II. NEONATOLOGY

HISTOLOGICAL MODIFICATIONS OF THE UMBILICAL CORD IN PREGNANCY INDUCED HYPERTENSION

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Abstract

Objective. The main structural modifications of the umbilical cord in pregnancy induced hypertension (PIH) are presented versus the normotensive pregnancy.

Material and method. Over 160 histological sections were obtained from 42 umbilical cords, distributed into two equal monitored groups: one group (n= 21), from mothers with (PIH); and another group (n=21), from normotensive mothers, representing control-group. The histological sections were made from the placental and fetal side of the umbilical cord. The histological method for preparation and the colored stain was that for Hematoxylin-Eosine (H.E.); for the examination of the samples we used an optical microscopy.

Results. In the study, were registered the following structural modifications in the pregnancies with PIH versus normal pregnancies:

- diameter and volume reduction of the umbilical cord and umbilical vessels;
- numerical reduction and structural disorders of the smooth muscular fibers and fascicles, from the vascular (and especially, arterial) media;
- vascular endothelium thickening and vascular caliber reduction;
- numerical reduction and structural disorders of the collagen and elastic fibers (especially to the umbilical cord vein). It is a special interest in the constant association of these lesions to the pacients with PIH, versus the normotensive cases, where they occur rarely and isolatedly.

Conclusions. The above described lesion complex has at least three physiopathological consequences:

- fetal blood stream reduction;
- fetal oxygenation and nutrition reduction, with an impact upon the general development;
- a fetal chronic hypoxemia, with a direct impact upon the fetal cerebral development.

Key words: Pregnancy Induced Hypertension (PIH); Umbilical cord

Introduction

PIH is registered in various studies as an evolutive complication of 6-12% of the pregnancies. Although the etiology is not specified, the emergence of the disease is incontestably related to the presence of the placenta and the complex: placenta – umbilical cord (after the birth and the delivery of the placenta, the arterial hypertension disappears).[1] PIH represents one of the most important causes of: intrauterine growth limitation, premature birth, low birth weight, perinatal mortality. PIH is associated to the increase of the placental – uterine vascular resistance[2]. A lot of studies have shown the existence of some structural differences between the placenta and the umbilical cord of the normotensive and respectively, hypertensive, pregnant women. These differences refer to the thickness (diameter) of the umbilical cord .No relations of causality have been established by now, between the morphological modifications of the placenta, umbilical cord and the degree of the fetal ischemia/hypoxia.2 Authors like Di Naro, Junex and others, have shown a significant global reduction of the umbilical cord and of its structures, during its entire length to the mothers with PIH versus the normotensive ones. At the level of the cord vessels, these differences are noticed especially in the media and intima, significantly contributing to the alteration of the hemodynamic conditions in the PIH.[3]

Even in a normal pregnancy (normotensive), the thickness of the umbilical cord undergoes an insignificant reduction, achieved mainly due to the Wharton's jelly; the vascular modifications are quite rare, inconstant and do not realized long lasting hemodynamic alterations. Probably, a certain degree of fetal ischemia/hypoxia, not quantified yet, represents a trigger factor of the birth at the normal time of gestation.[4]

Material and method

The study was carried out upon 42 umbilical cords sampled with the written consent of the mothers: 21 umbilical cords sampled from mothers with PIH and 21 normotensive mothers. Pieces of umbilical cord of about 2cm were achieved, both from the placental and fetal side, for the both groups of study; of each umbilical cord piece, at least two histological sections were carried out.

The main clinical characteristics of the two groups are presented in table 1.

Table 1. Clinical characteristics of normal pregnancy and PIH (mean values).

Clinical Characteristics	**Without PIH (n =21)**	**With PIH (n=21)**
Mother's age (years)	24,09	26,23
Parity (Nullipar/multipar)	13/8	15/6
Birth's type (Spontan/Cesarian section)	15/6	5/16
Gestational age (weeks)	38,09	36,38
Fetal weight (grams)	2928,57	2669,04
APGAR	8,04	7,66
Sistolic Blood Pressure (mmHg)	110,71	152,85
Diastolic Blood Pressure (mmHg)	69,76	99,52

The main factor of differentiation was the value of the blood presure:

- For the group of normotensive pregnant women, the values of the systolic TA ranged between 100-135 mmHg, and of the diastolic TA, between 60-85 mmHg;
- The difference to the hypertensive pregnant women group was made only in the cases whose values of the systolic TA > 140mmHg and diastolic TA > 90 mmHg.

