Anatomic markers for the retrospective and prospective evaluation of pathology involving the feto-placental and utero-placental circulatory systems inside human placenta.

Forensic implications

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Abstract: Authors studied a large number of human placenta (750) and they identified and nominalized four anatomic markers as morphologic and functional indicators for the structures inside the utero-placental and feto-placental circulatory systems: umbilical cord, subchorial veins thrombosis for the feto-placental circulatory system, perivillous fibrin deposition and retroplacental hematoma for utero-placental circulatory system. These markers contribute to the knowledge of the mechanisms for intrauterine asphyxiation, fetal death and intrauterine fetal growth restriction.

Key Words: placenta, umbilical cord, fibrin deposit, retroplacental hematoma

The evaluation of the disturbances involving the feto-placental and the utero-placental circulatory systems is possible by the knowledge of some anatomic markers as determining factors for the time and space genesis of the pathologic processes implicated in the death of the fetus or newborn.

Our paper proposes to ensure arguments for the necessity of rigorous examination of placenta that can provide morphologic information, both retrospective on fetus before birth as well as prospective on newborn after birth.

Anatomic analysis of placenta should be a part of the autopsy in cases of fetus or newborn death, as it helps clarify some difficult situations such as: legal controversies regarding acute or chronic diseases; the specific etiologic diagnosis in pathologic pregnancies; the localization of zygote in twin pregnancies; pregnancy management and last but not least, the newborn risk evaluation.

The anatomic study of placenta lesions and consequently the nominalization of markers are useless when we employ classifications based exclusively on macroscopic characteristics and we leave behind the main principles of pathology and the systemic terminology (Fox and Sebire, 2007) [10].

Nowadays, the old terminology dominates the literature of obstetric pathology; thus the nominalization of lesions by its pathogenesis is imposed. Fox and Sebire (2007) [10] proposes the classification of placenta lesions into four groups: 1. lesions determined by alterations in the fetal blood flow to or through placenta; 2. lesions determined by changes in maternal blood flow; 3. hematoma or thrombosis; 4. non vascular lesions.

Based on our experience gathered in the analysis of placenta structures, we intend to name and discuss anatomic markers that belong to the two circulatory systems – umbilical chord and

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thrombosis of subchorial vessels for the feto-placental circulatory system on one side, and fibrin and retroplacental hematoma for the utero-placental circulatory system, on the other side.

**Materials and methods**

The nominalization and the evaluation of anatomic markers in the female procreation system was achieved on 750 human placenta (605 after normal birth, 140 after C section, 5 after hysterectomy) registered in the Pathology Department of City Clinical Hospital from Craiova during 2003-2010.

The pieces were fixed in formaldehyde 7% solution at a ph of 7.3. The study of the placenta markers was accomplished based on their belonging to two circulatory systems: fetus placenta and uterus placenta. Tissue fragments adjacent to those circulatory systems were harvested and processed after classic micro anatomic methods of dehydration and paraffin embedding. The sections 5 mm thick were stained with Hematoxiline eosine, van Gieson and Gomori.

**Results**

The knowledge of placenta anatomic markers and its implication in the pathomorphogenesis of lesions involving feto-placental circulatory systems is needed for the evaluation of the maternal and/or fetal blood flow that can be altered during gestation.

We selected the umbilical chord and the thrombosis of subchorial blood vessels as fundamental anatomic markers for the feto-placental circulatory system and fibrin and retroplacental hematoma for the utero-placental circulatory system; these markers are implemented in orthogenesis and/or pathomorphogenesis of placenta structures.

**A. Analysis of markers characteristic of the feto-placental circulatory system**

1. **Phenotype analysis of the umbilical chord as an anatomic marker**

   The umbilical chord that bound placenta to fetus is an anatomic marker due to its trajectory in relation to the fetus body, the variability of its placental insertion and the umbilical arterial vessels coiling index.

   a. **Analysis of the relations between umbilical chord and fetus body**

   Two space relations of the umbilical chord brought our attention: the relation to the nuchal region and to the inferior limb (Fig. 1). We identified the nuchal chord equally at twin or single pregnancies.

