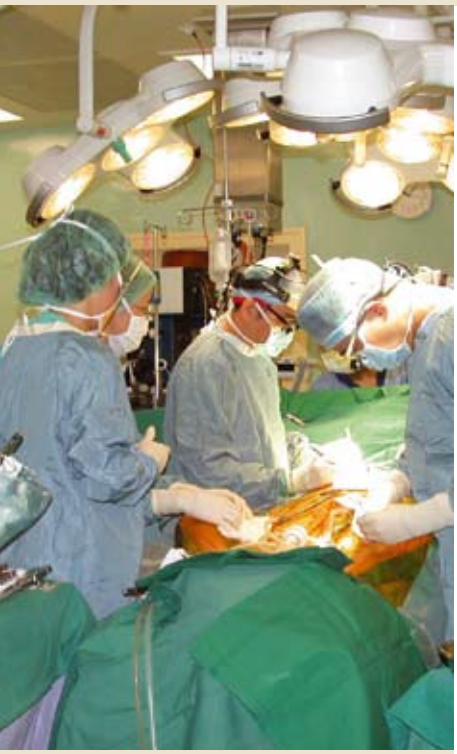
Cardiovascular Malformations in Congenital Rubella Syndrome: A Case Report



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Abstract:

Congenital rubella syndrome (CRS) has a wide variety of severe systemic complications. Cardiovascular defects have always been a part of the rubella syndrome. Patent ductus arteriosus (PDA) remains the most frequent cardiac anomaly. It may occur alone or accompany other heart defects. Pulmonary stenosis and septal defects have been noted with greater frequency since the earlier reports. The classic triad is hearing impairment, heart defect, and cataract.

Here we report an infant girl with classic presentations of CRS. We discuss about her malformations and compared them with other combination of manifestations in the literature.

Key words: Congenital, Rubella infection, Cardiac anomaly

Introduction:

Congenital rubella syndrome (CRS) is an ensemble of congenital malformations which results from a primary viral infection in non-immunized pregnant women (1). Rubella virus is one of the organisms responsible for intrauterine infection or TORCH syndrome. The acronym TORCH refers to toxoplasmosis, other agents (e.g. syphilis) , rubella , cytomegalovirus , and herpes simplex virus types 1 and 2 (2).Congenital rubella can result in deafness, congenital heart disease (CHD), retinopathy, and neurologic abnormalities. Diagnosis is confirmed by culture and/or identification of specific immunoglobulin M within the first 2 weeks of life(2). Maternal rubella was responsible for less than 2% of CHD. The accepted risk of CHD following maternal rubella in the first trimester was considered to be about 20 to 30% and declined steadily there after (3). Nerve deafness is the single most common finding among infants with CRS. Unilateral or bilateral cataracts are the most serious eye finding, occurring in about ⅓ of infants. Cardiac abnormalities occur in half of the children infected during the 1st 8 week of gestation. Patent ductus arteriosus (PDA) is the most frequently reported cardiac defect followed by lesions of the pulmonary arteries and valvular disease. Neurologic abnormalities are common and may progress following birth. Psychomotor retardation has been reported in up to 45% of cases (4).

In a prospective study by Kramer et al. 1016 infants and children with CHD were examined to detect the pattern of their additional malformations. Twenty seven had embryopathy and thirteen of these 27 embryopathies were due to rubella infection (5). In a study in USA from 1985 through 1996 one hundred twenty two CRS cases were reported to the national CRS registry. The most frequent CRS related defect was CHD (6). The literature suggests that approximately 30% of infants with CRS have PDA (7). As part of the national plan for elimination of rubella and CRS, Oman established a national registry of CRS cases. As of May 2005, the registry included 43 surviving CRS cases with a mean age of 11.9 years. Clinical examination found that 84% had ocular defects, 84% had auditory/speech defects, 70% had neurological mani-

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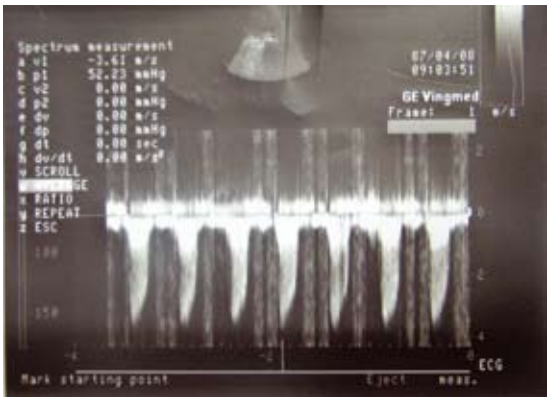
festations, and 42% had cardiac defects (8).
In our country rubella vaccine was included in the routine immunization program of children in recent years. The sporadic cases of CRS are the off springs of young mothers who did not receive rubella vaccine in their infancy. Here we report a CRS case with the classic manifestations. Our aim is to discuss the pathogenesis of cardiac involvement, and to describe the variable combinations of congenital malformations in this syndrome.

