CASE REPORT

The Astonishing, Classical Blueberry Muffin Rash: An Obstetric Case Report on Fetal Outcome in Congenital Rubella Syndrome

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Abstract

Background: A family awaits perhaps the biggest moment of joy of their lives on New Year's Eve when a 37-year-old female with twin gestation is conceived after several years through *In vitro* fertilization. But a rude shock hits the doctors as well as the expecting parents when one of the twin babies, is found to have congenital rubella syndrome, which had gone undiagnosed throughout the antenatal period. A classical blueberry muffin appearance, after moments of confoundment, reveals the diagnosis and a lesson on the importance of pre-conceptional immunization and monitoring of the second twin from its affliction.

Aim: To understand intrauterine infections, especially rubella, its prevention, and clinical presentation.

Case description: A 37-year-old female with twin gestation conceived via assisted reproductive techniques, delivered a child with congenital rubella syndrome.

Clinical significance and conclusion: Intrauterine infections can be a significant cause of sporadic abortions and congenital abnormalities. The prevention, diagnosis, and timely treatment can prevent its deleterious fetal effects. Also, an attempt to understand a rare, but classical presentation of congenital rubella—blueberry muffin rash—and its other autopsy findings.

Keywords: Blueberry muffin rash, Case report, Congenital cataract, Congenital rubella syndrome, Hepatomegaly, *In vitro* fertilization, Measles, Mumps, Rubella vaccination, Toxoplasma, Rubella, Cytomegalovirus, Herpes zoster infections.

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Introduction

Blueberry muffin rash, a rare occurrence, where clinicians might even struggle to diagnose, is a classical manifestation of a morbid intrauterine infection, rubella. More so, if you're a certain female, who's struggled to conceive for a decade, and finally with the utility of assisted reproductive technique (ART), good news awaits, but with a catch to it.

Case Description

On the New Year's Eve, at our tertiary care center, a 37-year-old nulligravida, with a very low ovarian reserve, who had conceived by ART by intracytoplasmic sperm injection (ICSI), after a decade of unsuccessful attempts to conceive, by using a donor ovum, came with an ultrasound report as described later. Her conception was by double embryo transfer, which eventuated in a dichorionic diamniotic gestation.

The patient had an uneventful antenatal course, and she was prophylactically kept on progesterone support and low-dose aspirin at a single tablet of 150 mg per day. Her targeted anomaly scans done at the 18th week of gestation for both twins were normal, and her blood investigations were within the normal range. The pregnancy was uneventfully progressing toward term, until the 36th week of gestation, when she presented with an ultrasound that showed fetal growth restriction and Doppler changes in the second twin, suggesting the absence of end-diastolic blood flow in the umbilical artery with intermittent reversal in the flow as well with an expected fetal weight of 1.4 kg. The first twin, in breech presentation, had a normal ultrasound with an expected fetal weight of 2 kg. As the antenatal corticosteroid cover was completed a couple of days earlier, a decision for emergency lower segment cesarean section was taken owing to the presence of doppler changes and breech presentation in the first twin.

Intraoperatively, the delivery of the first baby was uneventful by breech extraction and the baby cried immediately at birth. But, the moment amniotomy was performed on the amniotic sac of the second twin, the one with doppler changes, viscous and straw-colored amniotic fluid was observed that puzzled the obstetricians. That was merely the beginning of a rude shock yet to arrive. The moment the second baby was delivered, there was

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Patient consent statement: The author(s) have obtained written informed consent from the patient for publication of the case report details and related images.

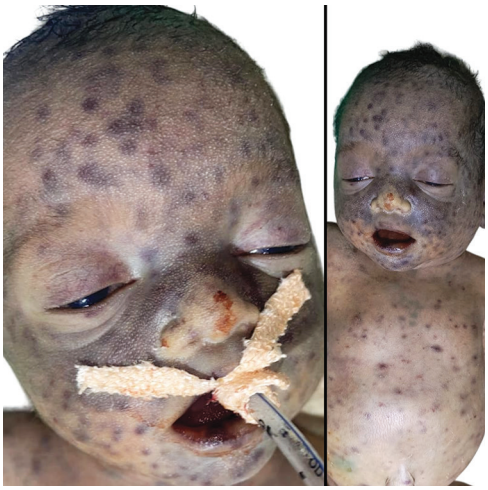

Fig. 1: Blueberry muffin rash

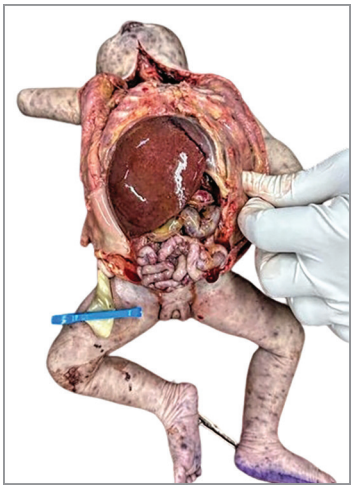

Fig. 2: Enlarged liver span on autopsy

evidence of dermal purpura throughout the body and obvious abdominal distension. The baby did not cry and was handed to the neonatology team for immediate resuscitation. Unfortunately, the baby succumbed to cardiorespiratory failure.

