Case Report

Rubella virus, infecting the placental villi

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Abstract

A 20-year-old woman infected with rubella virus at 19 weeks of gestation presented the clinical symptoms of rubella infection and whose placenta was obtained at 37 weeks for the observation. A light microscopical study using a standard light photomicroscope (MC63A Zeiss) was employed to detect morphological changes in the structure of the placental villi. Presence of mononuclear cells in the decidua of the basal plate showed acquired placental infection confirmed by RT-PCR. Death of stem villi appeared under fibrinoid deposition. Degenerative changes were noted in the stromal region of these villi. Clear spaces in this zone indicated tissue destruction and cellular death. Some villi were seen with inflamed syncytiun and others were noted in severe edematous condition. The tree villous was severely affected by the viral activity damaging the normal interchange of gases and nutrients.

Keywords: infection, placenta, Rubella

Introduction

Rubella virus, the sole member of the genus Rubivirus of the family Togaviridae, is a spherical, 40 to 80 nm, positive sense, single-stranded RNA virus with spike-like hemagglutinin containing surface projections and an electron-dense 30 to 35 nm core surrounded by a lipoprotein envelope. This virus produces pregnancy illness in women characterized by rash, lymphadenopathy and fever which can be transmitted to the fetus transplacentally in early pregnancy and can cause birth defects [1].

Acquired Rubella infection during pregnancy can result in stillbirth, spontaneous abortion or anomalies associated with the congenital rubella syndrome as cataracts, heart defects, deafness and other abnormalities. The virus produces chromosomal abnormalities, lysis and cellular death [1].

After serologically confirmed rubella in pregnancy, it can be detected in isolated placental tissues during the first trimester. In 13 amniotic fluids, there were three cases in which virological analysis of the fluid was infected [2]. The diagnosis and management of a case of acute rubella infection in the second trimester have been discussed [3]. However, it has been indicated that primary rubella infections during the first trimester of pregnancy are an indication for the termination, although not all of the fetuses will be infected [4,5].

Rubella vaccine is contraindicated during pregnancy, but if a pregnant woman who is inadvertently immunized is not a candidate for pregnancy termination because no defects consistent with congenital rubella have been reported to date in the offspring of other similarly vaccinated women.
Case

A 20-year-old woman at the 19 weeks of gestation who was infected with rubella presented slight fever, headache, nasal congestion, red and inflamed eyes, inflamed lymphatic nodules four days before the apparition of the rash at the level of the face which was spread to arms and furtherrly to all body with pain.

The samples of her blood were sent to the institution for prenatal diagnosis of rubella virus infection by direct detection of viral RNA in clinical samples by RT-PCR (Real-time polymerase chain reaction) and detection of antibodies by ELISA (Enzyme-linked immunosorbent assay) technique. Serology of the patient was negative for other viruses and toxoplasmosis. There were no other metabolic, genetic or parasitic diseases.

Histological slides of normal placenta were used as control according to the protocol of observations described in the previous article of Castejon and López [6].

In the region of basal plate analysis, we could observe lymphomononuclear cells in the zone of decidual cells (Figure 1a). These cells contained their cytoplasm well notorious. However, there were regions where the decidual cells lost their cytoplasm and a necrotic nucleus could be observed surrounded by a perinuclear clear space, indicating cellular death. Numerous decidual cells were observed in this condition (Figure 1b).

![Figure 1a. Decidual cells are seen invaded by lymphomononuclear cells (H&E 400x).](image1.jpg)

![Figure 1b. Decidual cells are destroyed by the viral activity (H&E 400x).](image2.jpg)

Placental villi were seen associated by fibrinoid deposition which contains debris of stromal region of villi with dead cells (Figure 2a). Stem villi were seen suffering severe degenerative changes. In immature villi, the clear zones in the stromal region were seen and the interruptions to the level of Hofbauer channels were observed (Figure 2b).

