

Presenting with Isolated Hepatitis Caused by Congenital Rubella Infection Due to Maternal Rubella Vaccination

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Abstract

Congenital rubella syndrome is a transplacental infection that may cause serious devastating damage in the fetus, including intrauterine growth retardation, cataracts, patent ductus arteriosus, hearing loss, microcephaly, thrombocytopenia, and hepatitis. Rubella vaccine is administered for preventing congenital rubella syndrome. It is suggested that patients must be screened for pregnancy before vaccination and should be informed regarding contraception for 3 months after vaccination. Herein, we presented a 1-month-old boy to whom rubella vaccine was administered. After performing multiple diagnostic studies to exclude other liver disorders, the patient, who had high liver enzymes, was diagnosed with congenital rubella infection by his mother's history and positive anti-rubella IgM. His liver enzymes returned to normal at 2 months of age of the follow-up period. Negative anti-rubella IgM was revealed at 6 months of age. As a result, when rubella vaccine is administered in pregnancy, high liver enzymes might occur without other congenital rubella syndrome signs in newborns. Infants who are borne by pregnant women with rubella vaccination should be monitored.

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Keywords: Rubella vaccine, congenital rubella infection, hepatitis

Introduction

While rubella creates a clinical picture with a mild form of the disease in children and adults, it can damage all the organ and systems of the fetus when experienced during pregnancy. When the disease is experienced in the first 3-4 months of the pregnancy, the virus infects the fetus around 80-90% and the condition results in spontaneous miscarriage, stillbirth and congenital rubella syndrome (1, 2). Congenital rubella syndrome may develop out of intrauterine growth retardation, ophthalmic problems (cataracts and microphthalmia), hearing loss, congenital heart disease (patent ductus arteriosus and pulmonary stenosis), retardation and central nervous system anomalies. Although the infection picked up early trimester may rarely cause congenital rubella syndrome, intrauterine rubella infection symptoms may develop later (6).

There has not been a live attenuated vaccine of rubella in use since 1969 (7). The most important reason for the administration of the vaccine is to prevent the development of intrauterine rubella syndrome. The vaccine ensures 95% protection in those people in whom the vaccine is administered. The rubella vaccine may cause viremia in the recipient (8, 9). This virus may well get through placenta and enter into the fetal tissues (10, 11). Therefore, after the vaccine is administered to the group of non-pregnant young adult women, they are recommended not to conceive at least for three months following the vaccination (7).

In this article, the case of a one-month old infant who developed intrauterine rubella infection with high liver enzymes due to the administration of rubella vaccine to the mother in the first trimester was presented.

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Table 1. Follow-up of the liver function tests and serological values found in the patient

Age	ALT (U/L)	AST (U/L)	GGT (U/L)	Total bilirubin (mg/dL)	Direct bilirubin (mg/dL)	Rubella IgM	Rubella IgG (IU/mL)
Normal	6-50	5-55	12-123	0.1-1	0-0.4		0-1
1. month	79	86	177	3.2	0.8	+	344
6. month	32	40	84	0.9	0.3	-	326

ALT: alanin aminotransferaz; AST: aspartat aminotransferaz; GGT: gama glutamil transpeptidaz

Case Report

One-month old male infant was admitted to our hospital with the story of the mother having been administered rubella vaccine in the first trimester (10. gestation week). The infant born to the mother in her second pregnancy through cesarean section on the 39th week weighing 3,800 gram did not have any complaints on the admission and had a good weight gain. The body weight was measured as 4,200 gram (50-70 percentiles), height 54.5 cm (75 percentile), and head circumference 35.4 (10-25 percentile). In the physical examination, the front fontanel was 2x2 cm and had normal head roundedness; bilateral red reflex was being received and other system examinations were normal. No hepatosplenomegaly was found. There was no physiological or extended story of hepatitis that developed after the birth in the personal background of the patient. There was second degree consanguinity between the mother and father, and given the blood types of the parents, no Rh or ABO incompatibility was found. The mother did not have any complaints of rashes, high fever or joint pains during pregnancy. The total blood count and urine analysis were normal in the laboratory tests. In biochemical examination, the following findings were obtained; alanine aminotransferase (ALT) 79 U/L (N:6-50), aspartate aminotransferase (AST) 86 U/L (N:5-55), gamma-glutamyl transpeptidase (GGT) 177 U/L (N:12-123), total bilirubin: 3.2 mg/dL (N:0.1-1) and direct bilirubin: 0.8 mg/dL (N:0-0.4). The abdominal ultrasonography done to eliminate possible other causes of liver disease was normal and hepatitis virus and cytomegalovirus serology were negative. Plasma ammoniac level, tandem together with acylcarnitine profile and plasma amino acids were normal. Rubella immunoglobulin M (IgM) was positive, rubella was IgG 344 IU/mL (N:0-1). Echocardiography, cranial magnetic resonance imaging, hearing test, and eye and optic fundus examinations were within normal limits. The patient was followed up due to vaccine-driven intrauterine rubella infection. The liver enzymes of the patient returned to normal when he was two months old (Table 1). The infant who is now six months old currently has body weight, height and head circumference within normal limits and continues to have age-appropriate neurological and mental development.

