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Placental abruption: etiopathogenic aspects, diagnostic and therapeutic implications

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Abstract

The severe form of retroplacental hematoma is a serious accident in the second stage of pregnancy and at birth with frightening for the mother and fetus that often lead to death. The pathological mechanism presumes conditions for a "special ground" capital for the "efficiency" of the acute intradecidual vascular accident with the rupture of the uterus–placental arterioles. The complete clinical picture of this severe form of retroplacental hematoma – the placental abruption, observed and mentioned by the classics (vascular drama of Couvelaire) consists of five syndromes, 18 signs and symptoms, four paradoxes, phenomena not fully met in the other forms of retroplacental hematoma (minor and intermediate). The rate of incidence of retroplacental hematoma is in between 0.13–1.38% and depends on the environment, on the socio-economic and medical conditions, on the "obstetric education" and associated pathology. Our study aims at re-evaluating the clinico-paraclinical phenomenon imposed by the dramatism of the phenomenon of *in utero* placental apoplexy, the impact on neonatal mortality and on the functional prognosis from the point of view of surgical climax.

Keywords: placental abruption, intravascular coagulation, fibrinolysis, hysterectomy, fetal mortality.

Introduction

The placenta is a temporary, unique organ, with a complex cellular and molecular composition, which ensures the mutual coexistence of the maternal and fetal organisms, being essential for the fetus development and growth [1–3]. It allows the passing of gases, nutrients and hormones, from mother to fetus, during the entire period of intra-uterine development. The placenta adapts to the maternal environment, through the permanent change of its structures and functions, thus contributing to maintaining the rhythm of fetal development [4, 5].

Placental abruption represents the early separation of the placenta from the uterus wall before finalizing the second stage of labor. Placental abruption occurs when there is a compromise of the vascular structures supporting the placenta.

The typical pathological injury is the retroplacental hematoma, which is situated in the basal decidua (basal decidua hematoma) [6–8]. This condition appears because of the acute intradecidual hemorrhage produced by the rupture of the uterus–placental spiral arterioles. In placental abruption, which is the severe form of retroplacental hematoma also known as "Couvelaire's vascular drama", the rupture of the spiral arterioles between the compact and the spongious of the basal caducei concerns at least 1/3 of the arterial vascular system in the uterus and placenta. The intensity of the hemorrhage determines the detachment of 30% or more of the placental basal plaque, retroplacental hematoma being more than 150 mL. This physiological mechanism occurs usually in natural birth, after the fetus expulsion. In a pathological manner, it occurs in placental abruption on a "particular field", while the fetus is still in the uterus.

In placental abruption, the mortality of the fetus is 100%, and the maternal mortality can reach up to 5% [9–11]. This hematoma quickly consumes the maternal coagulation factors that can induce fibrinogen deficiency from secondary fibrinolysis to afibrinogenemia. The accident occurs very fast since it is an internal bleeding more or less externalized through the cervical canal. For the diagnosis, the clinic proves its capital importance as well as the interventional decisions. In the obstetrics practice, the intermediate forms of retroplacental hematoma are the most numerous, also known as "trap type", their identification being essential since the fetus could still be alive and it could be saved through an immediate surgical procedure [6].

The absence of diagnosis together with the waiting time, the transportation from a hospital to another means time that is often lost with dramatic consequences, knowing that once the intradecidual hemorrhage began it is irreversible and after an unpredictable period of time, turns from a minor stage to a severe form of placental abruption [12–14].

Having in mind certain etiopathological factors, there

are recent genetic, immunological and biochemical studies which confirm the condition of "particular field" for women with preexistent or induced arterial hypertension by pregnancy that can complicate with retroplacental hematoma. These researches show the presence of a multifactorial polygenic disorder, with vascular implication in gestation, initially in the uterus–placental territory, with direct implication of "vasa vasorum", at the level of the uterus–placental arterioles. These changes appear from the second trimester and even less than 25 weeks of gestation [15, 16]. Using the electron microscope, in order to study the arterioles at the nidation site, profound changes, such as the permanent destruction of the endothelial tissue, followed by the attachment of the plasmatic components to the vascular walls, the myointimal cells proliferation, the macrophage accumulation in the arterioles of the uterus and placenta, phenomena that induce ischemia and then necrosis of the arterial wall, had been observed. This phenomenon was described by Hertig, as early as 1945, and defined as atherosis [5]. The affected vessels may evolve towards aneurysmal dilatations during some future pregnancies [17, 18].

All these changes were correlated to Doppler velocimetric studies in the uterus–placental territory, comparing the normotensive pregnants and those with gestational hypertension. Thus, the ultrasound and the multivessel Doppler study in pregnancy may have predictive value in case of subsequent onset of an acute vascular accident [19–23]. Interesting studies appear on the influence of smoking in triggering placental abruption [24], as well as in the prophylaxis of the fetal death *in utero* by using acetylsalicylic acid in low doses for pregnant women with gestational hypertension [25–27].

