Anatomical and histological considerations of placenta vascular diseases with implications in forensic medicine

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Abstract
Placenta, as a highly specialized organ in connecting the maternal and fetal organism, is frequently affected by a specific vascular pathology. The correlation between the macroscopic and the microscopic aspects of the fetal placenta vascularization together with the appearance of fibrin deposits is used to determine the pathological cause of death. Different studies suggest the hypothesis of precocious development of fibrin deposits during pregnancy, due to some immune-like reactions or due to the circulatory variations in the villous territory. The present research was realized on 467 placentas – out of 467 placentas collected in the past 10 years, 287 were from term births, 98 from premature births and 82 from abortions. The fibrin deposits in the placenta resulting from abortion can also be interpreted as alterations caused by the same circulatory variable conditions. In the therapeutic abortion, the placental fragments do not contain fibrin deposits. The correct approach of the macroscopic exam in the vascular pathology, accompanied by the recognition of the microscopic changes in the placenta, contributes to determine the cause of abortion, the premature birth or the term birth, followed by the death of the fetus and/or the mother. The study assesses the macroscopic and microscopic aspects of the vascular pathology at the placental level in cases with medical and legal implications. Our study also reported these placental aspects in aborted fetuses or in cases of intrauterine deaths, for various reasons considered forensic cases.

Keywords: fetal placenta, fibrin deposit, abortion, premature birth, vascular pathology.

Introduction
The interrelations between macroscopic and microscopic placental vasculature and the appearance of fibrin deposits represent two significant factors, which can sustain or suggest the presence of a distinctive placental vascular pathology that may cause spontaneous abortion, premature births, maternal or fetal deaths, in relation to social and environmental conditions.

The fetal blood vessels, two umbilical arteries (allantois arteries initially) and the umbilical vein, situated in the umbilical cord, may vary in size or number. Over time, many researchers have studied the Hyrtl arterial anastomosis. They were interested in anatomical variants and the direct physiological implications for the placenta as well as the indirect implications for the fetus.

Four characteristic signs of mature placenta have been described:
• the decreasing villous diameter;
• the villous capillary diameter takes the aspect of large, well-developed sinusoidal vessels, which are situated at the periphery of chorionic villous;
• the development of the syncytial capillary membrane;
• fibrin degeneration of villous, fibrosis and thrombosis.

From a forensic perspective, the macroscopic and microscopic exam of the vascular pathological changes occurring in the placenta during pregnancy may be useful to determine the cause of abortion, premature birth, maternal or fetal death. These vascular alterations that occur in the placenta can be used to emphasize the pathological thanatogenesis, especially in case of the violent abortions or newborn abandon cases [1]. Recent studies focus on the correlation of clinical data and laboratory investigations obtained during pregnancy, with the results obtained after necropsy [2, 3].

Materials and Methods
The study was conducted over a 10-year period (2003–2012) in the Laboratory of Pathological Anatomy of Timișoara Forensic Institute, Romania. The present research was realized on 467 placentas – out of 467 placentas collected in the past 10 years, 287 were from term births, 98 from premature births and 82 from abortions. To relieve the sinuous arterial system, we have used the injection of liquid gelatin into the placentas. For microscopic studies, there were collected a total of 150 samples of placenta, 25 samples from spontaneous abortions, 25 samples from abortion on request, 50 samples from premature birth sand 50 samples from term births. All these samples were fixed in 10% formalin. Then, histological samples were processed according to paraffin-embedded technique and Hematoxylin–Eosin (HE) staining. The microscopic exam was performed using an Olympus BX51 optical microscope.

