CASE REPORT

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Uteroplacental apoplexy associated with invasive cervical neoplasm

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Abstract

The cervical cancer is the worldwide second neoplasia in women, after the breast cancer. The incidence of invasive carcinoma in pregnancy is 1/2000 to 1/10 000 pregnancies. In most of the studies, almost all the patients had microinvasive carcinoma or limited cervical carcinoma at the cervix level. In the uteroplacental apoplexy, pathologically, retroplacental hematoma is formed while the fetus is still in the uterus. When speaking about the uteroplacental apoplexy, the fetal mortality is 100% and the maternal mortality can reach 5%. The particularity of the presented case is the association of the invasive cervical neoplasm, pathology unknown to the patient, with uteroplacental apoplexy, diagnosis for which she was hospitalized as an emergency. After the extraction of the dead fetus by segmental-transversal cesarean section, we continued to perform the total hysterectomy with adnexectomy. The fetus, the placenta, the uterus and the ovaries were sent for histopathological examination. Subsequently, the histopathological bulletin revealed cervical lesions in the neck of type cervical intraepithelial neoplasia (CIN) I, CIN II, CIN III, metaplastic squamous epithelium and moderately differentiated squamous cell carcinoma.

Keywords: uteroplacental apoplexy, total hysterectomy, pathological examination, squamous carcinoma.

Introduction

The cervical cancer is the worldwide second neoplasia in women, after the breast cancer. In the USA, the cervical cancer was ranked as the third in genital tract neoplasms, following the uterine and ovarian cancers [1]. The incidence of the invasive carcinoma in pregnancy is 1/2000–1/10 000 pregnancies. In most of the studies, almost all patients had microinvasive carcinoma or limited carcinoma in the cervix [2].

The uteroplacental apoplexy is the severe form of the retroplacental hematoma, caused by the breakage of the spiral arterioles from the basal placental obstruction. The hemorrhage intensity determines the placental basal plaque take off by at least 30% and the retroplacental hematoma formation of over 150 mL. In uteroplacental apoplexy, pathologically, the retroplacental hematoma is formed while the fetus is still in the uterus. In the uteroplacental apoplexy, the fetal mortality is 100% and the maternal mortality can reach 5% [3, 4]. This retroplacental hematoma consumes maternal coagulation factors, secondary fibrinolysis up to afibrinogenemia. The incriminated etiopathogens are the age over 35 years, the multiparity, the hypertension, preeclampsia, the premature ruptured membranes, smoking, the uterine leiomyomas [5–11].

The particularity of the presented case is the association of the invasive cervical neoplasm, pathology unknown to the patient, with the uteroplacental apoplexy, diagnosis for which she was hospitalized as an emergency.

Case presentation

We present the case of the uteroplacental apoplexy associated with the invasive cervical neoplasia in a 34-year-old pregnant woman, from the urban environment, secundiparous, 10 years after the first birth. The pregnant woman was admitted with voluntary termination of pregnancy (VTP) diagnosis, second pregnancy (IIP – secundipara) with 31 weeks gestation, cranial presentation, dead fetus, intact membranes, painful uterine contractions, severe form of preeclampsia, central placenta praevia, abnormal metrorrhagia, acute secondary anemia, negative Rh, uteroplacental apoplexy.

The sudden cataclysmic hemorrhage caused us to decide and practice surgery as an emergency.

After the extraction of the dead fetus by segmental-transversal cesarean section, we continued to perform total hysterectomy with bilateral adnexectomy for atonic uterus, not reactive to the oxytocin perfusion and intramural oxytocin injection, marbled uterus, with numerous violet areas, dark subseries present in both large and utero-ovarian ligaments.

The fetus was dead, 1300 g, female. The placenta with

voluminous retroplacental hematoma, with a footprint on the basal plate, was practically spontaneously removed. The fetus together with the extirpated placenta, the uterus and the ovaries were sent for pathological examination.

The laboratory investigations on admission show: hemoglobin (Hb) 10.8 g/dL, hematocrit (Ht) 32.5%, platelets 98 000/mm^3, urea 53 mg/dL, creatinine 2.2 mg/dL, glucose 94 mg/dL, glutamic-oxaloacetic transaminase (GOT) 87 U/L, glutamic-pyruvic transaminase (GPT) 21 U/L, Na^+ 136 mEq/L, K^+ 4.8 mEq/L, Quick time 92%, International Normalized Ratio (INR) 1.05. Evolving, after nine days, we noted the degradation of the kidney function, as it follows: urea 199 mg/dL, creatinine 6.98 mg/dL, uric acid 10.7 mg/dL. Postoperatively, the patient was evaluated cardiologically and nephrologically. In the nephrological exam, there were observed acute papillary necrosis and acute renal failure, the hemodialysis being recommended.