Our study aims at re-evaluating the clinico-paraclinical phenomenon imposed by the dramatism of the phenomenon of *in utero* placental apoplexy, the impact on neonatal mortality and on the functional prognosis from the point of view of surgical climax.

Patients, Materials and Methods

The study was conducted over a period of four years (2012–2015). From a total of 5184 births (1291, 1442, 1276, and 1175, respectively), 19 cases of severe retroplacental hematoma were hospitalized and resolved, respectively 0.3% (five cases in 2012, six patients in 2013, four patients in 2014, four cases in 2015). The main analyzed parameters were: the age of the patients – 26–30 years old (two cases), 31–35 years old (12 cases), 36–40 years old (five cases); the gestation – 18 cases had a history of more than five abortions or curettage for abortion; the parity – primiparous (0 cases), secundiparous (three cases), tertiparous (13 cases), four and more than four births (three cases); associated pathology – preexisting gestational hypertension or induced by the pregnancy (19 cases), uterine polyfibromatosis (two cases), cervical uterine cancer (one case).

The positive diagnosis was laid on the clinical trial especially. At the time of admission, the patients presented pale tears and mucous membranes, cold extremities, hypotension, lumbar abdominal pain, permanent uterine contracture, low vaginal bleeding, absent fetal movements, absent fetal heart rhythm.

Undoubtedly, to all the clinical aspects, were added, as an emergency, the blood and urinary laboratory samples and ultrasound investigation. In emergency, blood pressure was recorded, blood was collected for immunohematology tests (blood group, Rh), hematological tests (complete blood count, hematocrit), hemostasis tests (prothrombin time, thrombocytes, fibrinogen, fibrin degradation products), biochemistry tests (urea, creatinine, uric acid, glycemia, alanine aminotransferase, aspartate aminotransferase, serum proteins, serum ionogram). Urine samples for ionography and complete urinalysis were collected.

The ultrasound exam showed placental localization, retroplacental hematoma (the accumulation of blood between the uterine wall and the placenta as a homogeneous area of echogenicity, the clots having a different echogenicity than the placenta), the absence of fetal viability (absent fetal movements, absent fetal heart rhythm).

All patients were urgently operated. Postoperatively, patient evolution was monitored by hematological tests, coagulogram, biochemical tests, urinal tests and neurological, nephrological, cardiologic, ophthalmic specialist consultations.

For the histopathological (HP) study, the surgical pieces were sent to the Laboratory of Pathological Anatomy, Emergency County Hospital of Craiova, Romania, where there were harvested fragments of uterus and placenta that were fixed in 10% formalin and included in paraffin, according to the HP protocol. For the immunohistochemical study, of the harvested material and included in paraffin, there were performed serial sections in the microtome, transferred afterwards on poly-L-lysine slides. There were used the following antibodies: anti-CD34 (monoclonal mouse anti-human CD34 class II, clone QBEnd 10, 1/50 dilution, Dako) for highlighting endothelial cells; anti-CD68 (monoclonal anti-human CD68, clone KP1, 1/100 dilution, Dako) for highlighting macrophages.

Results

All the 19 cases were urgently hospitalized. The diagnosis was made based on the clinical trial, possibly after the ultrasound confirmation in the labor ward. Of the 19 cases, 17 (89.5%) patients were older than 30 years.

Except for one case (cervical cancer), all the other had a history of more than five abortions or curettages for abortion. In light of the parity, tertiparous prevailed (13 cases – 68.5%). Arterial hypertension was found in gestation in all 19 cases and two cases were with uterine polyfibromatosis.

The laboratory investigations on admission showed: hemoglobin (Hb) 6.4–9.8 g/dL, hematocrit (Ht) 22–30.5%, platelets 56 000–92 000/mm^3, Quick time (Qt) 87–98%, International Normalized Ratio (INR) 1–1.4, urea 50–112 mg/dL, creatinine 1.8–4.6 mg/dL, uric acid 6.8–10.7 mg/dL, glucose 80–98 mg/dL, alanine aminotransferase (ALAT) 22–38 U/L, aspartate aminotransferase (ASAT) 36–98 U/L, serum proteins 6.2–6.6 g/dL, Na^+ 136–148 mEq/L, K^+ 3.3–5.1 mEq / 1.8 g/L.

All the patients were admitted and urgently operated. The Caesarean section was followed by the total hysterectomy with (five cases – 26%) or without (14 cases – 74%) bilateral adnexectomy.

In none of the cases subcutaneous hysterectomy was performed. Postoperative paraclinical monitoring was systemic for the evaluation of cardiac, renal, hepatic and hematological functions. In seven cases, increased levels of urea (180–199 mg/dL), creatinine (6.2–6.98 mg/dL), and uric acid (8.4–10.7 mg/dL), polyuria (4500–5500 mL). Evolutionally, kidney parameters have improved, and will be followed in the ambulatory through the nephrology cabinet.

Postoperative arterial pressure values were maintained between 180/110–145/95 mmHg. The cardiology consultation did not reveal significant anatomical and functional changes.