Results
The vascular pathology of the placenta is due to the functional and organic circulatory disorders that may
occur at different stages of pregnancy. Out of the total of 467 placentas macroscopically examined, 279 (60%) placentas did not reveal any vascular pathology, while 188 (40%) placentas revealed evidence of vascular pathological alterations (Figure 1). On the fetal placental surface, the macroscopic exam emphasizes a distinct vascular pathology (intervillous blood stasis, also called hemorrhagic aneurysm, intervillous thrombosis, retro-placental hemorrhage, marginal decidual hemorrhage, and recent placental infarction); on the maternal surface, the infarction areas are also present (Figure 2). We consider that the factors determining placental vascular pathology can frequently intricate, contributing to the complexity of placental disease and its consequences.

Intervillous blood stasis, called hemorrhagic aneurysm, determines the damage of the villous syncytium and epithelial bridges (Figure 3). The ischemia of intervillous space occurs because of the compression exerted by a subchorial hematoma (Figure 4). Intervillous thrombosis of the placenta can be considered pathological when it occurs in the early stages of pregnancy (Figure 5). Deciduous marginal hematoma and the several weeks old hematomas were also observed (Figure 6). Maternal surface infarction of the placenta was observed in a case of an intrauterine death (Figure 7).

The microscopic exam of the samples prelevated from the placentas provides a better understanding of placenta vascular pathology. Intravillous hemorrhages are frequently observed (Figure 8, A and B). Extensive intervillous hemorrhage produces local circulatory disturbances, focal necrosis or premature placenta detachments (Figure 8, C and D). Fibrin degeneration correlated with the low age of pregnancy is considered pathological (Figure 8E and F). Vascular thrombosis is usually present (Figure 8G). Recent placental infarctions are associated with fetal intrauterine death (Figure 8H). Hydropic dystrophy can be associated with placenta alteration (Figure 8I). All these degenerative changes are limiting the lifetime of the placenta.

**Discussion**

Macroscopic aspects are characteristic for the placental vascular pathological intricate. Intervillous blood stasis called hemorrhagic aneurysm occurs due to disturbances in circulation because of maternal blood overload or deposit. This may be the cause for placental infarction or placental hematomas, as in the extended pregnancy illness, eclampsia, toxic conditions and toxic infection conditions, drug intoxications. These causes determine different types of damages of the villous syncytium and epithelial bridges [4, 5]. Intervillous hemorrhagic aneurysm called subchorionic hematoma appears as a red or purple hematoma that protrudes under the amniotic membrane. Ischemia of intervillous space occurs because of the compression exerted by a subchorial hematoma [6].

Figure 6 – (A and B) Marginal hematoma. Fetal surface: 1. Fixed blood clot; 2. Old hematoma. Maternal surface: 3. Area with ischemia; 4. Recent hematoma.

Figure 7 – Infarction of the maternal surface of placenta. 1. Recent hemorrhagic infarction; 2. Old cicatrical infarction; 3. Hemorrhagic areas.

Figure 8 – (A) Intervillous hemorrhages; (B) Diffuse perivillous hemorrhages; (C) Intravillous stasis; (D) Dispersed intravillous stasis; (E) Compact fibrin deposit; (F) Large fibrin deposits around intervillositary spaces. HE staining, ×200.
Intervillous thrombosis occurs frequently in case of the maternal isoimmunization or in fetal erythroblastosis [7, 8]. By studying the four well known entities in literature: the subchorial fibrin plaque, the central intervillous thrombosis, the basal intervillous thrombosis and the marginal intervillous thrombosis, and we can pinpoint their distribution and frequency. The subchorial plate of fibrin is presented as a pink or whitish deposit centrally located in the placenta, visible due to the amnios transparency. The marginal intervillous thrombosis occurs because of the extension of the fibrin deposit from the centre to the periphery, due to prolonged stasis in this area.