On the evaluation of this baby, blueberry muffin rash[1] as seen in Figure 1 was recognized, and congenital cataracts were seen. An autopsy was performed, which showed gross hepato-splenomegaly as seen in Figure 2. While the average liver span[2] for a 36-week-old baby is around 5 cm, the span for this baby was an astonishing 15 cm. There was also the presence of a large ventricular septal defect in the baby. To rule out other differential diagnoses for the blueberry muffin rash, which included neuroblastoma and leukemia, further autopsy and blood investigations were carried out which canceled those differentials. The polymerase chain reaction test for rubella was found positive for this baby, and rubella Ig G titers were raised as well, thereby confirming the diagnosis of congenital rubella syndrome (CRS).[3]

The first baby was tested for transplacental infection with toxoplasma, Rubella, Cytomegalovirus, Herpes zoster titers (TORCH), individual systemic evaluation was done, and the baby was found to have chorioretinitis on ophthalmic evaluation with positive rubella Ig G titers. All other individual organs were normal, and a conservative approach was carried out for the treatment of the chorioretinitis with resolution seen after 2 weeks. Maternal TORCH titers were tested as well, which showed the presence of rubella Ig G, with no history of having taken any vaccination against rubella. The patient and her surviving baby were discharged with an uneventful postpartum period.

Discussion

Rubella,[4] also called German measles in literature, is a disease caused by an RNA virus called rubella virus from the family *Togaviridae*. It is characterized in its classical form by maculopapular rash, fever, and lymphadenopathy. Its most severe form of acquisition is congenital when acquired in the 1st trimester. Its pathogenesis is by necrosis of the chorionic epithelium and endothelium and eventual fetal affliction, inhibition of mitosis, and early precursor cells of organs by inhibiting actin assembly and increasing cytokines and interferons in the fetus and causing congenital anomalies.

The classical "blueberry muffin appearance" seen is merely dermal erythropoiesis which is physiological till 5th month of intrauterine life until the liver and spleen take over that function. But in patients with affected liver and spleen, as seen in this baby, there is persistence of the dermal erythropoiesis, thereby leading to dermal purpura and hence the name. Other systems that can bear the brunt of this disease congenitally, can be sensorineural hearing impairment, various cardiac defects, cataracts and chorioretinitis with microphthalmia, thrombocytopenia, hemolytic anemia, microcephaly, and cerebral calcifications. The fetal abnormalities are due to vasculitis that causes tissue necrosis and also direct viral damage.[5]

Several studies have been done on infants with CRS. Singh et al.[6] in his case report describes a baby with CRS who has fetal growth restriction, hepatosplenomegaly, and cardiac murmur due to atrial septal defect, pulmonary hypertension, and patent ductus arteriosus (PDA). The baby also had bilateral cataract. A study done in India that studied over 50,000 children below 5 years of age with hearing impairments, developmental delays, and mental retardation revealed 0.58% of kids with CRS.[7] Another study by Manjunath and Balaya.[8] which assessed infants with mental retardation, cardiac anomalies, hepatitis, and cataract showed that 64.3% of infants had CRS. Chandy et al. reported that 9.4% of affected infants out of 646 studied have CRS and cataracts, cardiac defects, deafness, hepatitis, and neurodevelopmental delay.[9] Similarly, Toizumi et al. mention in their study of infants with CRS who had PDA and thrombocytopenia.[10]

Currently, the Measles-Mumps-Rubella vaccination,[11] also famously called the measles, mumps, rubella (MMR) vaccination, is a part of the national immunization schedule which mandates three vaccinations, first at 9 months of life, next at 15–18 months, and last between 4 and 6 years of age. This vaccine confers lifelong immunity toward these illnesses, but unfortunately owing to it being a live attenuated type of vaccine, it's contraindicated during pregnancies due to its theoretical teratogenic potential. Women hence are advised to be vaccinated with MMR at least 4 weeks prior to their plans for conception by the Center for Disease Control (CDC).

Toxoplasma, Rubella, Cytomegalovirus, Herpes zoster testing isn't advised for all pregnancies currently in India and isn't considered a part of routine antenatal surveillance. As ultrasound findings are suggestive of congenital TORCH infections, chorionic villous sampling or amniocentesis is performed to test for the viral genome and confirm its presence. It also provides for a valid reason for medical termination of pregnancy if detected till 24 weeks of

gestation in the intrauterine environment. In babies born with the stigmata of CRS, they can shed the virus in their secretions till 1-year of age, and hence their contact with other pregnant women must be prohibited due to its contagious nature.

Conclusion and Clinical Significance

No current treatment exists for CRS so the aim should be toward the prevention of transmission with vaccination and contact prevention. Perhaps, the infection here must've been remotely prior from the time of the targeted anomaly scan, which led to the missed diagnosis at a point when medical termination of pregnancy or selective fetal termination could've been an option.

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