Hepatic function was not altered in the 19 cases, the laboratory tests performed being in normal parameters. The ophthalmologic examination revealed papillary edema and small retinal hemorrhage areas in 12 cases and in a retinal decollation case, but the remaining six cases without significant alterations.

The fetal prognosis was of poor outcome, fetal mortality of 100%. The maternal vital prognosis was good (no mortality), the functional one remains dependent on the consequences of the surgical climax in women aged between 35–40 years old.

There are typical lesions in placental abruption, both fetal and maternal, that are described from the pathological point of view. The anatomical lesions found are variable as location and topographic extension. These are found in the uterus, placenta, fetus and maternal viscera.

Macroscopically, there are echocardiographic areas in the horns of the uterus, associated with hemorrhagic infiltration in the form of red-violet-like to black ecchymoses, sub-peritoneal disposed in the anterior and posterior uterine, broad ligament, sometimes at the vesicouterine peritoneum, at the level of lumbar–ovarian ligaments. The myometrium is edematous, violet, with hemorrhagic infiltrates, often functional. In this regard, it should be noted that there is no direct relationship between the macroscopic aspect of the uterus and its functional condition (Figures 1 and 2). Macroscopically, the dead fetus presents both visceral and vascular lesions in the brain (bleeding, cerebral meninges strokes, in the regions of the great Sylvian artery, of the bulb-protuberances, and of the ventricles) hemorrhagic lesions and infarcts in the liver, kidney, adrenals, lung, myocardium.

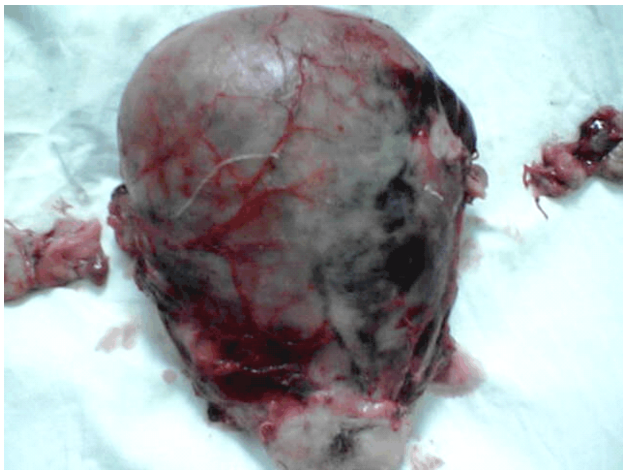

Figure 1 – ***Uterus with apoplectic aspect.***

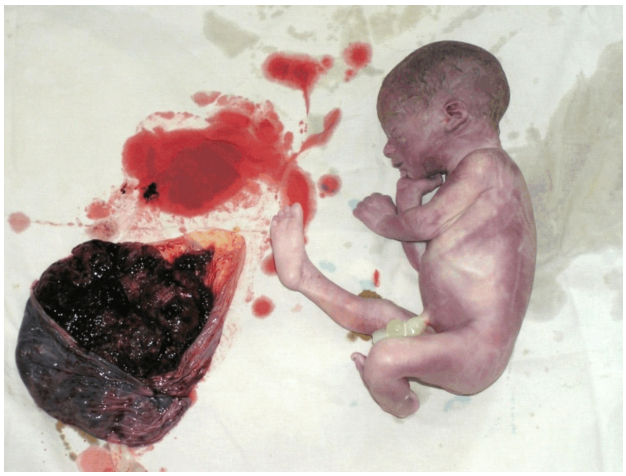

Figure 2 – ***Dead fetus with retroplacentar hematoma.***

Microscopically, the take-off takes place between the compact and spongy layers of the caduca. The collection of agglutinated red blood cells merges in a fibrinous network, prominating in the villositary space, compressing it. It is separated from this space by the state of fibroinoid Nitabuch and compact caduca, both of which form a kind of ceiling of the hematoma. The compacted intravitreal space villi are compressed, packed together with capillary internal vasodilatation. Hematoma is a consequence of uteroplacental arterioles rupture, with the occurrence of acute intradecidual hemorrhage, microscopic characteristic of the apoplectic uterus.

The HP studies performed by us on pieces included in paraffin, harvested from the patients in our group and stained with Hematoxylin–Eosin (HE) or with the Goldner–Szekely (GS) green light trichrome, showed a multitude of microscopic changes, both in the uterus and in the placenta. The myometrium frequently presented phenomena of hydropic degeneration (Figure 3), edema and interstitial fibrosis (Figure 4), microhemorrhages (Figure 5) and intraparenchymatous hematomas, as well (Figure 6). In the placenta, there were identified large areas of infarction (Figure 7), fibrin deposits in the form of stripes or islands that covered the placental villosities (Figure 8), the presence of old thrombi partially remodeled by fibrin deposits (Figure 9), villosities with phenomena of obliterating endarteritis, stromal fibrosis and diffuse calcifications (Figure 10).

Through the immunohistochemical examinations, we wanted to highlight the possible changes of the microvascularization and inflammatory reaction, in the myometrium and placenta. The microscopic examination highlighted that the greatest part of the myometrium presented a vascular network poor in small blood vessels, especially in the areas with hydropic degeneration (Figure 11); still, in the peridecidual areas, the uterine microvascularization was well-developed (Figure 12).

