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Case Report

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Congenital Rubella syndrome: A short report and literature review

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Abstract

Rubella infections are rarely seen where immunization programmes are in place. Congenital rubella syndrome is however still observed where the vaccination programme against rubella is not administered or interrupted. We present such a case, with typical clinical anomalies including congenital cataracts, sensorineural hearing loss and bone lesions. The diagnosis was verified by detection of rubella immunoglobulin M positivity in the mother in the first trimester and positive rubella serology in both baby and mother.

Keywords

Congenital disease, Rubella, immunization

Introduction

Congenital rubella syndrome (CRS), presents with cataracts, hearing loss, heart abnormalities, and central nervous system disorders.[1,2] The risk of congenital defects after maternal infection is essentially limited to maternal infection in the first 16 weeks of pregnancy.[3]

Case report

The first child of a non-consanguinous couple, a male, was born to 28-year-old primigravida mother delivered at 35 weeks' gestational age by normal spontaneous vaginal delivery. The mother had been diagnosed with Type 1 Diabetes Mellitus and hypothyroidism. She had been treated with subcutaneous insulin and levothyroxine during her pregnancy, as well as vitamin D and iron supplements. A blood sample at 10 weeks' gestation tested negative for serology of toxoplasmosis, rubella and herpes simplex. Maternal rubella specific IgM and Rubella specific IgG were positive, and rubella avidity rate was low. Following this, a ten-fold increase in rubella-specific IgG titre was detected with the disappearance of IgM positivity at the next follow-up. The fetal ultrasound scan detected no abnormality.

Premature rupture of membranes less than 18 h before term prompted delivery. The child had an Apgar score of 9 and 10 at 1 and 5min of age. His birth weight (3.5Kg) and length (49cm) were compatible with the 94th centile, with the head circumference at 33cm (the 77th percentile for his gestational age). He was hospitalized for three days in our neonatal intensive care unit because of indirect hyperbilirubinaemia in order to receive phototherapy at eleven days of age.

A month later, bilateral cataracts and glaucoma were noted. By then, he had mild hepatomegaly, his weight having increased only to 4.2Kg (thus dropping to the 30th centile), with smaller head circumference at 31cm.

Blood investigations revealed a neutropenia (1×10^9/L) and congenital anaemia (haematocrit: 27,4%). By brainstem-evoked response, audiometry revealed a right ear hearing loss.

Cranial ultrasonography demonstrated bilateral millimetric echogenic cysts within the caudothalamic notches. Cranial MRI revealed sub-ependymal cysts 3mm in size, and echocardiography interventricular septal hypertrophy.

Serology and polymerase chain reaction tests for infectious agents including cytomegalovirus, parvovirus, herpes simplex, varicella zoster, hepatitis and human immunodeficiency virus, syphilis, rubeola, and toxoplasma proved negative.

Rubella specific IgM titres of the neonate's serum were negative, but serum Rubella specific IgG was positive

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Table 1. Published congenital Rubella syndrome cases in literature.

Study No	Author	Date	Place	Laboratory Test Results of the Patient	Clinical and Radiological Findings	Mother's Vaccination Status	CRS Case Type (Probable or Confirmed)	Age Group	Mortality Status
1	Bypareddy et al.[4]	2016	India	Not performed	Bilateral cataracts, salt and pepper like pigmentary retinopathy, sensorineural hearing impairment, PDA	Not performed	Probable	10 years	Non
2	Reddy AK et al.[5]	2014	India	Not performed	Bilateral cataracts, developmental delay, PDA, hearing loss	Unknown	Probable	10 years	Non
3	Singh A et al.[6]	2017	India	Rubella PCR was positive	Bilateral cataracts, ASD, PDA, microcephaly, hepatosplenomegaly	Not performed	Confirmed	Neonate	Non
4	Ionescu C et al.[7]	2016	Romania	Rubella IgM was positive	Bilateral cataracts, ASD, VSD, Pulmonary artery stenosis, sensorineural hearing loss	Unknown	Confirmed	2 years	Non
5	Mekonnen D [8]	2017	Ethiopia	Not performed	Peripheral pulmonary stenosis, PDA, microcephaly, cataracts, developmental delay	Unknown	Probable	9 months	Non
6	Hussain AS et al.[9]	2019	Pakistan	Rubella IgM was positive	PDA	Not performed	Confirmed	Neonate	Non
7	Lazar M et al.[10]	2015	Romania	I. Rubella PCR was positive II. Rubella PCR and IgM were positive	I. ASD, PDA, bilateral cataracts II. Cataracts, glaucoma, hearing loss, PDA, microcephaly, radiolucent bone disease, jaundice, splenomegaly	I. Unknown II. Unknown	I. Confirmed II. Confirmed	I. Neonate II. Neonate	I. Died II. Died
8	Chauhan N et al.[11]	2016	India	Not performed	PDA, VSD, tricuspid regurgitation, left atrium to right atrium shunt, developmental delay, sensorineural hearing loss, microcephaly, pigmentary retinopathy	Unknown	Probable	7 years	Non
9	Khurana S et al.[12]	2019	India	Rubella IgM was positive	Bilateral cataracts, hepatosplenomegaly, microcephaly, ASD, PDA	Unknown	Confirmed	Neonate	Died
10	Ahuja R et al.[13]	2015	India	Unknown	VSD, severe hearing disorders	Unknown	Probable	4 years	Non
11	Fang J et al.[14]	2013	USA	Rubella IgM and PCR were positive	Hypoplastic transverse aortic arch, PDA, dilated right ventricle, bilateral nuclear cataracts, radiolucent bone lesions, sensorineural hearing loss	Not performed	Confirmed	Neonate	Non
12	Ajij M et al.[15]	2014	India	Rubella IgM was positive	Blueberry muffin skin lesions, microcephaly, hepatosplenomegaly, acyanotic congenital heart disease	Not performed	Confirmed	Neonate	Non

