CASE REPORT

Congenital Rubella Syndrome with Positive Serology and Virus Isolation

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Summary

An effective live attenuated rubella vaccine was available since 1969 and congenital rubella syndrome can be prevented with appropriate vaccination. We report a baby with congenital rubella syndrome born in Klang valley to indicate that the Universal Rubella Vaccination Programme adopted by the Ministry of Health Malaysia since 2002 has yet to achieve its effect of eliminating transmission of rubella and preventing congenital rubella infection in the community. To our knowledge, the virus isolate represents the first successful isolation of rubella virus in this country and will serve as the reference strain for future comparison in molecular epidemiological tracking of rubella virus activity this country.

Key Words: Congenital rubella syndrome

Introduction

Rubella virus is classified as a non-arthropod-borne virus under the family *Togaviridae* and is the only member of the genus *Rubivirus*. The disease due to the virus was described as early as 1881 but did not receive much attention because of the relatively mild and self-limiting nature of the illness. Its significance was only realized in 1941 when it was noted to be an important cause of congenital defects by N. MacAlister Gregg[1].

Maternal rubella infections may result in fetal death and spontaneous abortion, or the delivery of a severely malformed infant, or an infant with minimal damage or even a healthy infant. The different outcomes depend on a combination of factors which may include the level of maternal viraemia, genetic susceptibility of fetal cells to infection by rubella virus, and most importantly the gestational age at which maternal infection occurs[1].

Following intrauterine infection in early pregnancy, rubella virus persists in multiple fetal organs throughout gestation. The virus may be isolated from nasopharyngeal secretions, urine, stools cerebrospinal fluid and tears of affected infants for substantial period of postnatal life. Study by Cooper and Krugman showed that rubella virus could be isolated from nasopharyngeal secretions of most neonates with severe congenitally acquired disease at birth, but by the age of three months the proportion excreting the virus declined to 50-60% and approximately 10% by 9 to 12 months of postnatal life[2]. Due to the persistent presence of virus in the body, rubella specific IgM could be detected in the circulating blood even after infancy. We report a newborn baby girl with Congenital Rubella Syndrome admitted to Hospital Tengku Ampuan Rahimah, Klang with positive detection of rubella specific IgM in her blood and isolation rubella virus from her nasopharyngeal secretions.

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Case Report

B/O IG was delivered at home on 24 April 2005 with birth weight of 1.45 kg. She cried spontaneously at birth. Mother was unsure of date but her Ballard score was 39/52. She was brought to hospital at 4 hours of life.

IG was 36 year old Gravida 9/Para 8. All her previous babies were healthy. Her antenatal history was uneventful until 33/52 where the uterus was noted to be smaller than date. She had immunization during secondary school days but was unsure of the type of vaccine received. She had no fever, skin rash or contact with person with rash during her current pregnancy. Rubella specific IgM was detected by IgM-capture ELISA (Dade Behring, Germany) in her venous blood sample collected two days after delivery.

On admission, B/O IG was small for age. Her head circumference, weight and length were far below 3rd centile. She was tachypneic with generalized "blueberry muffin" spots on the face and body (Figure 1). Her anterior fontanelle was wide and suture separated. There was an ejection systolic murmur grade 2/6 over left upper sternal edge. Liver (3cm) and spleen (2cm) were enlarged. There was no cataract.

Her blood investigation reviewed thrombocytopenia with normal liver function test. Chest X-ray showed cardiomegaly with features of mild respiratory distress syndrome. Cardiaechography confirmed presence of patent ductus arteriosus. X-ray of long bones was normal. Computerised axial tomography of brain showed multiple calcifications in both basal ganglia and head of corpus callosum (Figure 2), but there was no hydrocephalus. Her eye examination was normal but hearing screening in the ward showed abnormal results and awaiting formal hearing assessment. Results of screening tests for human herpesvirus 5 (cytomegalovirus), *Toxoplasma gondii*, human herpes virus 1 and 2 (Herpes Simplex type I and II) and syphilis were negative. Rubella specific IgM was detected in her blood sample collected at two days of

Fig. 1: Photograph of a newborn baby with congenital rubella infection showing "blueberry muffin" cutaneous haemorrhagic spots on the face and body.