Similar images were also observed in the placenta. Some placental villosities that developed a high fibrosis presented a poor or even absent vascular network (Figure 13), while other villosities presented a network of normal microvessels (Figure 14).

Regarding the inflammatory reaction, both in the uterus and the placenta, there were highlighted few macrophage cells (Figures 15 and 16).

We believe that one of the pathognomonic injuries stand is the rupture of the walls of the uterus–placental arteries. The venous thrombosis and the obliterating endarteritis observed near the retroplacental hematoma, does not represent the cause of the rupture, but its consequence.

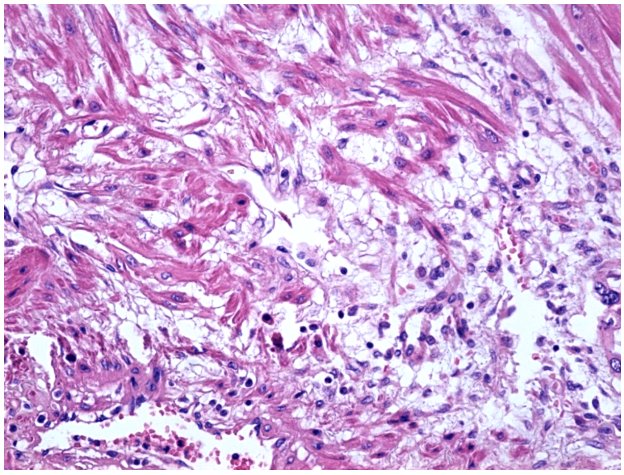

Figure 3 – ***Myometrium with hydropic degeneration (HE staining, ×200).***

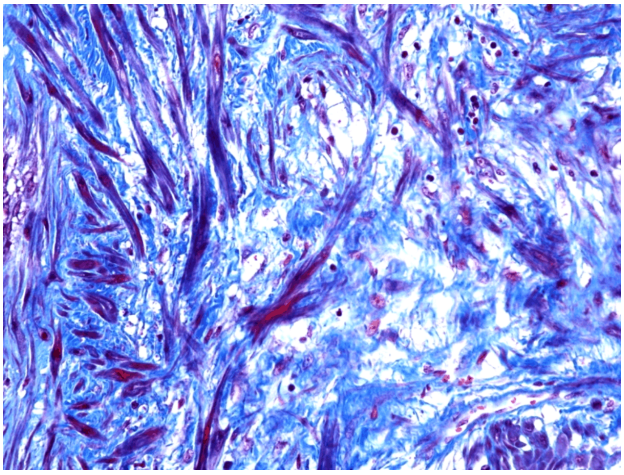

Figure 4 – ***Myometrium with disorganized muscular fibers by the presence of interstitial edema associated with processes of collagen fibrosis (GS trichrome staining, ×200).***

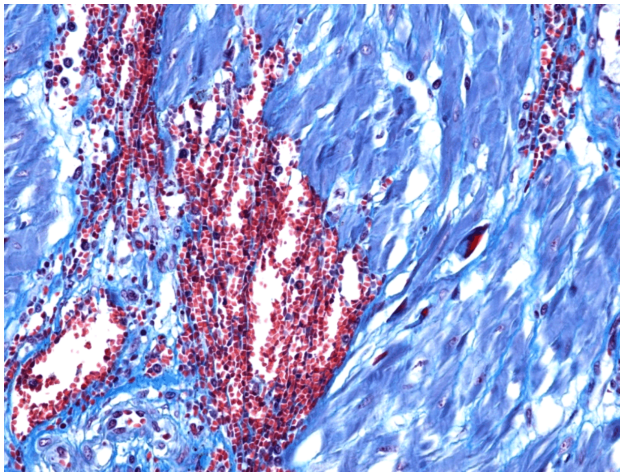

Figure 5 – ***Microscopic image of myometrial micro-hemorrhage (GS trichrome staining, ×200).***

