Letters to the Editor / Cartas al Editor

THE VESSELS OF STEM VILLUS IN PLACENTA ASSOCIATED WITH OBESITY AND HYPERTENSION.

Olivar C. Castejón Sandoval

Center for Research and Analysis Assistance Teaching of the Nucleus Aragua (CIADANA)
Labaratory of Electron Microscopy.
Faculty of Health Sciences. University of Carabobo.

olivar.ciadanauc@gmail.com


To the Editor:

During normal placental development stem villus originates from first-trimester mesenchymal villi, characterized by its loose stroma. Subsequently the vessels are centrally placed with fibrous connective tissue surrounding them. When the placenta is structured these stem vessels arise from chorionic vessels. Stem villi has one to several large muscular vessels surrounded by a condensed fibrous adventitia containing superficially located paravascular capillaries, similar to vasa vasorum. The vessels of stem villi are composed of endothelium, muscular media and adventitia without elastic membrane.

Obesity is a risk factor for hypertension. A corporal mass index > 29 increase that risk in 10%. Hypertension is associated with vessel lesions (hyalinization or deposit of homogeneous, strongly eosinophilic and thinly granular material) and with proliferation of fibrous tissue or smooth muscle. These changes, described in uterine pathology but not in stem villi of placenta, lead to vessel wall thickening and lumen narrowing. Other physiopathologic mechanisms have been purposed for hypertension as low placental perfusion or ischemic-hypoxic processes producing lysis of endothelial cells, fragmentation of the endothelium and increase of the permeability. These events, originating endothelial dysfunction and occlusive compression of vessels, lead to low blood flow. In this regard, an increase in the number and size of syncytial knots and a thinning of the syncytiotrophoblast and infarcts has been observed.

The aim of this paper is to investigate degenerative changes occurring in stem villi vessels.

For carrying out this descriptive, retrospective and no experimental study with non probabilistic sampling, two placentas were obtained from two pregnant women at 38 weeks of gestation for microscopic analysis. Both pregnancies led to live-newborn with malformations. Women weighed 75 and 85 Kg and their hypertension exceed 90/150 mmHg. The placental weights were 600gr and 650gr after draining all their blood. Specimens were removed immediately post cesarean section from each other and fixed in buffered formaldehyde at 10% in the delivery room according to the conventional procedures for light microscopy.

Five specimens were obtained from each placenta and three slides per placenta were processed for Haematoxylin-Eosin staining. Twenty fields per slide were visualized in a standard clinical MC63A Zeiss microscope (Carl Zeiss, Oberkochen, West Germany) with 16X ocular and 10X - 40X objectives. The observations were focused in the stem villi and its results compared with samples removed from normal placentas.
A protocol linked to the structural characteristics of stem villi vessels was applied. Description of the normal stem villi here employed follows that of Benirschke and Kaufmann1.

Our result stated that stem villi showed vessels with degenerative changes in the endothelial layer. This appeared dilated or expanded in the stromal region and sometimes reveals aneurismal zones. Interruptions or perforations of this layer were seen affecting their continuity (Fig. 1).

In other cases the endothelial layer has disappeared. The muscular media looked disorganized and its smooth muscle cells were orientated in different directions. These cells occupied the vessel lumen forming a net of cells (Fig. 2).

Fig. 1. Stem villi vessels show aneurismal prolongations. A thin and interrupted endothelial layer is seen (arrow). Some vessels are empty. 160x H&E.
Fig. 2. Endothelial layer is not observed. Smooth muscle cells constitute a net in the lumen of a degenerative vessel (arrow). 160x H&E.

This lumen was obliterated by them in some of the stained sections. Images revealing early formation of thrombus were visualized (Figs. 3, 4).

Fig. 3. A growing thrombus into a stem villi vessel. 100x H&E.
Edema affected the muscular layer detaching the smooth muscle cells and almost all the stromal region of the stem villi. In the closed vessels smooth muscle cells replaced the endothelium. The vessel lumen was empty of erythrocytes in some of the stem villi and full of them in others. Edema disorganized the vessel adventitia (Fig. 5).

There were stem villi where vessels have disappeared and the stromal region appeared infiltrated by an accentuated deposit of fibrinoid (Fig.6).
Necrosis fibrinoid also was seen in placental villi connected with the stem villi. Peripheral smaller vessels in these stem villi, similar to vasa vasorum, revealed prominent and with same degenerative changes as those detailed above.

Aneurismal vessel dilatations were occasionally seen. Some of these stem villi revealed calcified in the stromal region supplied by vessels (Fig.7).

Those vessels losing smooth muscle cells showed changes in lumen morphology revealing polygonal form.
Reduced utero-placental blood flow has been recognized in cases of severe hypertension. In these cases, narrowing of fetal capillaries has been demonstrated. This reduced blood flow provokes placental ischemia and low intervillous blood flow leading to degenerative functional changes as those observed in the endothelial layer due to bad placental perfusion. Abrupt diminution of the oxygen tension in this blood induce rapid and reversible vasoconstriction which might produce disorganization of the muscular media. The duration of this vasoconstriction is inversely proportional to the oxygen tension and regulate the blood flow during life. Since hypoxia increases significantly the prostaglandins PGF2α during vasoconstriction this may explain the presence of closed vessels.