The latest liver enzyme tests were normal and rubella immunoglobulin M in his serology was negative (Table 1).

Discussion

In this article, the case of a newborn that was found to have a disorder in his liver function tests due to the administration of rubella vaccine to the mother in the first trimester was presented. Findings of the latest studies where women were administered the rubella vaccine within the trimester before pregnancy or in the early months of pregnancy concluded that the risk of developing congenital rubella syndrome following vaccination was 0.5-1.6% (7, 12, 13). This is much smaller than the 25% risk posed when the infection occurs in the early phases of pregnancy. However, young adults are recommended not to get pregnant at least for three months following the vaccination (7).

The patient was found to have high liver enzymes in the neonatal period; however, no other clinical or laboratory findings of congenital rubella syndrome were found. This is a finding seen in the 50-75% of the hepatosplenomegaly patients in the congenital rubella syndrome (14). However, hepatitis picture is rarely seen (15, 16). There are few cases admitted for neonatal cholestasis (17, 18). In acquired rubella infections, on the other hand, hepatitis picture and hepatitis failure have been reported (19, 20). However, no hepatitis picture was in infants in comprehensive studies in which rubella vaccination during pregnancy was administered (21, 22). Therefore, our patient was the first case where hepatitis picture was seen following the vaccination of the mother. Based on the story of the mother, the blood sample taken from the mother helped us to serologically make a definite diagnosis via rubella IgM positivity. Rubella-specific IgM antibodies in infants infected in the intrauterine period remain in the body for 6-12 months. The rubella IgM antibody in our patient became negative in the 6th month. Badilla et al. (23) carried out a research regarding the congenital rubella infection risk caused by the rubella vaccine during pregnancy without knowing if there was a pregnancy in Costa Rica in 2001 and found some complications such as miscarriage and congenital rubella infections. In a study done in Brazil, 171 cases who were administered

rubella vaccine during pregnancy were followed up until the end of pregnancy and it was found that 11.1% of the pregnancies ended up in miscarriage (19/171 cases) (24). In this study, in the blood serologic examination of 6.7% of the infants, rubella immunoglobulin M was found positive as the finding of the virus during pregnancy; however, clinical and radiological investigations produced no finding of congenital rubella infection in the trimester period (24). In another Brazilian study, 4.7% congenital rubella infection was found in the infants of the women who were administered rubella vaccine during pregnancy (27/580 cases) (25). In a retrospective study done in Argentina, no congenital rubella infection or congenital rubella syndrome was found in the infants of 56 women who were administered rubella vaccine during pregnancy (26). In a study done in Brazil, 4.1% rubella IgM positivity was found in the infants of mothers who were administered rubella vaccine during pregnancy (67/1647 cases) (27). In another Brazilian study, rubella IgM positivity was found in the 9 infants of 1636 mothers who were administered rubella vaccine during pregnancy (28). In our case, echocardiography, cranial magnetic resonance imaging, hearing test, and eye and optic fundus examinations were within normal limits and neurological and mental development were found to be age-appropriate. In conclusion, congenital rubella syndrome is a congenial infection that affects almost all the systems and cause serious mortality and morbidity. Rubella vaccine is administered all over the world in order to prevent rubella infection. Vaccination during pregnancy may develop hepatitis picture or cause congenital rubella infection in the infant. Therefore, the women in childbearing age should not conceive within the three month period following the vaccination.