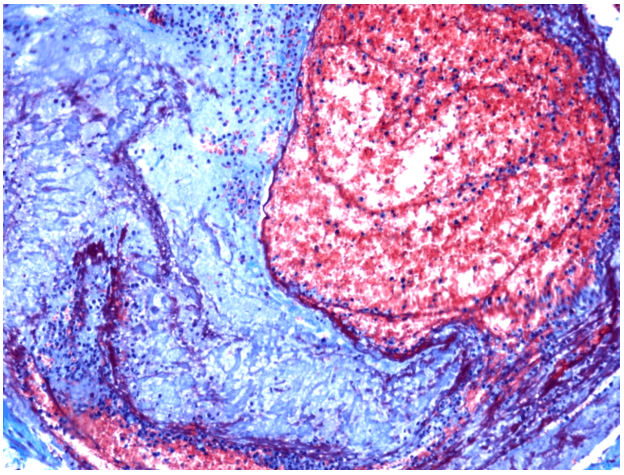

Figure 6 – ***Myometrial hematoma (GS trichrome staining, ×100).***

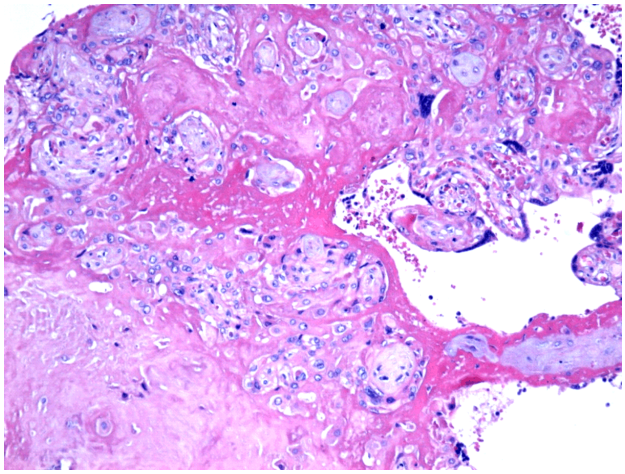

Figure 7 – ***Placenta with large area of placental infarction (HE staining, ×100).***

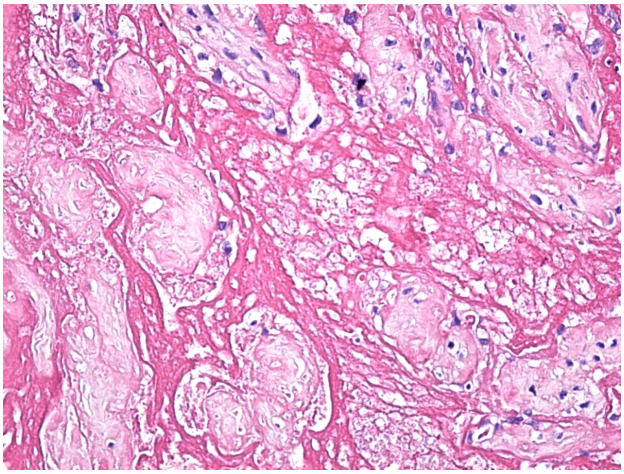

Figure 8 – ***Fibrin stripes arranged unevenly, covering and jugulating the placental villosities (HE staining, ×200).***

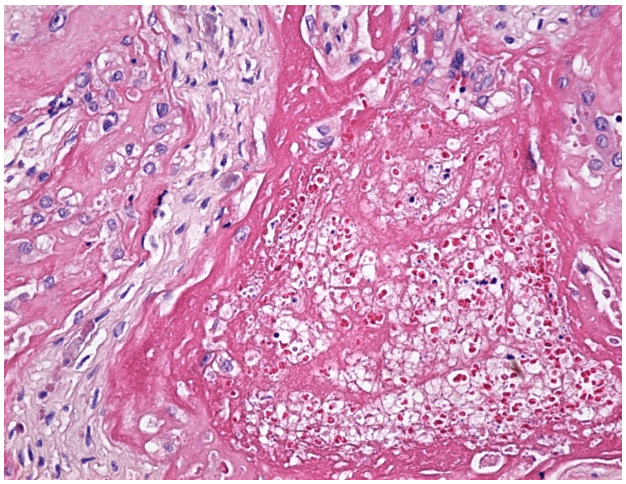

Figure 9 – ***Intravillous old thrombus with partially degenerated red blood cells, reshaped by the onset of laminary fibrin stripes (HE staining, ×200).***

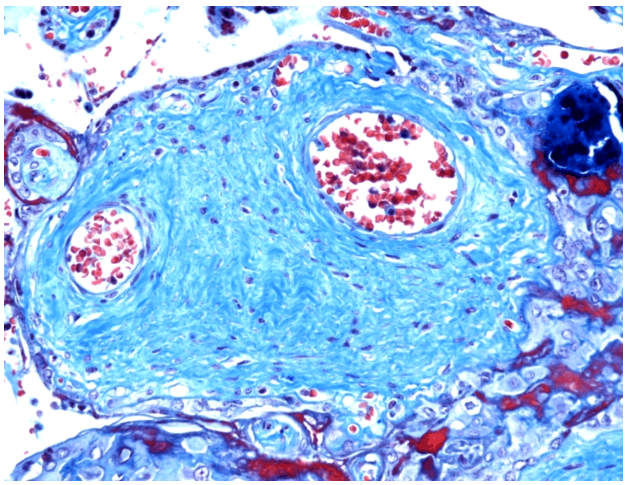

Figure 10 – ***Basis of placental villosity with emphasized stromal fibrosis and microcalcifications (GS trichrome staining, ×200).***