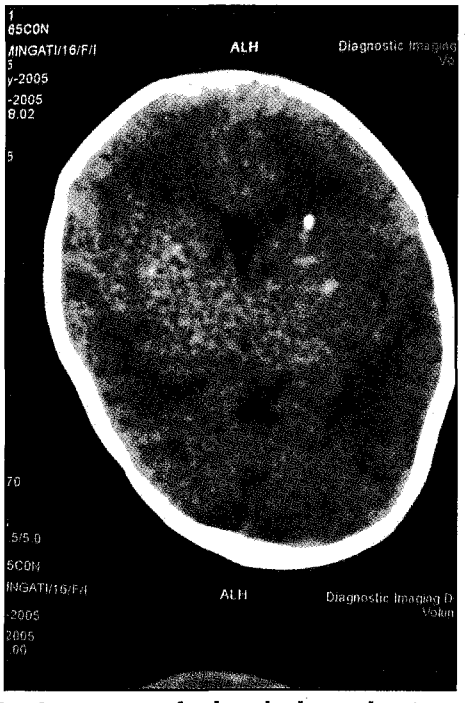

Fig. 2: CT scan of the baby's brain with congenital rubella syndrome showing multiple calcifications in both basal ganglia and head of corpus callosum.

life. Rubella virus was isolated from her nasopharyngeal aspirate collected at sixty-three days of postnatal life using Vero/SLAM cells. Virus replication as evidence by the presence of cytopathic effect on cultured Vero/SLAM was noted after a blind passage. The identity of the isolated virus was confirmed by indirect immunofluorecence test using a commercial rubella specific monoclonal antibody (Cat. No: MAB926, Chemicon USA).

B/O IG required ventilation for three days due to respiratory distress followed by NCPAP for another three days. Since then she remained in hospital until she was discharged at D36 OL with weight of 1.8 kg. She was discharged with Syrup Frusemide and hematinics and will be followed up in the clinic in six weeks' time. We had counseled her parents regarding her long term prognosis.

Discussion

Congenital rubella syndrome can be prevented with appropriate vaccination. The live attenuated rubella vaccine was developed in 1969 and licensed for used in United States of America under the Universal Rubella Vaccination Programme to stop the indigenous transmission of virus and prevent occurrence of congenital rubella infection. Five years after its introduction, the incidence of congenital infection dropped dramatically and there has been no report of endogenous congenital infection for the last decade in USA. A recent review shows that rubella is no more endemic in the country[3]. The United Kingdom adopted the Selective Rubella Vaccination Programme since 1970 and despite its intensive vaccination programme, outbreaks of rubella with congenitally infected babies continue to occur. By 1988, UK has switched over to the Universal Vaccination Programme as adopted by USA. Malaysia adopted the previous UK system of Selective Rubella Vaccination Programme in 1985 and was intensified in 1990 (Source: Department of Health, Ministry of Health Malaysia). Similar to the scenario in UK, the Selective Programme failed to prevent the occurrence of congenital rubella syndrome[4]. In 2002, Universal Rubella Vaccination Programme was adopted as part of the childhood measles, mumps and rubella (MMR) vaccination strategy. The occurrence of congenital rubella infection in this baby indicates the Universal Rubella Vaccination Programme has yet to take effect to stop the local endemic transmission of rubella.

This report confirmed that Vero/SLAM cell-line is sensitive for isolation of rubella virus from clinical samples (personal communication with Dr Masato Tashiro, director of NIID, Japan). To our knowledge, the virus isolate represents the first successful isolation of rubella virus in this country. The successful isolation of rubella virus is timely as this isolate will serve as the reference strain for future comparison in molecular epidemiological tracking of rubella virus activity and monitor the success of Universal Rubella Vaccination Programme in this country.

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