![Figure 2a. Dead stromal region of immature villi is surrounded by fibrinoid deposition (H&E 400x).](image3.jpg)

![Figure 2b. Immature intermediate villi showing the stromal region with severe degenerative changes (H&E 400x).](image4.jpg)

Stem villi were observed with changes to the level of vessels and the clear regions in the stroma of the placental villi were indicative of lithic viral activity (Figure 3a). In this figure, the interruptions of the syncytium can be seen. Some edematous villi were exhibited as a ball in severe degenerative changes (Figure 3b). This feature was affected by numerous villi presented in these observations which were not noted in the control placenta.
Discussion

The presence of proliferative and necrotic infection in the decidual region of the basal plate is evidence of intrauterine rubella transmission to the intervillous space of the villous tree [5].

These viruses inhibit cellular macromolecule synthesis and produce acute infections that persist in host tissues for short or long periods of time causing infection. It has been described that under the viral attack of two different viruses (VIH-VPH) the villi suffer numerous interruptions of the syncytium and the placental villi tend to fusion with others to conform new villi [6]. This fusion is realized with previous production and deposition of fibrinoids by both structures.

The observation of large stem villi death is indicative of a diminution of terminal villi since they are a carrier of terminal villi in their ramifications. The degeneration affecting these villi damages the interchange of gases and nutrients in the intervillous space.

The presence of immaturity inhibits the normal development of the villi and the viruses have eliminated the cellular defense represented by Hofbauer cells. It is possible that syncytium is enhanced in some regions of the placental villi since the viral attack has interrupted it and the penetration of fluid has disorganized their internal structure which loss their cytoskeletal organization and elastic properties [7].

The invasion of the virus to the stromal region has provoked the rupture of stromal channels, death of their cells and exaggerated inflammation affecting any villi. Edema of cells lining the blood vessels in the stromal chorionic region can result in karyorrhexis and villous necrosis [8].

The persistence of IgG antibody beyond six months or the demonstration of IgM antibody can be used for the diagnosis of congenital rubella infection [1]. The rubella virus can infect the fetus at any stage of pregnancy provoking hearing loss, mental retardation, cardiac malformations and eye defects.

Developmental defects are less severe if the mother contacts rubella in the second trimester. One common defect is a hole in septum or wall separating the left and right ventricles of the heart. Besides, the overall decrease in the amount of gray matter in the brain which leads to microcephaly, motor coordination and inflammation of spleen and liver. Maternal infection does not always indicate that the child will be born with these defects [9].

Rubella virus was detected in the placenta in two cases in which the fetus was uninfected, and there was no evidence of rubella virus in the placenta from one case in which the fetus was infected. Thus, the detection of rubella virus in chorionic villus sampling by RT-PCR may not always correctly predict fetal rubella infection [10].

A placenta with congenital rubella was found a tendency to hypoplasia, nodules of villi agglutinated by fibrin, immaturity of the villous stem and terminal villi, villitis of reactive, necrotic, proliferative and reparative types [11]. No animal models are available to study how rubella virus causes tissue damage and the placenta has permitted to obtain these dates in the woman pregnancy of this first teratogenic virus described.

In a case of placentomegaly with fetal death at the 29 weeks of gestation, rubella virus was amplified by RT-PCR from the placenta and histological diagnosis of the placenta showed active chronic villitis and chorioamnionitis, villous fibrosis, focal calcifications and thrombotic vasculopathy with avascular villi and hemorrhagic endovasculitis [12].

Recent development procedures for the propagation of rubella virus in the laboratory permits virologic and serologic investigation of congenital rubella infections. It has been described that the interval of viral transmission from the onset of rash in the mother is about 10 days to the placental villi and 20-30 days to the fetus [13].

The diagnostic serologic examination of congenital infection is not always definitive since there are cases where the viral infection was diagnosed in the neonatal period and the prenatal examination was negative. Other possible methods are the mentioned RT-PCR, virus
culture in amniotic fluid or in fetal blood obtained by cord puncture [14]. So, RT-PCR in amniotic fluid has replaced conventional prenatal diagnostic techniques including fetal blood sampling [15].

**Conclusion**

The placental infection with rubella virus has provoked severe interruptions of the syncytium, edema, disorganization of the structure of the placental villi, immaturity and a destructive effect on the stromal region damaging the normal interchange of gases and nutrients in the intervillous space.

**Conflict of interest**

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**References**