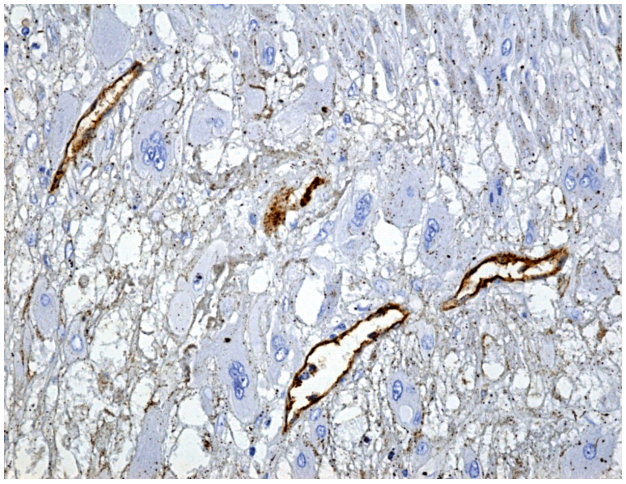

Figure 11 – ***Area of myometrium with hydropic degenerescence and a poor vascularization (Anti-CD34 antibody immunostaining, ×200).***

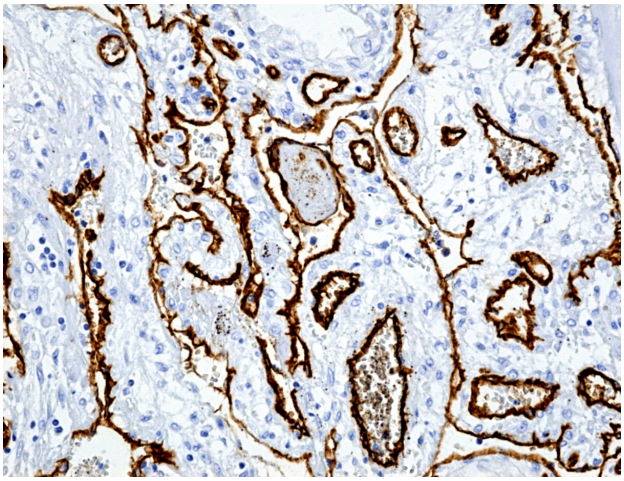

Figure 12 – ***Myometrium from the peridecidual area, with a network of well-developed microvessels (Anti-CD34 antibody immunostaining, ×200).***

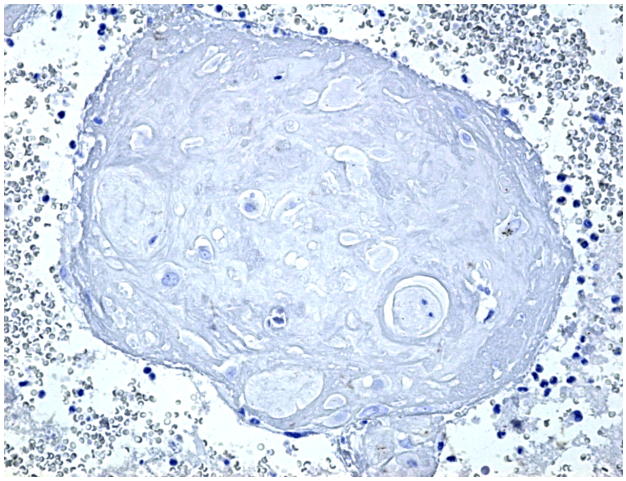

Figure 13 – ***Image of placental villosity in a transversal section, where there may be observed a total lack of blood vessels (Anti-CD34 antibody immunostaining, ×200).***

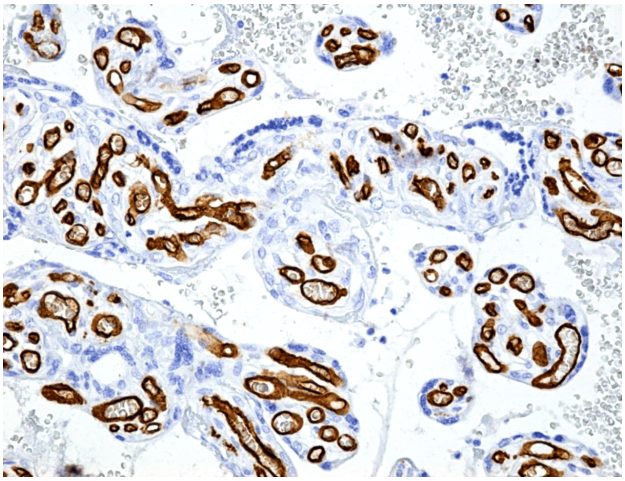

Figure 14 – ***Placental villosities with a network of microvessels with a normal aspect (Anti-CD34 antibody immunostaining, ×200).***

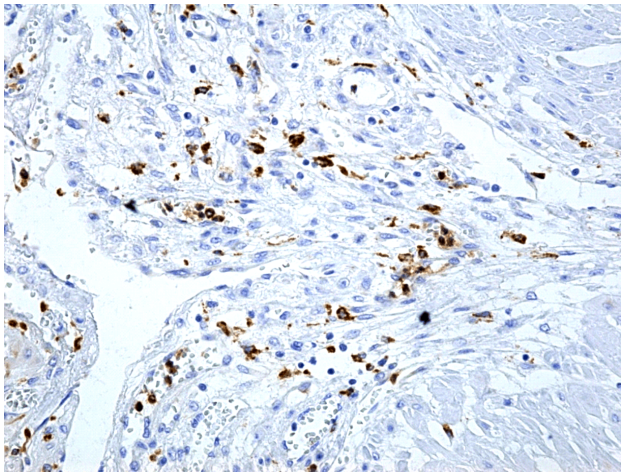

Figure 15 – ***Myometrium with rare macrophage cells (Anti-CD68 antibody immunostaining, ×200).***

