gestational age (SGA), and had multiple discrete purplish spots all over the body.

It was a spontaneously conceived and supervised pregnancy and mother was immunized for tetanus. The baby was 2nd in birth order; elder sibling was 4y healthy male child. Mother was not immunized for MMR vaccine and serology for rubella was not done during antenatal period. There was no history of any fever, rash, arthralgia, lymphadenopathy, bleeding diathesis, vaccination received during the pregnancy. HIV and VDRL were non-reactive. Antenatal Ultrasonography showed normal study .The birth weight was 2015 grams (< 10th percentile), length was 44cm (b/w 10th and 25th percentile) and the head circumference was 28 cm (< 3rd percentile). Microcephaly was missed in the antenatal USG. On examination, the child had no pallor, icterus, cyanosis, and edema, no dysmorphic features, eye examination was also normal. Skin had multiple well defined violaceous, non blanchable macules, and barely palpable plaques to nodules ranging in size from 0.3×0.3cm^2 to 0.5×0.5 cm^2, present all over the body including palms and soles, predominantly over face [Table/Fig-1].

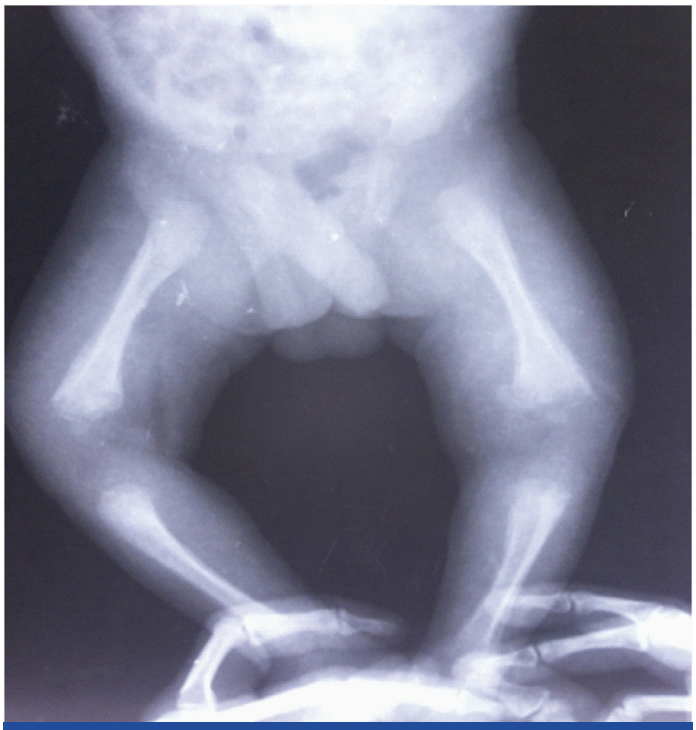
Pan systolic murmur in 2nd, left intercostal space was present. Liver was 3cm palpable below the right costal margin, with firm consistency and sharp margin, Spleen: 1.5 cm palpable below the left costal margin. Complete blood count revealed severe thrombocytopenia (17,000). First sepsis screen was negative, second sepsis screen was positive. Coagulation study was deranged. Prothrombin Time was 21.3 (against normal of 11.7) and Partial Thromboplastin Time was >180 (normal 30). Chest X-ray showed cardiomegaly with infiltrates. Infantogram showed extensive metaphysitis predominantly involving long bones [Table/Fig-2].

Various differentials for trans-placental acquired dermatosis include infectious, neoplastic and inflammatory causes. Reasons favoring infectious cause in this case included a low birth weight, small for gestational age child with microcephaly, hepatosplenomegaly, thrombocytopenia with skin rash and metaphysitis. So, we had a term 37-week-child, with early onset sepsis, pneumonitis with acynotic congenital heart disease with thrombocytopenia, hepatosplenomegaly, coagulopathy with transplacentally acquired dermatosis and the differentials for this included various intrauterine infections- congenital rubella syndrome (CRS), congenital Cytomegalo Virus Infection(CMV), congenital toxoplasmosis, early syphilis, hemolytic disease of newborn. Further workup for the diagnosis showed Rubella serology of baby as IgM =1.98 (<1.20), IgG =19.10 (0-4.99), Rubella serology of mother was IgM =79.70, IgG =209.00. Serology for CMV, Toxoplasma and VDRL were negative. Ultrasonography of skull on Day 2 showed bilateral calcification in caudothalamic region, plain CT scan of brain was normal. Echocardiography showed atrial septal defect with patent ductus arteriosus and mild tricuspid regurgitation. Skin Biopsy in epidermis showed mild hyperkeratosis with keratotic plugging, and biopsy of dermis had severe ill-defined nodes of extra medullary haematopoiesis suggestive of blueberry muffin (BBM) lesions. Hence, CRS was confirmed in this case. A written informed consent was obtained from the parents for publication of this case report and the images.

DISCUSSION

Rubella, a viral infection, not of much clinical significance in adults, but its infection in pregnancy, especially the early pregnancy, causes serious outcomes in the newborn. Infection occurring in the first trimester causes congenital rubella infection in 90%, with almost a 100% risk of congenital defects. From 13 to 17 wk, the risk of infection is about 60%, and risk of defects, about 50%. From 18 to

[Table/Fig-1]: Blue berry muffin skin lesions



[Table/Fig-2]: Infantogram showing growth plate irregularity

24 wk, the risk of infection is about 25%, with minimal chances of congenital defects [1].

Manifestations of CRS include cataracts, congenital glaucoma, congenital heart disease, microphthalmia, microcephaly, deafness, mental retardation. Thrombocytopenic purpura, hepatosplenomegaly with jaundice, and bone defect may also be present [2].

According to the study by P. Vijayalakshmi et al., [3], 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 [4]. 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 [5].

CRS spectrum may include early abortions, still births to various disabilities. This is an important cause of blindness, deafness, congenital heart defects and mental retardation. Late manifestations include movement and behavioral disorders, diabetes, thyroid abnormalities [6].

According to the study by Dewan P et al., [7], CRS accounts for 10-15% of paediatric cataract, 10-50% of children with congenital anomalies have laboratory evidence of CRS, 10-30% of adolescent females and 12-30% of women in the reproductive age group are susceptible to rubella infection in India. There have been reports of CRS occurring in spite of maternal antibodies, suggesting re-infection during pregnancy [8,9].

In spite of endemicity of rubella in India there are no comprehensive studies for assessing the prevalence of CRS in general population. All studies have focused on symptomatic cases of CRS [10] and currently there is no effective nationwide policy against rubella. In America, the use of vaccine since 1969 after the rubella pandemic between 1962 and 65 has brought the rubella cases down by 99% [11].

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.

Although MMR vaccine has not been included in national immunization schedule of India, The Indian Academy of Pediatrics (IAP) recommend to offer MMR vaccine to all parents who can afford it as two dose schedule, one at 15-18 month and second at school entry (4-6yrs of age) [12]. State immunization programme of Delhi has also introduced MMR as a single dose between 15-18 month.

CONCLUSION

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. 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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