Case report:

An 11-month old girl was admitted at pediatric cardiology ward of Shahid Modarres Hospital in June 2008. She was the full term product of her mother's first pregnancy and was delivered by normal vaginal delivery. Her 21-yr old mother had no previous history of abortion. The mother had not received rubella vaccine, and she remembered several days of nonspecific maculopapular rash in the late period of first trimester of her pregnancy. The mother had no previous history of other illnesses like diabetes mellitus or hypertension. The parents were not relatives. At birth the body weight was 2700 gram, head circumference 31 cm, and length 43 cm. The neonate developed jaundice in the 3rd day of birth and had 5 days of hospitalization for treatment.
On admission in our ward the general condition was good but the patient suffered from failure to thrive. Her body weight was 7 kg, head circumference 42cm, and length 72cm. At physical examination there was leukokoria (white pupillary reflex) in both eyes [figure 1]. The cataract of right eye had been operated previously. The patient suffered from mild developmental delay. There was a failure to elicit auditory brainstem evoked responses (ABR test) indicating hearing impairment. Heart auscultation revealed a grade 4/6 harsh systolic murmur with a loud second heart sound (P2) at left sterna border. Liver was 2 cm. below costal margin. Chest X-ray showed severe cardiomegaly with biventricular enlargement, increased pulmonary blood flow with hillar engorgement. ECG showed right axis deviation with biventricular hypertrophy. Echocardiography demonstrated a large perimembranous VSD with PDA and pulmonary hypertension. Cardiac catheterization confirmed the above diagnosis and ruled out the peripheral pulmonary stenosis. Cell blood count (CBC) showed mild anemia with thalassemia minor. Serologic study at the neonatal period had shown positive rubella IgG antibody titer for both mother and child. Repeated serologic test after one month showed positive rubella 1gM antibody titer for the child.

Figure 1: Leukokoria of both eyes are evident

The patient underwent cardiac surgery for PDA legation and division and PA banding [figure 2]. Preoperative pressure of aorta was 8o mmHg and PA pressure was 90 mmHg. Postoperative pressure of aorta was 100 mmHg and PA pressure was 45 mmHg. The postoperative course was uneventful and the patient was discharged in good condition with treatment of congestive heart failure (digoxin, diuretic, and captopril). The patient had regular follow–up and in near future the second heart surgery for closing of VSD will be performed.



Discussion:

In the course of gestation, many bacteria, parasites, and viruses may infect the pregnant woman, but few cross the placenta to affect the fetus and fewer still affect the fetal heart. Although the incidence of fetal cardiac infection is low, the effect on the fetus is major. The pathogenesis of infection of

the fetal heart relates to the agent and to the time of gestation when the infection occurs. The agent affects the heart along one or more of three separate pathways; inhibition of cell growth, cytolysis, and interference with blood supply. Most agents cause cytolysis, stimulating inflammation and scarring. Although several agents carry the suspicion of teratogenicity, only rubella virus has been incriminated with certainly as capable of functioning along each of the three pathways with potential to serve as teratogen (9). The ductus arteriosus is present for many months of fetal life and for a short time after birth, and whatever the mechanism of final closure, it is conceivable that it could be damaged at any stage. The greater incidence of PDA in these children may thus merely reflect the longer time that this structure is at risk. In this regard the histologic structure of the ductus has been reported as abnormal in babies damaged by maternal rubella (3).