Retroplacental hemorrhage leads to a premature detachment of normally inserted placenta (1.5–2%), specific to multiparous women, and women younger as 16 years or over 30-year-old, with a history of chronic disease like nephropathies, hypertension, and diabetes, accidental or obstetrical traumatisms. The retroplacental hematomas can infiltrate the entire myometrium and in severe cases spread to the Fallopian tubes, ovaries, and large ligaments, causing the woman’s death. Deciduous marginal hematoma could cause hemorrhage at the end of pregnancy or during labor. It appears in the marginal area of the placenta as a fixed blood clot, dark red or purple, adhering to placental membranes and tissue [9]. The several weeks old hematomas, visible on the fetal surface of the placenta are yellow-white and they do not get to infiltrate the basal plaque. Intraplacental hematoma occurs because of the umbilical vein alteration [10]. The resulted hematoma is voluminous and it is bulging the fetal surface of the placenta, sometimes becoming pedunculated in the amnios. Small hematomas are generated by ruptures of small veins and the more numerous the ruptures, the higher the incidence of abortions or premature deliveries. They occur in vascular, toxic and degenerative lesions, in infections (syphilis) and are less common in traumatic events [11, 12].

Recent placental infarctions of the fetal surface occur frequently in chronic diseases associated with nephropathies, hypertension and diabetes. On fresh samples, the recent infarct appears as clear pink outbreaks with precise edges. Chronic infarction has a yellowish-brown color, firm consistence, regular contour attached to the basal plate. At times, old pale areas alternating with fresh dark red areas appear. Central portion may be thrombotic or hemorrhagic. Maternal surface infarction of the placenta causes the thickening of the same surface of placenta and often leads to intrauterine fetal death or premature births [13, 14]. It is white-grayish, pale, with a smooth surface, often associated with diffuse subchorial thrombosis or subchorial cytotrophoblastic cysts.

Under physiological conditions, the microscopic study reveals small inter villous spaces, histological and functionally stable. Increasing intervillous dimensions on the histological samples is the result of the breaking intervillous bridges and of the retraction of the villous produced during tissue processing (the fixative and the paraffin embedding). The fibrin degenerative lesions, focal of recent infarction alternating with focal of old infarction, vascular thrombosis, interstitial hemorrhages with hemosiderin deposits in villous chorion and villous atrophy are found on the placental samples obtained from spontaneous abortions or premature births. Some microscopic aspects can be considered pathological or normal depending on the age of pregnancy. The fibrin degeneration appears on the syncytial layer of the chorionic plate, of the placental villous and septa, extending on the surface, as the pregnancy progresses. If initially it represents the degradation product of the syncytial implantation, in time it spreads to the peripheral regions of chorionic villous [15, 16]. The fibrin has no blood coagulation properties, slowing down the blood flow; fibrin deposits have no leukocyte content. The degenerative trophoblastic processes are correlated with the physiological or pathological aging of the placenta that would become more and more insufficient to feed the fetus, causing its detachment, followed by the expulsion of the fetus.

Recent placental infarctions are characterized by intervillous fibrin deposition, intravillous capillaries filled with red blood cells, syncytial cells with karyopyknotosis, karyorhexis and tinctorial changes resulting in increased eosinophilia, focal areas of necrosis and thrombosis in the chorionic plate [17, 18].

The interstitial hemorrhages with intravillous hemosiderin deposits appear in venous occlusions as congestive focal zones, with blood vessels filled with red cells alternating with avascular pale focal areas, and sometimes with minimal inflammatory reaction. Intravillous hydropic dystrophy can also be observed [19–21]. The villous ischemic necrosis of fetal origin appears because of premature thickening of the vascular wall that causes the...
decrease of the vascular lumen (arterioles, capillaries), the trophoblastic degeneration and the appearance of fibrin deposits [22–26]. It is often associated with chronic diseases of the pregnant woman.

**Conclusions**

Our study sustains the existence of distinct placental aspects in aborted fetsuses or in cases of intrauterine deaths, for various reasons considered forensic cases. The vascular pathology of placentas must be taken into account in the forensic thanatogenesis. Correlating medical information (acute or chronic affections) from the pregnant woman with pathologic exam and necroptic data, when needed, are important to specify the pathological thanatogenesis of abortions, premature births, term births, fetal or/mother deaths.

**References**

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