For the rest of the clinical parameters, significant differences between the two groups were registered also for the gestational age, birth weight, type of the birth and immediate neonatal adaptation.

Because during the study, only a limited number of cases (no. = 7) benefited from Doppler ultrasonography, the fact did not allow us to use this variable in our analysis. We mention that in all subjects to Doppler investigation, an important reduction of the vascular caliber and of the blood stream at the level of the umbilical arteries was registered; we are suggesting for the systematic utilization of this investigation in the PIH cases.

For both groups, the following cases were not included: those with essential hypertension, multiple pregnancy, diabetes mellitus, chronic renal diseases, epilepsy and hematological disorders.

The working method for all of the histological sections followed the usually procedure:

- fixation in a 10% formalin solution;
- dehydration in ethanol gradated series;
- sedimentation in xylene;
- paraffining;
- deparaffining;
- hydration and coloring with hematoxylene – eosine .

We mention that the samples and the measurements were carried out immediately after the birth.

Results and discussions

The comparative analysis of the main morphometric and histological parameters is presented in table 2.

Table 2. Umbilical cord's morphological parameters.

PARAMETERS	**Without PIH**		**With PIH**	
	Placental side (n = 21)	*Fetal side (n = 21)*	*Placental side (n = 21)*	*Fetal side (n = 21)*
Cord's diameter (mm)	11,09	9,71	8,04	7,71
Cord's total area (mm^2)	95,76	73,96	50,74	45,99
Reduction of the muscular area in arteries	2/21	2/21	17/21	19/21
Smoth muscular celles hipoplastic and discontinuous	1/21	2/21	18/21	18/21
Thickening of the vascular endothelium	0/21	1/21	17/21	20/21
Reduction and disorder of the collagen and elastic fibers	2/21	2/21	15/21	19/21
Reduction of the arterial caliber	2/21	3/21	18/21	19/21
Reduction of the veinous caliber	1/21	2/21	19/21	19/21

The diameter and volume reduction of the umbilical cord, is significant in the group with PIH, and it is realized especially due to the Wharton's jelly. All the conditions which lead to the limitation of the uterine growth are characterized by a narrow umbilical cord and a Wharton's jelly very much reduced, until its complete disappearance.

In this sense, PIH represents a real natural model of fetal malnutrition and hypoxia. The histological lesions are registered almost constantly in the cases with PIH versus the normotensive group. The reduction of the vascular dimensions is constantly accompanied by significant structural disorders which have an impact upon the vascular intima, media and fibrillary structures.

These structural modifications are associated quasi-constantly with the cases with PIH versus the normotensive cases, in which they appear quite rarely and isolatedly (Figure 1-4). There are some minimum structural modifications, quite rare and never associated with the normotensive cases, suggests processes of prenatal vascular senescence, common at the normal term of gestation.

