The Placenta in a Case of Pregnant Woman Infected by Chikungunya Virus

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Abstract

In this work our proposal is to describe the changes provoked by chikungunya virus on the structure of the placental tissue with light and scanning electron microscopy. Placenta was obtained of patient of 32 years old infected during the third trimester of pregnancy with low increase of weight. Numerous immature intermediate villi were seen. Some placental villi were noted, in part, without the sincytothrophoblast layer, with fibrotic stromal region and death cells. Interruptions of the placental surface were found. Regions of fibrinoid, microinfarcts, syncytiun of different thickness and long mature intermediate villi without terminal villi were located. Stem villi showed collapsed vessels, calcification and severe damage in their vessels. Sub trophoblastic edema, degenerative changes in stromal zone and villous bad-development were located. The viral attack has transformed the placental villi in one structure which is not in their better condition for the fetal transference of gases and nutrients.

Keywords: Chikv; Placental villi; Degenerative changes

Introduction

Chikungunya virus (CHIK V) or chikunguña is a virus belonging to the group of Arbovirus transmitted by vectors Aedes aegypti and Aedes albopictus wich are arthropods transmitters of dengue [1]. Is an alphavirus belonging to the togaviridae family. Alphavirus are small spherical enveloped viruses, with 60-70nm diameter [2]. The fever produced by this virus presents a transplacental [3].

Chikungunya fever was described by first time in the south of Tanzania in 1952. More of 776000 cases of this fever have been realized about chikungunya virus but there is absence of histopathological work in the placental villi showing the structure of these affected by chikv. Is our proposal to describe the change provoked by Chikv on the structure of the placental villi.

There are reports of spontaneous abortus after of an infection by chikv in the mother [6].Chikungunya fever is accompanied by articular pain, abdominal pain, muscle pain, head pain, nausea, tiredness, and subcutaneous eruptions. Occasionally complicated with cardiac and neurological affectations, ocular and gastrointestinal annoyance [4].

Epidemiologicals [7], clinics [2], and laboratory studies [8] have been realized about chikungunya virus but there is absence of histopathological work in the placental villi showing the structure of these affected by chikv. Is our proposal to describe the change provoked by Chikv on the structure of the placental villi.

Material and Methods

Two groups of population of placental villi were taken of placenta normal and placenta study. The group study proceed from hospitalary institution whose placenta was obtained to the 37 weeks of pregnancy, with an poor increase of weight of only 6 kg. The newborn was born alive with 51 cm and 3600gr. The placenta normal was obtained at 38 weeks of pacient with an increase of weight of 10 kg, without antecedent of disease. The Chikv diagnostic was confirmed by seroconversion test (ELISA IgM/IgG) and nucleic acids detection (RT-PCR). The serology of pacient with placenta study was negative for Hepatitis B, C, cytomegalovirus, Epstein Barr virus, rubella and toxoplasmosis. Without other metabolic disease, genetic, parasitary or with malformations and being seronegative to the six weeks of birth.

The infected woman pregnancy had knowledge of informed...
consent and approval by the ethical committee of the hospitalary institution for the realization of this investigation according to the Helsinki declaration. Diagnostic was made by Micro-Elisa of fourth generation, with equipment automatic AXSYM (Abbot, EUA) and confirmatory Western Blot Assay (Germany-Singapore Science Park). Of each placenta were taken five small specimens of the maternal surface selected to the azar from the region central parabalasal in the vertical plane. Three slides by specimen were prepared for light microscopic, 30 histological slides in total which were stained with H&E for their observation.

Five small fragments in similar form were taken for Scanning Electron Microscopy (SEM) according to conventional stains and seen with a Hitachi S2300 scanning electron microscopy. Cross sections of placental villi stained with H&E will be associated with similar regions taken with SEM. The concepts of immaturity, Edema, Fibrinoid deposition and chorangiosis are used as in previous work [9] employing the same nomenclature of placental villi.

Results
Numerous immature intermediate villi were seen. Some placental villi were noted, in part, without the syncytiotrophoblast layer, with a fibrotic stromal region and death cells (Figure 1). Frequent koilocytic figures were observed. The placental surface of the villi showed interruptions or breaks. These villi are little developed or immature and regions of fibrinoid were seen indicating necrosis of villous zone (Figure 2). Regions of microinfarcts and placental villi showing a syncytium of different thickness were found (Figure 3). The single, long, mature intermediate villi showing the characteristic bends of its longitudinal axis and multiple grape-like terminal villi were not seen. There are not terminal villi arising from the convex side of each bend as is seen in normality (Figure 4). The paucity of mature intermediate villi associated with terminal villi is highly characteristic. Bad-development of increased number of filiform terminal villi of minimum diameters with absence of capillary branching were seen.

In some zone these types of villi are seen interlaced and notorious stromal clear areas or empty are noted (Figure 5).

Stem villi showed collapsed vessels and intravillous fibrinoid replaces villous stroma neath debris of trophoblastic cover (Figure 6). These villi also showed severe damage in the blood vessels and villous calcification could be seen associate to degenerating villi (Figure 7).