Chronic hypoxia or alternate periods of hypoxia / reoxygenation within intervillous space is expected to trigger tissue oxidative stress and increase placental apoptosis. Previous reports pointed out that an increased release of syncytiotrophoblastic micro particles of 0.2 to 2 um in size formed by plasma membrane blubbing during apoptosis are triggered in excess into maternal circulation. These detached fragments, debris of trophoblast, micro villi from syncytiotrophoblast microparticles could be considered as causing endothelial damage, among other factors. Damaged endothelium leak out plasma to muscular media provoking disaggregation of smooth muscle cells and their disorganization associated with the edema originated. This also affected the adventitia of the vessel. These degenerative changes in the wall of the vessel lead to the formation of thrombosis. Occlusive vascular lesions as here observed can be seen in intrauterine growth retardation, intrauterine fetal demise, fetal abnormalities and thromboembolic disease.

The observation of stem villi with some emptied vessels of erythrocytes indicate that fetus can not absorb gases and nutrients or that placental villi are with bad perfusion promoting an ambient of hyperoxia which brake the process of branching angiogenesis resulting in filiform terminal villi. Long standing hypertension with severe elevations can directly damage blood vessels. Changes in the intima and media can lead to significant narrowing of vessels and ischemia in placental villi which produce severe necrotic damage contributing with the disappearance of villi.

Perfusion of the placenta at abnormally low oxygen tension is associated with increased basal perfusion pressure, consistent with placental vasoconstriction. Chronic vasoconstriction and increased intraluminal pressure could lead to vascular obliteration through progressive mural hyperplasia. Increased intraluminal pressure likely predispose to endothelial damage and luminal obliteration. So, there are a prediction of that hypoxia stimulate the liberation from the placental villi to the maternal blood of a factor that interacts with the endothelium.

Low blood flow in the intervillous space provoke a diminution of placental villi by fibrinoid necrosis of them or the formation of zones of infarct. This low blood flow can to be caused by deficient dilatation of utero-placental vessels associated with sharp arteriosclerosis during hypertension which would be increased in these cases associated with obesity.

Rupture of endothelial layer which is here seen dilated possibly contribute to a hemorrhagic endovasculitis. Blood vessel structure is altered in obesity with increase in vessel diameter, limiting caliber and distensibility of vessel walls. Mechanisms that could affect placental blood vessel structure in maternal obesity. Enhanced understanding of normal and aberrant placental structure of vessel in early pregnancy of obese woman is required.

On the other hand growing evidence in human and animal models of maternal obesity have indicated increased placental vascularity, or chorangiosis which would be an adaptative response to low blood flow in the intervillous space.

Normal placental weights have increased over the last decades and this may correlate with increasing maternal obesity. Increased placental weight and placental hypertrophy have been more common in obese groups and could be attributed to the increasing edema here observed.

Aneurysmal prolongation of vessel is a consequence of elevated blood pressure that modifies the wall of the vessel as seen in Fig.4.

Greater muscularity, higher numbers of neutrophils within the intervillous space and a heightened inflammatory response within the adipose and placental tissue has been demonstrated. We found not this fetal environment of inflammation in our placentas associated with obesity and hypertension however recent studies suggest that heightened inflammatory response may be involved in adverse clinical outcomes during pregnancy.

In obese individuals endothelial function is significantly impaired. Blood vessel structure is altered in obesity with an increase in vessel diameter, basement membrane thickness, vascular permeability, and vessel stiffness. A progressive microvascular rarefaction develops increasing the risk of local tissue ischemia by atrophy and vessel

http://biomed.uninet.edu/2015/n2/castejon.html
diameter narrow. The mechanisms underlying impaired endothelial function in obese woman still are not well understood.

In conclusion, degenerative changes in the wall vessel characterized by morphological changes in endothelial layer; edema, losing and invasion of cells in muscular layer as well as adventitia affected by edema have provoked a disorganization of the wall of the vessel with fibrinoid necrosis or calcification originating reduction of the blood flow which could to be affecting the normal development of the fetus.

REFERENCES


ACKNOWLEDGMENTS

The author deeply acknowledges to the Medical staff of Gynaecology and Obstetrics of the Maracay Central Hospital and "Carabáño Tosta" Hospital of the IVSS; to the Administrative Coordination, Faculty of Health Sciences Nucleus Aragua by their financial support for CIADANA, and to TSU Laury R Gutierrez S by the transcription of the manuscript.

CORRESPONDENCE:

Prof. Olivar C Castejón,
General Coordinator of the CIADANA, (Center for Research and Analysis Assistance Teaching of the Nucleus Aragua) Laboratory of Electron Microscopy,
Faculty of Health Sciences. University of Carabobo
Aragua State,
Maracay, Venezuela.
Apdo. 4944.
olivar.ciadanauc@gmail.com