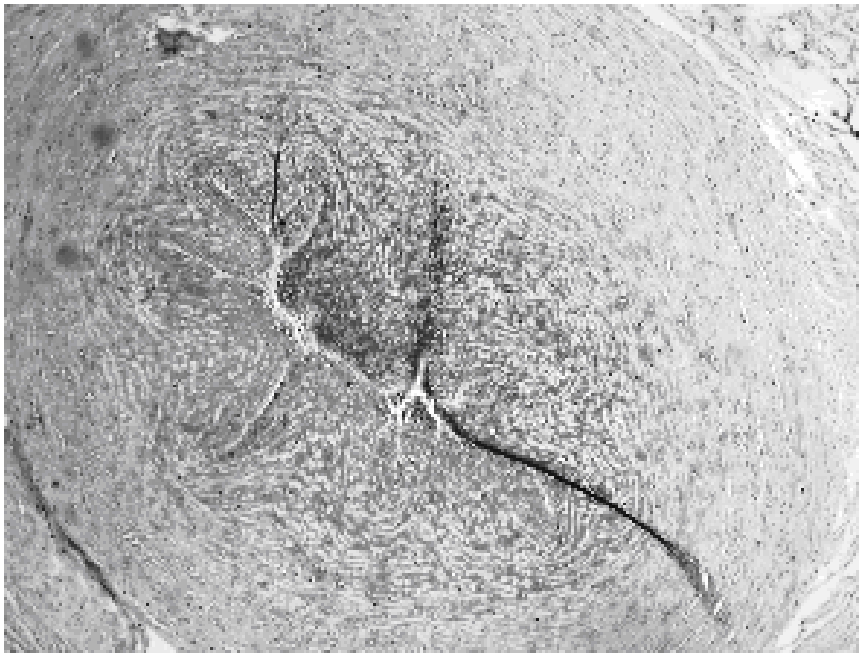

Fig. 1. H.E. X 10, General view of the umbilical cord artery, with significant narrowing lumen and muscular disorders.

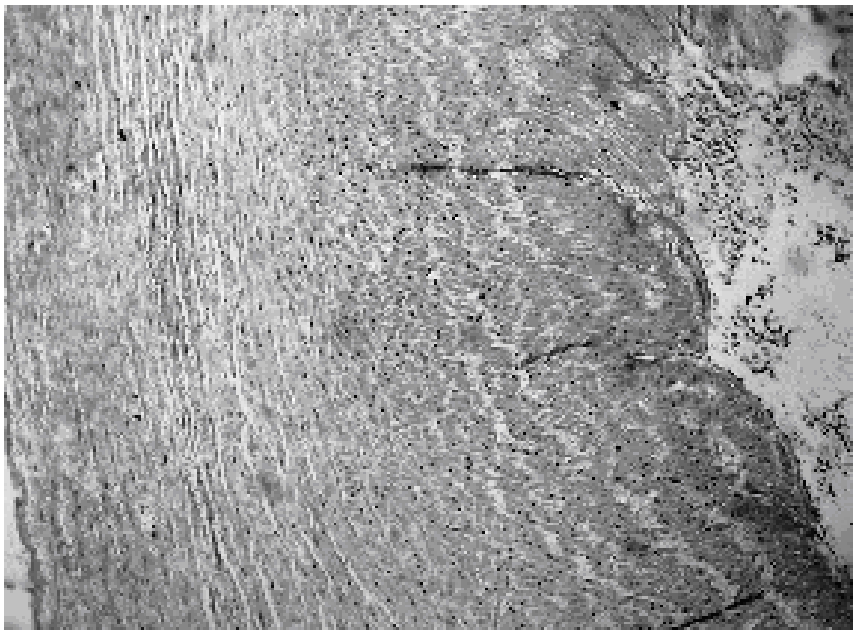

Fig. 2. H.E., x 40, the muscle area disposed in separated layers, due to the increase of the connective tissue and to the edema.