   In case of monochorionic monoamniotic twin pregnancy only one fetus had a nuchal chord. The twist of the nuchal chord had one or two loops (Fig. 1 A, B; Fig. 1 E-H). The umbilical arterial vessels inside the umbilical chord go in large spirals around the umbilical vein. After removing the umbilical chord we noticed a true “strangulation groove” (Fig. 1 H). Analyzing Fig. 1 D, we noticed the umbilical chord twisted around the right thigh and leg.

   b. **The analysis of the umbilical chord insertion on the chorial plate**

   We described four locations for the insertion of umbilical chord: interpositional (Fig. 2 A), velamentous (Fig. 2 B), marginal (Fig. 2 C, E – G ) and central in triplets placenta (Fig. 2 H).

   c. **Phenotype analysis of the umbilical arterial vessels twisting inside umbilical chord**

   Analyzing the studied cases, we noted a great variability of twisting of the umbilical arterial vessels around umbilical vein inside umbilical chord. The trajectory of umbilical arteries follow a helical curve in logarithmic direction (Fig. 3 A, D, G, H, I).

   We identified three spiral types: high, medium and absent. In cases with high spiral index (Fig. 3 A, G) we described prominent parts separated by deep grooves. This aspect is diminished in cases with low spiral index (Fig.. 3 D, H). We encountered frequent cases where the spirals were absent (Fig 3 A left, Fig. 3 J).

2. **Analysis of location and relations of subchorial veins thrombosis**

   Subchorial veins thrombosis is well visible at macroscopic examination of the fetus side of placenta (Fig. 2) and of the sections through placenta (Fig. 4). Subchorial venous blood vessels have contiguity relations to basal plate. The lumen of those vessels is occupied blood cloths adherent to the vascular wall (Fig. 4 A-D). Analyzing the micro anatomic serried sections one can easily observe thrombosis of the subchorial veins (Fig. 4 E, F). Equally, we noted small arterial vessels with a partially obliterated lumen in villous trunks (Fig. 4 G, H).
Figure 1. Topographic relations of the umbilical cord to fetus. A, B: Nuchal cord at dizygotic twins - separate diamnionic – dichorionic placentation. C-D: Cord entanglement around thigh and leg – single fetus pregnancy. E-H: Nuchal cord – single fetus pregnancy. Mark left by the umbilical cord in the nuchal region.

Photographs taken with a Canon Mark II DSLR system – Macro Lens 100 mm, f: 2.8.
Figure 2. Variability of umbilical cord insertion site. **A**: Interpositional; **B**: Velamentous; **C-E**: Marginal in single fetus pregnancy; **F**: Marginal and convergent in twins pregnancy; **G**: Marginal and divergent in twins pregnancy; **H**: Excentric in twins pregnancy.

Photographs taken with a Canon Mark II DSLR system - Macro Lens 100 mm, f: 2.8.
Figure 3. Phenotype transformations inside the umbilical cord. A, D, E, G, J: Variability of the spiral index achieved by the umbilical arteries around the umbilical vein. B: True knot, C; E; F: False knot.

Photographs taken with a Canon Mark II DSLR system - Macro Lens 100 mm, f: 2.8.
Figure 4. Subchorial veins thrombosis. A-D: Blood clots adherent to the vascular walls are easily seen on macroscopic examination; E, F: Subchorial space contains numerous veins, transversely sectioned, presenting blood clot inside its lumen; G, H: Villous trunks with small arteries presenting partial thrombosis. Photographs taken with a Canon Mark II DSLR system - Macro Lens 100 mm, f: 2.8 (A-D); Paraffin section. Hematoxilin Eosine stain, x28 (E), x70 (G), x140 (F), x280 (H).
B. Analysis of markers characteristic of the utero-placental circulatory system

1. Analysis of perivillous fibrin stereo distribution

The establishment of the location and extension of fibrin distribution was achieved by means of three terms: perivillous fibrin deposition for the diffuse distribution; subchorionic fibrin plaque for the compact distribution as plates; massive perivillous fibrin infiltration in case a deposition that occupies more that 30% of parenchyma.