Pulmonary hypertension in our patient was due to presence of two large left to right shunts. Cardiac catheterization and angiocardiography did not show peripheral pulmonary stenosis. One of the earlier review articles about cardiovascular defects and rubella syndrome indicated that of 112 patients with CRS patent ductus arteriosus was demonstrated in 46 infants (41%). Twelve patients (10.7%) had VSD and only four (3.6%) had pulmonary stenosis (3). In a report by Spelling et al; about nine patients under five months of age with cardiovascular manifestations of the rubella syndrome, six had PDA. Three of these six also had pulmonary artery stenosis (10). Aiming to document the incidence and type of associated CHD, 20 children affected with the CRS have been evaluated during a 5-year period by Granzotti et al. CHD was detected in 45% of the cases. PDA was the most frequent finding, followed by VSD and ASD. An association of 66% was found between ophthalmic and heart lesions (11).

TORCH infection including rubella can cause multi organ lesions, such as hearing impairment, hyperbillirubinemia and liver dysfunction, impairment of neurologic system, myocardial impairment, thrombocytopenia, and CHD. Neonatal jaundice of our patient may be a manifestation of rubella infection and she had multi organ involvement such as cataract, hearing deficit, developmental delay and CHD. In a study by Givens et al on 125 cases of CRS, ocular disease was the most commonly noted disorder (78%), followed by sensorineural hearing deficits (66%), psychomotor retardation (62%), cardiac abnormalities (58%), and mental retardation (42%). Mulltiorgan disease was typical (88%). Ocular disease and hearing loss were frequently associated (53% had bout). A similar association existed between ocular and cardiac disease (12). In a study in Brazil a total of 43 infants with CRS were screened for birth defects. Eye anomalies and CHD was shown to be the most appropriate sentinel, with the lowest sample size required to detect CRS in neonates (13). No specific therapy for congenital rubella infection has been established, and so treatment is primarily supportive.

In conclusion diagnosis and therapy of the cardiac complications of the rubella syndrome is possible in the first few months of life. Early recognition of cardiac defects in the young infant with the rubella syndrome permits medical management and in most instances surgical operation is indicated.

References :

1. Lahbil D, Souldi L, Rais L, Lamari H , El Kettani A, Zaghloul K. Manifestations of congenital rubella syndrome: clinical and epidemiologic aspects. Bull Soc Belge Ophtalmol. 2007; (303): 13 – 20.
2. Epps RE, Pittelkow MR, Su WP. TORCH syndrome. Semin Dermatol, 1995; 14 (2): 179 – 86.
3. Clifton Way R. Cardiovascular defects and the rubella syndrome. Canad Med Ass J. 1967; vol 97: 1329 – 1334.
4. Mason WH. Rubella. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF, (Eds). Nelson text book of pediatrics. Philadelphia: Saunders Elsevier 2007: 1337 – 1341.
5. Kramer HH , Majewski F , Trampisch HJ , Rammos S, Bourgeois M . Malformation patterns in children with congenital heart disease. Am J Dis Child. 1987; 141 (7): 789 – 95.
6. Schluter WW, Reef SE, Redd SC, Dykewicz CA. Changing epidemiology of congenital rubella syndrome in the United States. J infect Dis. 1998; 178 (3): 636 – 41.
7. Zimmerman L, Reef SE. Incidence of congenital rubella syndrome at a hospital serving a predominantly Hispanic population , El Paso , Texas . Pediatrics, 2001; 107 (3): 40 – 7.
8. Al – Awaidy S, Griffiths UK, Nwar HM, Bawikar S, Al – Aisiri MS, Khandekar R, Mohammad AJ, Robertson SE. Costs of congenital rubella syndrome (CRS) in Oman: evidence based on long – term follow – up of 43 children. Vaccine, 2006; 24(40 – 41):6437 – 45.
9. Rosenberg HS. Cardiovascular effects of congenital infections. Am J Cardiovasc Pathol, 1987; 1(2): 147 – 56.
10. Spelling DR, Verska JJ. Rubella syndrome: Cardiovascular manifestation and surgical therapy in infants. Calif Med, 1966; 105(5): 340 – 4.
11. Granzotti JA, Amaral FT, Sassamoto CA, Nunes MA, Grellet MA. Congenital rubella syndrome and the occurrence of congenital heart disease. J Pediatr (Rio J). 1996; 72(4): 242 – 4.
12. Givens KT, Lee DA, Jones T, Listrup DM. Congenital rubella syndrome: Ophthalmic manifestations and associated systemic disorders. Br J Ophthalmol, 1993; 77(6): 358 – 63.
13. Rittler M, Lopez – Camelo J, Castilla EE. Monitoring congenital rubella embryopathy. Birth defects Res A Clin Mol Teratol, 2004; 70(12): 939 – 43.