ZIKA VIRUS AFFECTS THE PLACENTAL VILLI

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ABSTRACT

The pathogenesis of Zika virus infection is not well known and the effects on the structure of the placental villi require to be investigated. Is our proposal to describe the histopathological changes that occur in the placental villi provoked by Zika virus. The patient of 38 years old was infected during the third trimester of pregnancy a week before parturition manifesting symptoms of infection by Zika. Light and scanning electron microscopy were used. Numerous stem villi are suffering degenerative changes with collapsed vessels. A conglomerate of syncytial knots and degenerated peripheric surface can be seen. Immature intermediate villi suffers fibrinoid deposition with macrophages together in Hoffbauer channels. Necrosis of the syncytium and stromal fibrosis were noted on the placental villi. Koylocytic cell, destroyed villi, damage in the wall of vessels and mature intermediate villi with scarcity of terminal villi were found. Bad development of the ramifications of the placental villous tree and regions of lysis in stromal region were located. Thrombus and edema could not be seen. The placental villous tree has been found suffering severe degenerative changes and bad development indicating a destructive effect on the structure of the placenta that could to explain the cytopathic effect provoked by zika virus.

KEYWORDS: Zika virus, Placental villi, Degenerative changes.

INTRODUCTION

Zika virus (Zikv) is an emerging arbovirus, flavivirus of the family Flaviviridae which includes dengue, West Nile, Yellow fever and Japanese encephalitis viruses, that causes a mosquito - borne disease transmitted by the Aedes genus, with recent outbreaks in the South Pacific [1]. It was first isolated from a rhesus monkey in 1947 from the Ugandan forest named Zika [2].

Zika fever is characterized by arthralgia, conjunctivitis no purulent, myalgia, headache, and maculopapular rash. This disease course with mild clinical symptoms. Despite these clinical symptoms, Zikv infection during pregnancy appears to be associated with grave outcomes, including fetal death, placental insufficiency, fetal growth restriction and central nervous system injury [3].

Vector-mediated transmission of Zikv is initiated when a blood-feeding female Aedes mosquito injects the virus into the skin of its mammalian host, followed by infection of permissive cells via specific receptors. From here could to follow until blood vessels and to reach the intervillous space of the placental villi. The first human Zikv infection was reported in Uganda in 1964 [4]. The virus was later isolated from humans in Southeast Asia [5]. In 2007 a large epidemic was reported on Yap Island of the Federated States of Micronesia with nearly 75% of the population being infected with the virus [6]. Zikv contains a positive single-stranded genomic RNA encoding a polyprotein and their viral replication occurs in the cellular cytoplasm. The size of these viral particles is between 70 and 100 nm [1].
Zikv has been isolated from sentinel monkeys, mosquitoes and sick persons in Africa and Southeast Asia. This emerging pathogen can be sexually transmitted [7].

There are evidence of Zikv infection in Brain and placental tissues from two congenitally infected newborns and two fetal losses. Placental tissue from one miscarriage showed heterogeneous choronic villi with calcification, fibrosis, perivillous fibrin deposition and patchy intervillitis of focal villitis, while tissue from the other miscarriage had sparsely normal-appeaning chorionic villi [8].

It has been clear that trasplacental and perinatal transmission can occur [9]. Zikv has been detected in newborns, placenta and umbilical cords, as well in pregnant women by RT-PCR [10]. Despite the pathogenesis of this infection this is not well known and the effects of Zikv on the structure of the placental villi have not been described. Is our proposal to describe the histopathological changes that occur in the placental villi provoked by Zikv.

MATERIAL AND METHODS

Two groups of population of placental villi were taken of placenta study and placenta normal. The group study proceed from hospitalary institution whose placenta was obtained to the 39 weeks more two days of pregnancy. The pacient of 38 years old was infected during the third trimester of pregnancy a week before parturition manifesting symptoms of infection by Zikv. This was confirmed by nucleic acids detection by 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 bad-formations and being seronegative to the six weeks of birth.

The newborn was born alive of 52 cm, 3100gr and placenta of 650gr. 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. The placenta normal was obtained at 38 weeks of pacient with an increase of weight of 10kg without antecedent of disease.

Of each placenta were taken five small specimens of the maternal surface selected to the azar from the region central parabasal in the vertical plane. Three slides by specimen were prepared for light microscopy and 30 histological slides in total 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 Hitachi S2300 scanning electron microscope. Cross sections of placental villi stained with H&E were associated with similar regions taken with SEM. The concepts of immaturity, edema, fibrinoid deposition and chorangiosis are used as in previous works [11],[12] employing the same nomenclature of placental villi.

RESULTS

The placental decidual region when was observed showed a light infiltration of mononuclear cells. Numerous stem villi are suffering degenerative changes. Collapsed vessels were seen in stem villi and a conglomerate of syncytial knots on the surface of placental villi with frequency can be seen [Fig. 1]. In these stem villi the endothelium of their vessels is severely damaged in many cases [Fig. 2]. Regions of the periphery surface of stem villi can be seen in degeneration [Fig. 3]. Stromal clear zones or regions of lysis were observed in stem villi. Macrophages are seen together in Hoffbauer channels of immature intermediate villi which is suffering fibrinoid deposition [Fig. 4]. Giant macrophages were seen in fibrous placental villi. A destructive effect on the placental villi with necrosis of the syncytium and stromal fibrosis can be observed in [Fig. 5]. A zone of stromal region appears to be empty in immature intermediate villi [Fig. 6], which is associate to another large region of immature villi. Anchoring villi associate to decidual region shows damage in the wall of vessels and some and some decidual cells contain nucleus with paucity of chromatin [Fig. 7]. Placental villi showed Koylocytic cell and another villi appear destroyed [Fig. 8]. Thrombus were not located in the vessels of the placental villi.