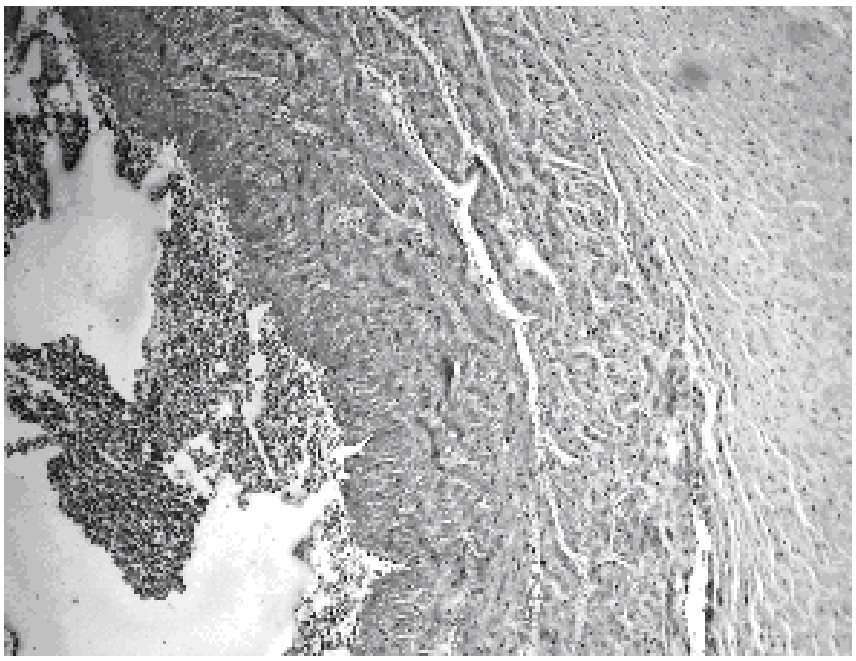

Fig. 3. H.E., x 100, detail of the umbilical vein, with smooth muscle cells contracted and separated from each other; endothelium, subendothelium and some muscle layers have join completely.

Fig. 4. H.E., x 40, umbilical vein lumen narrowed, with separations between the muscle cells and layers; muscle cells contracted with a waved like aspect of the nucleus; muscle area separated from the connective tissue.

It is recognized the fact that the key-factor, which contributes to the growth and development of the vascular tree on the axis: placenta → umbilical cord → foetus, is the progressive growth of the blood stream .In PIH cases, a placental vascular disorder is initially produced, which is accompanied by the growth of the placental resistance and the reduction of the umbilical blood stream, with a fetal hypo-perfusion. The maintenance of these hemodynamic conditions leads to the stabilization of the vascular and umbilical cord structural pathological modifications and to their constant association and extension, while they are following the above mentioned vascular vector.[5]

The following significant morphological modifications were registered in the cases with PIH (table 2):

- the significant diameter reduction of the umbilical cord and its vessels;the most important reduction was registered for the diameter of the umbilical cord and it was realized due to the Wharton's jelly reduction;[6]
- there is a reduction of the smooth muscular fibers and fascicles number in the media of the umbilical arteries;[7] under the arterial epithelium, among the muscular layers extended acellular spaces occur, probably due to the interstitial edema; the contraction of the

muscular cells cause a "wave"-like shaped orientation of the nuclei ;

- the muscular area, separated by a conjunctive tissue tends to become narrower and thus, contributing to the diameter reduction of the lumen, more noticeable in arteries;

- the smooth muscular cells seem to be diminished or hypoplastic; in many areas, these seem to be discontinuous;[8]

- the thickening of the vascular endothelium and the significant reduction of the vascular caliber, both for arteries and for the umbilical cord; because the vascular endothelium is the first layer which undergoes to the hemodynamic modifications, it is possible that the reaction to be produced precociously, even at the beginning of thePIH;[9]

- the numerical reduction and the structural disorder of the collagen and elastic fibers are more noticeable in the umbilical vein where, under normal conditions, they are better represented.

The above mentioned morphological modifications are suggestive for a predominantly hypoplastic mechanism at a vascular level. The first reaction to hypoxemia is the vasoconstriction. If the hypoxemia continues, it shall produce in time the above mentioned hypoplastic modifications, with immediate and late hemodynamic consequences. The morphological modifications of the umbilical vein wall and its caliber directly influence the fetal blood stream, which has an impact upon the fetal vascular system; the modifications of the fetal vascular system may represent a main factor, for vascular affections of the future adult.[10]

Conclusions

The morphological modifications of the umbilical cord in the PIH represent a marker of some important postnatal and fetal hemodynamic deficiencies.

The hemodynamic status of the foetus and of the new-born baby with mothers suffering from PIH are characterized by hypoxia/ischemia with an immediate and late impact upon their cerebral development.

A good quantification of the morphological modifications of the umbilical cord in PIH provides an informational support to the practitioner concerning the baby's neurological future.

A systematically prenatal monitoring of the hemodynamic of the feto-placental circulation (including Doppler) may reduce the incidence of the severe forms of the intrauterine development and growth in the new-born babies with mothers suffering of PIH.

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