a. Diffuse perivillous fibrin deposition

Analyzing the cases diagnosed as “perivillous fibrin deposition” we observed that the perivillous fibrin deposits appear as small grains when macroscopically examined on placenta serried sections (Fig. 5 A-C). Gathering the macro and micro anatomic information we concluded that fibrin is deposited around terminal villi (Fig. 5 F-H).

b. Plaque-like compact distribution of fibrin deposits

The variability of the space distribution of fibrin deposits as compact plaques was pointed on the series section through embryo disc (Fig. 6). By analyzing the surface of those sections one can easily see fibrin plaques at the level of chorionic lamina in close relations to the subchorionic blood vessels (Fig. 6 A, B), at the level of placenta circumference (Fig. 6 C, E-H), at the level of basal lamina (Fig. 6 F) as well as inside placental parenchyma (Fig. 6 D, E). Frequently we observed the coexistence of those fibrin plaques with subchorial umbilical blood vessels thrombosis (Fig. 6 G) and with hemorrhagic spots very well circumscribed (Fig. 6 H).

c. Massive distribution of fibrin deposits inside placental parenchyma

At the examination of the mother side of placenta in cases of fetus death in uterus we emphasized the excessive presence of fibrin deposits at the level of basal lamina (Fig. 7).

That deposition takes an encephalic aspect on the mother side of placenta (Fig. 7 C) and diminishes the spaces between villi. We equally observed the fibrin deposits expansion toward the chorionic plaque (Fig. 7 D). Micro anatomic analysis of the serried sections allowed the visualization of massive perivillous fibrin deposition and a narrowing of the spaces between placental villi (Fig. 7 E, F).

2. Retroplacental hematoma

The analysis of the hysterectomy piece allowed us to perform serried sections revealing the location and color of the retroplacental hematoma (Fig. 8).

At the external opening of dilated uterine canal one can easily notice the hanging of the umbilical cord together with the placenta border and a red blood cloth (Fig. 8 A-C). After sectioning the anterior uterus wall the fetus side of placenta became visible (Fig. 8 D, E) together with a massive blood cloth situated lateral (Fig. 8 F). The decollation of placenta borders and its union to the median plane of the hysterectomy piece permitted us to observe a giant retroplacental hematoma (Fig. 8 H). The mother side of placenta is covered with small blood cloths (Fig. 8 J).

Discussions

A. Considerations on the markers characteristics for the feto-placental circulatory system

Four markers are necessary and sufficient for the evaluation of the alterations inside the feto-placental (umbilical cord and subchorial veins thrombosis) and utero-placental (perivillous fibrin and retroplacental hematoma) circulatory systems.

The umbilical cord offers evaluation criteria for the feto-placental circulatory system such as: form – length, width, color and spiral index; trajectory inside the amniotic sac; relations to the fetus; its insertion on the fetus side of placenta. The length of the umbilical cord that varies between 60-70 cm in full term pregnancy is frequently associated with its tangling around the fetus raising the risk for blood flow obstruction, asphyxiation and the coloring of amniotic fluid due to meconium (Sarwono et al, 1991) [28]. The umbilical arteries spiral index around the umbilical cord offers information about its association with other pathologic conditions.

In case of hypocoiling there have been reported associations to: fetus death in uterus; low Apgar score and congenital fetus anomalies such as trisomy. Hypercoiling have been accompanied by: intrauterine growth restriction, fetus acidosis and asphyxiation (De Laat et al, 2005) [4]. The umbilical cord is a helical vascular structure made of three blood vessels – two umbilical arteries and an umbilical vein surrounded by Wharton gelatin. This spiral structure is visible after the 28th day of gestation.
Figure 5. Perivillous fibrin deposition. A-C: Perivillous diffuse distribution of fibrin deposits; D-H: Intervillous spaces are diminished by perivillous fibrin deposition.

Photographs taken with a Canon Mark II DSLR system - Macro Lens 100 mm, f: 2.8 (A-C). Paraffin section. Hematoxiline Eosine stain, x28 (D, E), x70 (F), x140 (G), x280 (H).
Figure 6. Variable distribution of fibrin as plates and conglomerates. A, B: Subchorial plate; C, E-H: Circumferential plate; F: Plate in lamina basalis; D, E: Fibrin conglomerates inside placental parenchyma.
Photographs taken with a Canon Mark II DSLR system - Macro Lens 100 mm, f: 2,8 (A-H).
Figure 7. Massive basal fibrin deposition (“Maternal floor infarction”).  
D: Massive fibrin deposits inside placental parenchyma;  
E: Intervals between placental villosities are diminished;  
F: Fibrin deposits around placental villosities and villous trunks.