(continued)

Table 1. Continued

Study No	Author	Date	Place	Laboratory Test Results of the Patient	Clinical and Radiological Findings	Mother's Vaccination Status	CRS Case Type (Probable or Confirmed)	Age Group	Mortality Status
13	Pitts SI et al.[16]	2014	USA	Rubella PCR, persistant Rubella antibody and Rubella IgM was positive	Microcephaly, hepatosplenomegaly, developmental delay, Peripheral pulmonary stenosis, PDA	MMR vaccine was performed	Confirmed	Infant	Non
14	Ushida et al.[17]	2003	Japan	Rubella IgM and PCR were positive	PDA, sensorineural hearing loss, Bilateral cataracts	Rubella vaccine was performed	Confirmed	Neonate	Non
15	Ayadi et al.[18]	2015	Tunisia	Rubella IgM was positive	Jaundice, splenomegaly, microcephaly, Blueberry muffin skin lesions	Unknown	Probable	Neonate	Died
16	Hwang SJ et al.[19]	2010	Taiwan	Not performed	PDA, Pulmonary artery stenosis, retinopathy, hearing impairment, developmental delay	Unknown	Probable	Neonate	Non
17	Marchant et al.[20]	2016	UK	Rubella IgM and PCR were positive	Bilateral cataracts	Unknown	Confirmed	Neonate	Non
18	Ooi HL et al.[21]	2005	Malaysia	Rubella IgM and Rubella PCR were positive in the baby	Blueberry muffin skin lesions, microcephaly, hepatosplenomegaly, PDA, hearing impairment	Unknown	Confirmed	Neonate	Non
19	Forrest JM et al.[22]	2003	Australia	Rubella IgM was positive	Bilateral sensorineural deafness	Not performed	Confirmed	Neonate	Non
20	Banerji A et al.[23]	2005	Canada	Rubella IgG and IgM were positive. Rubella virus was cultured from the urine and from both extracted cataracts	Microcephaly, Bilateral cataracts	Unknown	Confirmed	Neonate	Non

*ASD: Atrial septal defect VSD: Ventricular septal defect PDA: Patent Ductus Arteriosus.

twice**.** Long bone radiography showed osteopenia and longitudinal radiolucent bone lesions.

Discussion

Pediatric CRS cases reported in PubMed between 1997 and 2019 were searched; 20 case reports and series being found relevant and analyzed according to the CDC definition (Table 1).

Congenital rubella infection and CRS are defined by WHO and Centers for Disease Control (CDC) differently.[4,24] WHO developed clinical criteria to classify CRS as either a suspected CRS case, a clinically confirmed CRS case, a laboratory confirmed CRS Case or as a congenital rubella infection (CRI).[25] According to CDC, CRS cases are classified as probable, confirmed, suspected or infection only.[24]

CRI presents variously as spontaneous miscarriage, fetal demise, or the birth of a neonate with CRS. First trimester infections have the highest risk, as high as 90%.[26,27] There are a wide variety of ocular defects including glaucoma, cataracts, pigmented retinopathy and microphthalmia. Sensorineural hearing impairment, intrauterine growth retardation and cardiac anomalies such as pulmonary stenosis and patent ductus arteriosus are other clinical features. Later postnatal findings are generalized 'blueberry muffin' skin spots, pneumonia, bone lesions, hepatosplenomegaly, developmental delay, encephalitis, autism, diabetes mellitus, and thyroid dysfunction.[26,28]

Rubella-specific IgG antibodies that persist at a higher concentration or more prolonged duration than expected from passive transfer of maternal antibody, or isolation of rubella virus RNA confirm the diagnosis.[29] The CRC diagnostic criteria of CRS refer to the baby only, whereas WHO diagnostic criteria include both mother's findings in pregnancy and the baby's findings after birth.[25,26] As the former concentrates only on the baby's findings, cases may be overlooked or diagnosed late.

Our literature review suggested cardiac and eye anomalies are the most common; skin lesions less common. All confirmed cases had laboratory evidence of rubella virus infection such as IgM or PCR positivity. Developmental delay was detected in four out of seven probable cases, and is a warning sign for rubella.

We present this study to emphasize the importance of vaccination against rubella for eradication. Routine vaccination against rubella should continue and follow up of vaccination is essential. Since there is no treatment for congenital rubella infection, the main aim must be prevention.

Consent to participate

The patient's consent was obtained from his parents. All authors ensure the patient's anonymity.

Declaration of conflicting interests

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