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References

1. Cooper LZ. The history and medical consequences of rubella. *Rev Infect Dis* 1985; 7: 210. [\[CrossRef\]](#)
2. Miller E, Craddock-Watson JE, Pollock TM. Consequences of confirmed maternal rubella at successive stages of pregnancy. *Lancet* 1982; 2: 7814.
3. Galazka A. Rubella in Europe. *Epidemiol Infect* 1991; 107: 43-54. [\[CrossRef\]](#)
4. World Health Organization. Rubella vaccines. WHO Position Paper. *Wkly Epidemiol rep* 2000; 75: 161-9.
5. Atreya CD, Mohan KVK, Kulkarni S. Rubella virus and birth defects: molecular insights into the viral teratogenesis at cellular level. *Birth Defects Research (Part A)* 2004; 70: 431-7. [\[CrossRef\]](#)
6. Cole FS. Viral infection of fetus and newborn. In: Taeusch HW, Ballard RA (eds). *Avery's Disease of the Newborn*. 7th ed. Philadelphia: Lippincott Williams & Wilkins, 1999: 467-87.
7. CDC. Current trends rubella vaccination during pregnancy-United States, 1971-1988. *MMWR* 1989; 38: 289-93.
8. Modlin JF, Brandling-Bennet AD, Witte JJ et al. A review of 5 years experience with Rubella vaccine in the united states. *Pediatrics* 1975; 55: 20-9.
9. Tingle AY, Chantler JK, Pot KH et al. Postpartum Rubella immunization Association with development of prolonged arthritis, neurological sequelae and chronic rubella viremia. *J Infect Dis* 1985; 152: 606-12. [\[CrossRef\]](#)
10. Sheridan E, Aitken C, Jeffries D, et al. congenital Rubella Syndrome: A risk in immigrant populations. *Lancet* 2002; 359: 674-5. [\[CrossRef\]](#)
11. Phillips CA, Maeck JV, Rogers WA, Savel H. Intrauterine rubella infection following immunization with rubella vaccine. *JAMA* 1970; 213: 624-5. [\[CrossRef\]](#)
12. Robertson SE, Cutts FT, Samuel R, Diaz-Ortega JL. Control of rubella and congenital rubella syndrome in developing countries. Part 2. Vaccination against rubella. *Bull WHO* 1997; 75: 69-80.
13. CDC. Control and prevention of rubella: evaluation and management of suspected outbreaks, rubella in pregnant women, and surveillance for congenital rubella syndrome. *MMWR* 2001; 50 (No. RR-12).
14. Cooper LZ, Preblud SR, Alford CA. Rubella. In: Remington JS, Klein JO (Eds), *Infectious Diseases of the Fetus and Newborn Infant* (4th ed), WB Saunders Company, Philadelphia, 1995:p. 268-311.
15. Stern H, Williams BM. Isolation of rubella virus in a case of neonatal giant-cell hepatitis. *Lancet* 1966; 1: 293-5. [\[CrossRef\]](#)
16. Esterly JR, Slussner RJ, Ruebner BH. Hepatic lesions in the congenital rubella syndrome. *J Pediatr* 1967; 71: 676-85. [\[CrossRef\]](#)
17. Shah I, Bhatnagar S. Antenatal diagnostic problem of congenital rubella. *Indian J Pediatr* 2010; 77: 450-1. [\[CrossRef\]](#)
18. Abdullah AM, al Fadel Saleh M, al Madan M, el Mouzan M, Olasope B. Infantile cholestasis in the Central-Eastern Province Saudi Arabia. *J Trop Pediatr* 1997; 43: 138-42. [\[CrossRef\]](#)
19. Sugaya N, Nirasawa M, Mitamura K, Murata A, Takeuchi Y. Hepatitis in acquired rubella infection in children. *Am J Dis Child* 1988; 142: 817-8. [\[CrossRef\]](#)

20. Figueiredo CA, Cordovani NT, Castrignano SB, et al. Acute liver failure associated with rubella virus in a child. *Pediatr Infect Dis J* 2010; 29: 573-4. [\[CrossRef\]](#)
21. Mamaei MH, Ziaee M, Naseh N. Congenital rubella syndrome in infants of women vaccinated during or just before pregnancy with measles-rubella vaccine. *Indian J Med Res* 2008; 127: 551-4.
22. Nasiri R, Yoseffi J, Khajedaloe M, Yazdi MS, Delgoshaei F. Congenital Rubella Syndrome after Rubella Vaccination in 1-4 weeks Periconceptional Period. *Indian J Pediatr* 2009; 76: 279-82. [\[CrossRef\]](#)
23. Badilla X, Morice A, Avila-Aguero ML, et al. Fetal risk associated with rubella vaccination during pregnancy. *Pediatr Infect Dis J* 2007; 26: 830-5. [\[CrossRef\]](#)
24. Minussi L, Mohrdieck R, Bercini M, et al. Prospective evaluation of pregnant women vaccinated against rubella in Southern Brazil. *Reprod Toxicol* 2008; 25: 120-3. [\[CrossRef\]](#)
25. Sato HK, Sanajotta AT, Moraes JC, et al. São Paulo Study Group for Effects of Rubella Vaccination During Pregnancy. Rubella vaccination of unknowingly pregnant women: the São Paulo experience, 2001. *J Infect Dis* 2011; 204: 737-44. [\[CrossRef\]](#)
26. Pardon F, Vilariño M, Barbero P, et al. Rubella vaccination of unknowingly pregnant women during 2006 mass campaign in Argentina. *J Infect Dis* 2011; 204: 745-7. [\[CrossRef\]](#)
27. Soares RC, Siqueira MM, Toscano CM, et al. Follow-up study of unknowingly pregnant women vaccinated against rubella in Brazil, 2001-2002. *J Infect Dis* 2011; 204: 729-36. [\[CrossRef\]](#)
28. da Silva e Sá GR, Camacho LA, Stavola MS, Lemos XR, Basílio de Oliveira CA, Siqueira MM. 1. Pregnancy outcomes following rubella vaccination: a prospective study in the state of Rio de Janeiro, Brazil, 2001-2002. *J Infect Dis* 2011; 204: 722-8. [\[CrossRef\]](#)