Photographs taken with a Canon Mark II DSLR system - Macro Lens 100 mm, f: 2.8 (A-C). Paraffin section. Hematoxiline Eosine stain x120 (E, F).
Figure 8. Giant retroplacental hematoma. A-H: Layer by layer dissection of the hysterectomy probe for the visualization of retroplacental hematoma; I: Fetus side of placenta with proeminent vascular pattern; J: Mother side of placenta presents blood clots.

Photographs taken with a Canon Mark II DSLR system - Macro Lens 100 mm, f: 2,8.
Nakai et al (1997) [20] observed that the pulse model blood flow inside the umbilical vein is correlated to a high spiral index of the umbilical cord in two cases of growth restricted fetuses. Nishio et al (1999) [23] noted that mean resistance index for the umbilical arteries is low in cases of growth restricted fetuses and is associated to a hypercoiling of the umbilical cord. De Laat et al (2005) [4] considered that hypercoiling could be associated to the pulse model of the venous blood flow and correlated to a severe disturbance in fetus placenta circulation.

The direct correlation between the umbilical cord hypercoiling and the increase in blood flow can be interpreted as a piston effect or a pulsometer. The pulsations of the venous and arterial pressures take place in different directions and in this manner the arterial pulsations can serve as a pulsorter to sustain the venous blood flow (Reynold, 1952, 1978) [25,26]. The presence of the spiral arterial umbilical vessels in the perspective of human species evolution should be considered a progress for the optimization of blood flow.

Nevertheless, spiral extremes such as hypo or hyper coiling are associated to unfavorable events around parturition. The spirals of the arterial umbilical vessels around the umbilical vein regulate the blood pressure – the greater the number of spirals, the more intense the effect. Degani et al (1995) [3] remarked the existence of a linear relation between the spiral index and the venous flow. The first description of the helical trajectory of the umbilical vessels was made by Berengarius (1521) [7].

The interest for the spiral umbilical vessels was raised once with the introduction of modern techniques such as noninvasive ultrasound. Yun Sung et al (2011) [11] brought the attention on the role played by the umbilical cord as a protector against forces outside from the fetus placenta system: tension, pressure, torsion or twisting. The origin of the twisted umbilical blood vessels is unknown: fetus movement, embryo active or passive motion (Edmonds, 1954) [7], the different growth rate of the umbilical blood vessels (Lacro, 1987)[13], fetus hemodynamic forces (Malpas, 1966) [16] and the stero distribution of the muscle cells fascicles inside the umbilical arteries (Malpas, 1966; Roach, 1976) [16, 27].

An important topographic relation of the umbilical cord is with the fetus nuchal region after entangling around the neck. Nuchal cord by simple entangling was reported 8-30% cases, by double entangling in 10.6% cases, by triple entangling in 2.5% cases and by quadruple entangling in 0.5% cases (Shui et al, 1957) [29]. It is considered that the prevalence of nuchal cord raises with the gestational age 5.8% at 28 weeks and 29% at 42 weeks (Larson et al, 1997) [15]. This increase can be determined either by increase of fetus motor activity or by variations in the volume of amniotic fluid. The etiology of nuchal cord is controversy and unclear. Strong et al (1996) [30] proved that in fetuses with nuchal cord there is a low spiral index of the arterial blood vessels, or even the vessels have no spirals (65% of cases). It has been noted that nuchal cord was associated with a long umbilical cord, the presence of meconium inside amniotic fluid, cardiac malformations and low Apgar score. Larson (1995) [14] said that those associations do not increase the risk of abortion. Nelson and Grether (1999) [22] evaluated the association of nuchal cord to cerebral palsy as a primary pathogenic event due to oxygen deprivation. Nelson and Grether (1998) [21] concluded that in case of asphyxiation, the potential of association to spastic quadriplegia is considerable but not to hemiplegia. Clapp et al (1999) [2] consider that nuchal cord at birth is significantly associated to subclinical manifestations in mental and psychomotor performance at 1 year.