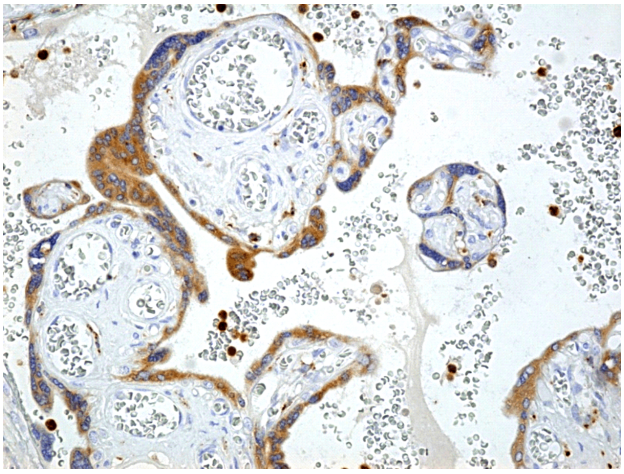

Figure 16 – ***Rare macrophage cells with a rare peri-villositary arrangement (Anti-CD68 antibody immuno-staining, ×200).***

Discussions

If the first pregnancy is an attribute of the eclampsy, multiparity would favor a higher incidence of placental abruption [28]. Yet not all the multiparous have retro-placental hematoma. We observed calving with 12–16 previous birth that had performed well without fetal–maternal complications [29–31]. Genetic predisposition and a certain accumulation of other factors pave the ground for the intradecidual acute hemorrhage condition by rupturing the spiral arterioles. The intense and prolonged spasm of the "vasa vasorum" induces ischemia and necrosis of arteriolar wall and their rupture.

The cases we studied were neglected cases, without home-based prenatal consultations, uninvestigated, untreated, brought by as emergency services.

As for the differential diagnostic, on the background of the hemorrhagic syndrome, we could take into consideration as it follows: placenta praevia (showing up at any age, not directly linked to arterial hypertension, has no relation to parity, occurring in first time pregnancy, is not related to the number of previous abortions), the uterine prerupture syndrome and uterine rupture (mechanical causes, such as high fetal to basin ratio) [32], the HELLP syndrome (showing up after preeclampsia, the uterus without generalized contractions, intraperitoneal hemorrhage through the rupture of the Glisson's capsule).

We found macroscopic lesions that are obvious in the form of violet to black ecchymoses, the uterus being atonic, inoperative. This is the so-called "Couvelaire uterus", between its appearance and the size of the retro-placental hematoma, being a great match.

This macroscopic aspect of the uterus is consistent with fluid-coagulant imbalances, preserving it with a catastrophic prognostic effect. The apoplectic uterus in Couvelaire's vascular drama is the result of blood extravasations in the tissues, unlike uterine infarction, which is secondary to massive vascular thrombosis, never seen aspect in retroplacental hematoma. In some cases, cracks or rupture of the ceiling were observed, the hematoma entering direct communication with the intra-villous area. These tears explain the rapid defibrillation in these cases through the passage of the chorio-decidual thromboplastin in the maternal circulation. This also explains the rapid consumption of coagulation factors by retroplacental hematoma.

The immunological conflicts in the utero-placental area can lead to the embrittlement of the spiral arterioles, the occurrence of the oxidative stress, mitochondrial pathology, and expression of genes responsible for the effects of hypoxia. The immunogenetic conflicts lead to this level to outfalls with antagonist effects on the utero-placental arterial vascular walls (vasodilator and anti-platelet from the vascular endothelium/prostaglandins PGE2, PGI2, nitric oxide; vasoconstrictor in the trophoblast and platelets/thromboxane A2, angiotensin II). In gestational hypertension, it was observed a decrease of the inter-mediate metabolite of prostacyclin/PGI2 in the maternal serum, in the placenta and the umbilical vessels. The polymorphism of the genes for Fas, hypoxia-inducible factor-1 alpha (HIF-1α) protein, interleukin (IL)-1β, lymphotoxin-α, transforming growth factor-beta 3 (TGF-β3), tumor necrosis factor (TNF) were studied with varied results. A number of seven genes were deeper analyzed: methylenetetrahydrofolate reductase (MTHFR) gene on chromosome 1p36.3 involved in vascular disease, Factor V Leiden on chromosome 1q23 involved in thrombophilia, angiotensinogen (AGT) on chromosome 1q42–q43 active angiotensin gene with determinism on the blood pressure, nitric oxide synthase 3 (NOS3) on chromosome 7q36 (nitric oxide is an important vasodilator agent in vascular endothelial function), human leukocyte antigen (HLA) on chromosome 6p21.3 involved in immunity, F2 on chromosome 11q 11p 12 being known that the prothrombin is involved in coagulation and thrombophilia, angiotensin-converting enzyme (ACE) on chromosome 17q23 involved in the angiotensinogen conversion in angiotensin [6, 11, 13].