The single, long, mature intermediate villi shows not the characteristic bends of its longitudinal axis and they were seen with scarcity of terminal villi. Bad development of the ramifications of the placental villi is frequently observed [Fig. 9].

In many placental villi the syncytium is attenuated or slender and terminate interrupting their surface to give origin to breaks. Some of them were seen as exploded. Zones of pre-infarcts exhibit numerous syncytial nodules and areas of calcification are almost absent. Edema could not be seen in placental villi.

Fig.1. a) Conventional SEM photography of placental villi are observed.
Fig. 1 b) Numerous syncytial sprouts are on the surface of them and vessels in stem villi are damaged. H&E:100x.

Fig. 2 a) Placental villi is showing their interior without part of the syncytiun.

Fig. 2 b) Interruption and degenerative changes of the syncytium can be observed. Fibrinoid deposition is noted in stromal region. H&E:400x.

Fig. 3 a) Immature villi with globulous extension.

Fig 3 b) Stromal region shows fibrinoid deposition and macrophages inside of dilated channels. H&E:400x.

Fig. 4 a) Placental villi exhibit severe internal damage.
Fig 4 b) Debris of placental villi and fibrotic region of other immature villi with death cells. H&E:400x

Fig 5. a) Some globulous terminal villi with bad-development.

Fig 5 b) Cross section showing degenerative changes in terminal villi. H&E:400x.

Fig 6 a) Immature terminal villi

Fig 6 b) Cross section that shows bad-development of placental villi. H&E:400x.

Fig 7. a) Damage of vessel in stem villi in their tunica intima H&E:400x.
DISCUSSION

Zikv has provoked directly damage to the structure of the placental villi causing on host cells lysis, cellular destruction and inhibition of vital processes. Histopathologic changes as focal necrosis, inflammation, fibrosis, bad development of the ramifications of the placental tree are indicative of viral cytopathic effect. Similar changes have been observed in placenta infected by virus of the togaviridae family [12]The changes morphological observed in the vessels of stem villi are considered as adverse events provoked or associate to Zikv infection between another fetal abnormalities as growth restriction or central nervous system lesion [13]Endothelial damage has also been produced by viral infection in Rubella (German Measles) as mentioned in the literature [14].The infiltration of mononuclear cells in the decidual placental region is indicative of transplacental perinatal transmission at final of the third trimester.

The prominently increased syncytial knots that were observed in placental infarction regions with acute ischemic change remember to us the changes seen in pregnancy-induced hypertension [15]

Peripheric and stromal regions appear in degeneration by effect of the viral activity of Zikv which contains proteases in their structure. Necrosis, fibrosis, deposition of fibrinoid, koylcytic figures and placental immaturity have also been described in cases of infection with HIV/HPV [16], Chikungunya virus [12] and VIH-1 [17]. The giant macrophages occasionally seen could be considered as a reservoir of Zikv particles. Large Hofbauer cells have also been depicted in villous immaturity of the placenta in a diabetic mother [14]. These cells are involved in reduction of fetal serum proteins contained in the villous stroma and the water balance of placenta with phagocytic activity and immunological role [14]. Macrophages have been confronting the viral attack which produces cellular lysis and a destructive affect.

Since the observation of thrombosis was not noted in stromal vessels villous edema was of difficult observation.

The persisting immaturity observed besides with some mature intermediate villi which lack of terminal villi are indicative of delay of villous maturation at the 39 weeks of gestation.

Thinning of the trophoblast was found in malnutrition with severe anemia or chronic oxygen deficiency (Chronic hypoxia) [18] finding that can be reversible increasing oxygen transfer [14] Rupture of this slender trophoblast could to be originating breaks that facilitate the passive transfer of free virus particles since the intervillous space to the stromal region during uterine contractions of parturition as has been suggested in vertical contamination of Chikungunya virus [12]. In contrast with the found in these virus calcification was almost absent and edema was not seen in this infection with Zikv.

Mild chronic lymphocytic deciduitis of the decidua basal, stromal fibrosis, edema of terminal villi, villous immaturity, calcifications, intravillous and perivillous fibrinoid deposits as well as giant Hofbauer cells were observed in a case of congenital infection of Zikv [19]There are recent reports of placental calcifications, fibrosis, fibrin deposition and villitis associated with maternal Zikv infections but no refer immaturity [8],[19] which was noted in this work.

Besides there are cases where perinatal Zikv transmission no produce adverse results in newborns [20],[21]. We not know if this contamination brief at term could produce in the newborn any abnormality at the future. Although it is possible that intrauterine Zikv infections that occur at later stage of pregnancy may present either with less severe manifestations, such as mental retardation, sensorineural deafness, opthalmological lesions or full term miscarriages [21]

There is no evidence to suggest that Zikv infection during pregnancy is associate with a more severe illness for the
mother, has long-term effects on fertility, or is associate
with adverse fetal outcomes at future pregnancies [22]

This infection is usually mild and lasts up to a week,
mortality is low and hospitalization is infrequent. Zikv is a
public health emergency of international concern: Global,
economics and of health security since in numerous
countries at the Americas has been detected [2]

In conclusion, an immature placental villous tree has been
found suffering severe degenerative changes and villous
bad-development a week before parturition indicating a
destructive effect on the structure of the placenta that could
to explain to us the cytopathic effect provoked by ZikaV
during first thirimester of pregnancy with fetal losses or
miscarriages.

REFERENCES