Following the dynamics, the kidney function improved: urea 112 mg/dL, creatinine 4.8 mg/dL, uric acid 7.61 mg/dL, proteinuria 1490 mg/24 h, urinary volume 5000 mL. Arterial pressure values were maintained at 160–140/90 mmHg.

The vital maternal prognosis was good. At discharge, there was a general good condition, without fever, the abdominal wound healed *per primam*, with physiological micturition, digestive transit, with the recommendation to re-evaluate from the cardiologically and nephrologically point of view.

The patient had only two prenatal consultations during the pregnancy and was not diagnosed with cervical neoplastic lesion.

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. The take-off occurs between compact and spongy layers of the basal caduca (decidua). The apoplectic uterus presents ecchymosis on extended areas, from the horns on the bottom of the uterus, the front and rear faces (Figure 1).

These lesions were associated with hemorrhagic infiltration of the subperitoneal region of the broad ligaments, the substance of the ovaries, and free in the peritoneal cavity. There may be widespread extravasation of blood into the uterine musculature and beneath the uterine serosa.

The histopathological examination of the placenta showed the presence of a collection of red blood cells in a fibrous network, which prevails in the villous space, compressing it. The chorionic villi were compacted, piled with capillary vessels having internal expansion, the hematoma having direct communication with the intravillous space, which explains the rapid defibrination of the choriodecidual thromboplastins passage into the maternal circulation. The myometrium presented hydropic degeneration, with trophoblastic infiltration areas and recent microthrombi and chorionic villi of terminal type (Figure 2).

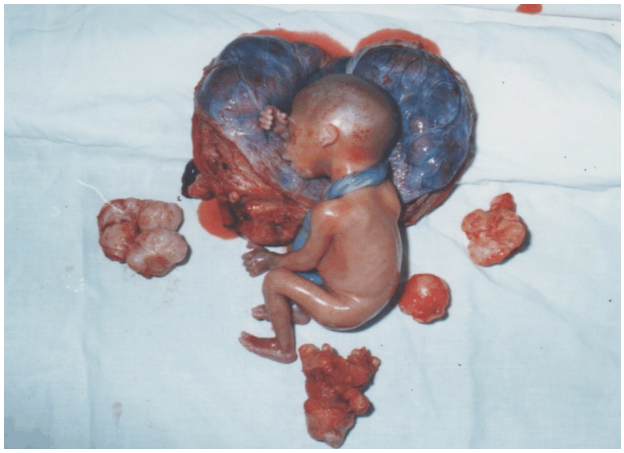

Figure 1 – ***Placental abruption, dead fetus, apoplectic uterus, placenta.***

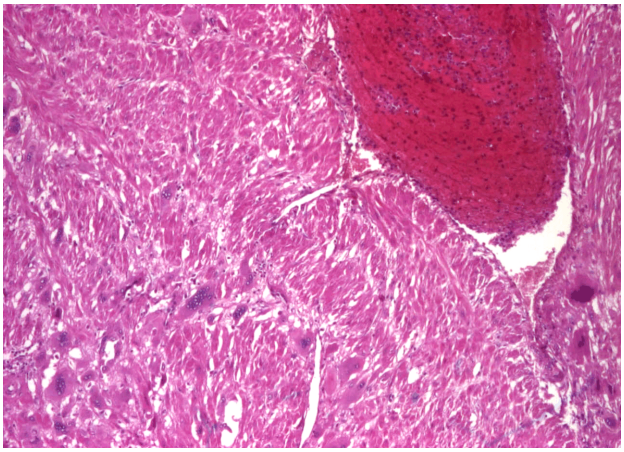

Figure 2 – ***Myometrium with hydropic degeneration, trophoblastic infiltration areas and recent microthrombi [Hematoxylin–Eosin (HE) staining, ×200].***

The placenta was exposing chorionic villi of intermediate, mature and terminal type and a large area of placental infarction (Figure 3). The ovary can be described as having corpus luteum and surface decidualization area, granulated cyst and hyperplasic area with nodular Leydig cell (Figure 4).