They are severely damaged with breaks at the level of syncytium, with accented subtrophoblastic edema and degenerative changes in stromal zone. Areas of prominent lysis are observed (Figure 8).

Besides, in regions of fibrinoid deposition, when seen, nucleus of cytotrophoblast were observed with scarcity of chromatin and occasionally placental villi that exhibits chorangiosis can be seen suffering severe degenerative changes in their blood vessels.

Discussion
Viruses cause disease directly affecting the physiology of the cells they infect and the most dramatic effect that have on their
plasma membrane permeability, fusion of cell membranes and depolymerization of the cytoskeleton have been described [11].

Chikv was found in placenta but was not found in some samples including maternal milk and synovial samples [12]. Ziegler et al [13] found in 14 – day – old mice inoculated subcutaneously with chikungunya virus histopathologic changes in skeletal muscle as focal necrosis, inflammation, fibrosis and dystrophic calcification. This offered a useful model for further study of the pathogenesis and treatment of Chikv. Koilocytic figures are indicative of viral reservoir or transformed cell organelles by the viral activity. The clear zones that were observed in the stromal region indicate that the placental villi has suffered necrosis under the viral cytopathic effect. Chikv can provoke direct cytopathic effect on the structure of the villi causing its destruction. These viruses have RNA genome positive sense translationed directly by host tissue and are very infectious. Extensive zones of the placenta with these features can to produce growth retardation, low birth weight and developmental anomalies as occurs with Rubella, CMV and HIV virus. Scanning electron microscopy has confirmed the presence of immature placental villi, low ramification and filiform terminal villi. This technique exhibits a placental tree corresponding to first trimester of pregnancy with villous bad-development.

Although has been described that the rarity of placental histologic lesions (in only 1 of 624 women with chikungunya infection during pregnancy) confirmed the absence of placental infection by the virus and explained the rarity of cases of fetal chikungunya infection before birth [14]; however others factors as lower education level [15], economic resources and nutrimental problems could are contributing with these morphological changes here observed.

Chikv has affinity by several types of cells as muscle cells, glioblastoma cells, meningeal and ependymal cells, kupffer cells, mononuclear cells, endothelial cells, fibroblast cells, keratinocytes and macrophages being the fibroblast chiefly targeted by Chikv [16]. This tropism so diverse add an aggressive character to these viruses which can destroy all the structure of one placental villi as seen in Figure 8.

Vertical contamination most probably occurs as consecuence of passive transfer of maternal blood-borne free virus particles through the placental barrier via the physiological breaches that arise at term of pregnancy and during parturition by uterine contractions and which are known to lead to maternal-fetal blood exchanges [16].

It is possible that factors such as maternal immune status and pre-term placental abruption may contribute to pre-partum infection. The mechanisms that promote fetal infection remains undefined [17]. So, mother-to-child infections were demonstrated with a fifty-percent probability of vertical transmission when the mother was highly viremic around the term of pregnancy [18].

Atrophy, necrosis, vacuolization and collagenosis were also observed in skeletal muscle fibers and muscle satellite cells probably could be eliminated by a direct cytopathic effect [19]. Persistence bylong time of Chikv into macrophages as cellular

![Figure 5: a) Interconnected long mature intermediate villi are noted. b) Lytic changes in the stromal region of several villi are shown. H&E. 100X.](image)

![Figure 6: a) Notable damage is observed in the layers of blood vessels in stem villi. H&E. 100X. b) Villous calcification is associate to degenerating villi. H&E. 100X.](image)

![Figure 7: a) Stem villi presents collapsed vessels H&E. 100X. b) At the center debris of placental villi which presents stromal region substituted by fibrinoid deposition H&E. 100X.](image)

![Figure 8: a) Stem villi is observed with interruptions of syncytium, subtrophoblastic edema and severe degenerative changes in stromal region. b) Placental villi presents disappearance of part of stromal zone, H&E. 100X disintegration or lysis. H&E.100X.](image)
reservoirs during chikv infection in vivo potentially explains long-lasting symptoms observed in humans [20].

In vitro studies using a panel of mammalian cell lines showed rapid induction of cytopathic effects and cell death via apoptosis in most adherent cell lines [21]. Aggregation of nucleus with scarcity of chromatin represent a type of cytopathic effect of Chikv on the placental structure known as cell fusion that involves the fusion of the plasma membrane of four or more cells to produce an enlarged cell with four or more nuclei [22]. Chorangiosis is a term of villous hipervascularization in response to low efficiency of oxygen transfer to the fetal circulation in the villi [23,24]. The viral attack has deteriorate blood vessels and the transference results impaired.

So, the vessels are damaged and the fetus will have problems in the absorption of gases and nutrients. Lysis of the syncytial plasma membrane by the viruses on it could produce holes and the entrance of fluids in these since the intervillous space disorganize the stromal region.

In conclusion, an immature placental villous tree with persistence of immature intermediate villi has been found. This was observed with low ramifications and villous bad-development with accentuated degenerative changes. The viral attack has transformed the placental villi in one structure which is not in their better condition for the fetal transference of gases and nutrients.

References