The research carried highlighted how important it is for the practitioners to know the signs for call for the retroplacental hematoma symptoms: vaginal bleeding (78%), ascending uterus (66%), fetal distress (60%),

hypertonic/hyperkinetic uterus (34%), premature labor (22%), fetal death (15%), positive ultrasound (25%), renal sufferance/cortical necrosis (23%) [6].

In all the cases there were observed the five syndromes, 18 symptoms and signs, four paradoxes, more or less intense, always present: the obstetrical syndrome (pain, permanent uterus contracture/tetanized womb/so-called "wood womb", fetal heart rate and active fetal movement absent, the elevated uterine bottom, the uterine volume increases from one examination to another, vaginal bleeding), the hemorrhagic syndrome (internal bleeding, hypotension, acute anemia), the shock (hypotension, pallor, lipotimic condition, cold teguments and extremities), toxemia syndrome (arterial hypertension, oligoanuria, hematuria, proteinuria), biological syndrome (disseminated intravascular coagulation, incoagulability/fibrinolysis).

The paradoxes were: the acute anemia with low volume or with no significant bleeding, arterial hypertension in a parturient with a relatively abundant vaginal bleeding (acute intradecidual hemorrhage occurred recently in a low basal caduca, as in the placenta praevia), hypotension/ hypovolemic shock with little to no vaginal bleeding (intradecidual bleeding occurs in a high-basal caduca, as in a normally inserted placenta), association of hypotension – fainting with proteinuria.

The causes of placenta abruption are, most of the time, unknown. Most often, there are alleged maternal traumas. According to some studies, the traumas suffered by the mother cause up to 59% of placental abruption [33–35]. Other studies showed that some maternal chronic conditions represent important risk factors for placental abruption [36–37]. Of these, diabetes mellitus, kidney diseases and high blood pressure are among the most frequent ones [38–40].

We should mention that epidemiological studies associated with HP studies of the placenta, umbilical cordons and membranes, suggested that placental abruption may be the result of a long time pathological process, which extends until the last stages of pregnancy [41, 42]. Because of this fact, we suggest that pregnant women should be carefully monitored starting from the first stages of pregnancy, especially when they suffer from chronic conditions.

We had a placental abruption association in one case of a parturient, who suffered from an asymptomatic cervical cancer, the diagnosis being established postoperatively on the track of the hysterectomy at the HP examination. The case of placental abruption coexisting with the cervical cancer was a secundiparous of 34 years, 10 years after the first birth. The patient was not detected with cervical cancer when she presented to be consulted for only two prenatal specialized checkups in order to observe the pregnancy. The reason for hospitalization was the patient had 34 gestational weeks with cataclysmic vaginal bleeding "out of the blue". In this case, we witnessed, post-total hysterectomy, cervical intraepithelial neoplasia (CIN III) developed on the squamous metaplastic epithelium and moderately differentiated squamous cell carcinoma [43]. A case like that is rare, but it does not mean that we are partisans of the subtotal hysterectomy; on the contrary, we prefer the total hysterectomy [44].

In the world literature, there are clinical and statistical studies that show a maternal mortality up to 5%, in placental abruption. Regarding the fetal mortality, as we already mentioned, the mortality is 100%. The severe form of placental abruption with a live fetus does not exist. It is a about the intermediate retroplacentar hematoma forms, the so-called "trap forms" in which the fetus is in great sufferance, but alive.

Conclusions

Placental abruption is one of the most dramatic accidents met in pathology and obstetrical practice. On the studied group, the severe form of placental abruption had an incidence of 0.3% somehow to the lower limit if we compare the literature data (0.13% to 1.38%). The intradecidual acute bleeding is the consequence of rupture the spiral uteroplacentar arterioles. Crucial in the effectiveness of this accident is a combination of factors: genetic constellation, gynecological history (abortion, curettage), multiparty (13 cases – 89.5%), patients' age (17 cases over 30 years old – 68.5%), hypertension associated pathology (19 cases – 100%), uterine polyfibromatosis (two cases – 10.5%). The positive diagnosis was overwhelmingly a clinical one, being about the major emergencies. In almost all the cases, the clinical trial is a specific one and it consists of five syndromes, 18 signs and symptoms, four paradoxes. In all the 19 cases, the total hysterectomy that continued the Caesarean section was practiced, with maternal purpose. The results were: fetal mortality 100% and maternal mortality 0%. As prophylactic measures, we note early taking into evidence of the pregnant women by the outpatient ward, ultrasound examination especially in the first trimester of the pregnancy in order to make the classification of the pregnant women group with high-risk.

Conflict of interests

The authors declare that they have no conflict of interests.

Author contribution

Anca Daniela Brăila and Adrian Gluhovschi contributed equally to this work.

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