The marginal and vellamentous insertions of the umbilical cord on the fetus side of placenta were associated to two types of complications: 1. Risk for the rupture of previa vessels when the vellamentous vessels cross the cervical canal; 2. Thrombosis with a decrease in blood flow and a low weight at birth. Vellamentous insertion is more frequent in twin pregnancies and is accompanied by many fetus malformations.

B. Prospective and retrospective value of markers characteristic to utero-placental circulatory system

Two anatomic markers are useful in the evaluation of the disturbances in utero-placental circulatory system: perivillous fibrin distribution and retroplacental hematoma.

1. Considerations on the perivillous fibrin distribution

Terminology used to characterize the perivillous fibrin deposition is variable. It is considered that it exists in almost all placentas at full term, as small amounts deposited around villi.
If the fibrin deposit does not exceed 30% of the placental parenchyma but it is sufficiently extended to be macroscopically visible as fibrin plaques, then we use the term perivillous fibrin deposition (Fox, 1967) [9]. Some authors prefer the term fibrinoid and use perivillous fibrinoid deposition (Benirschke and Kaufman, 1995) [1].

Nevertheless, Fox and Sebire (2007) [0] prefers the term fibrin for the amorphous, eosinophilic perivillous material that derives probably from the mother blood present in the spaces between villi. He uses the term fibrinoid for the intravillous depositions of eosinophilic material. Recently, immune histochemistry studies recommended the employment of two new terms: fibrin-type fibrinoid for the classic perivillous fibrin deposits and matrix-type fibrinoid for the intravillous deposits. Fox and Sebire (2007) [10] who is a prominent researcher in the pathology of reproduction at Manchester University remarked that although there is scientific motivation for the introduction of those two new terms, they are not used by pathologists that still continue to appeal to terms as fibrin and fibrinoid even if the sense is slightly incoherent.

Philine (1986) [24] employs the term villous ischemic necrosis with fibrin deposits for the cases with white, heterogeneous spots, diffuse limited inside the normal placenta tissue. They are visible since the 38th week and are frequent in the marginal, subchorial regions and inside placenta interlobular septa. We consider that this French terminology has the same semantic charge as the English one – perivillous fibrin deposition promoted by Fox (1966) [8].

When the fibrin deposit exceeds 30% of the parenchyma one can use the term massive perivillous fibrin deposition. Fox and Sebire (2007) [10] considers this term and the one stated by Benirschke and Kaufman (1995) [1] maternal floor infarction as parts of the same pathophysiologic process. In massive perivillous fibrin deposition fibrin is distributed diffusely and in maternal floor infarction, fibrin is mainly present at the base of the mother side of placenta.

The pathogeny for this entity is unknown especially for the excessive fibrin deposition around chorial villi. It is well known the high incidence for fetal death and intrauterine growth restriction (Naeye, 1980; Mandsager, 1994) [19, 17].

2. The significance of retroplacental hematoma

Retroplacental hematoma is present in 4-5% of births (Wilkin, 1965; Fox, 1966) [31,8]. The incidence is raised in women with preeclampsia, disseminated intravascular coagulation, uterine apoplexy, uterine necrosis, cocaine usage and cigarette smoking. The pathogenesis of placental bleeding is far from being clarified. It is considered that this bleeding is determined by the rupture of decidua arteries and is the foundation of fetus sufferance, low Apgar score and death around birth.

Conclusions

1. Anatomic markers of the female procreation system are morphologic and functional indicators for the fetus placenta and uterus placenta circulatory systems.
2. Umbilical cord, subchorial veins thrombosis, perivillous fibrin deposition and retroplacental hematoma are “memory cards” for the female procreation system.
3. The phenotype changes of those anatomic markers become evaluation criteria for the fetus placenta and uterus placenta circulatory systems.
4. The nominalization of the perivillous fibrin deposition is important for the evaluation of the uterus placenta circulatory system and for the knowledge of the causes for high incidence of fetal death and intrauterine growth restriction.

References