The histopathological examination of the uterine cervix revealed the presence of lesions type cervical intraepithelial neoplasia (CIN) I, CIN II, CIN III, metaplasic squamous epithelium and moderately differentiated squamous carcinoma (Figure 5 and 6).

For positive and differential diagnosis, we have decided to perform some immunohistochemistry studies. In our study, we used the antibodies: anti-Ki67 (clone MIB-1, 1/50 dilution, Dako), anti-human papilloma virus (HPV) (clone K1H8, 1/200 dilution, Dako), anti-cytokeratin 7 (CK7) (clone OV-TL 12/30, 1/100 dilution, Dako), anti-estrogen receptor (ER) (clone 1D5, 1/50 dilution, Dako), anti-progesterone receptor (PR) (clone PgR 636, 1/50 dilution, Dako) and anti-p53 (clone DO-7, 1/100 dilution, Dako).

Ki67 is a nuclear antigen, a marker for proliferating cells. In our image, we note squamous cervical epithelium with a CIN III degree lesion, an immunomarker characterized by the Ki67 affinity. At the level of the dysplastic cell nuclei in the thickness of the epithelium, cellular polarity and degree of cellular disorder as well as cellular atypia are observed.

Diagnosis of high-grade intraepithelial lesion is indicated by Ki67 proliferation factor by revealing atypical nuclei of epithelial thickness (Figure 7).

In an endocervical glandular epithelial metaplasia and aggravated metaplastic epithelium, the Ki67 proliferation

factor was clearly expressed in the nucleus of the dysplastic cells and occasionally in the normal endocervical cells (Figures 8 and 9).

The immunohistochemical exam was negative for HPV (Figure 10), but was positive for CK7, especially in the atypical cell cytoplasm, the cells stroma being negative for CK7 (Figure 11).

In our study, tumoral and dysplastic cells showed a poor affinity for the estrogen hormone factor (Figure 12) and the affinity for progesterone was less pronounced in tumor cells and better evidenced in stromal cells (Figure 13).

The immunoreaction for p53 was relatively poorly in the nuclei of tumor cells, and absent in stromal and inflammatory elements (Figure 14).

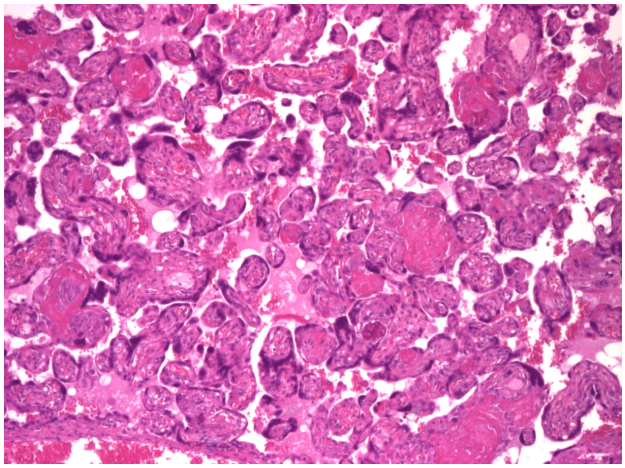

Figure 3 – ***Placenta with intermediate mature and terminal chorionic villi type (HE staining, ×100).***

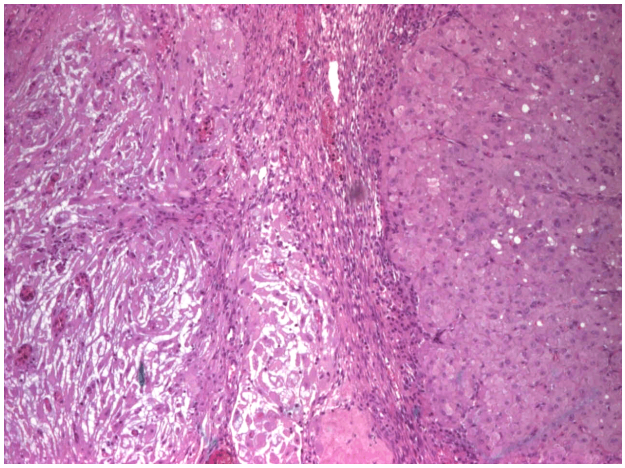

Figure 4 – ***Ovary with corpus luteum and surface decidualization area (HE staining, ×100).***

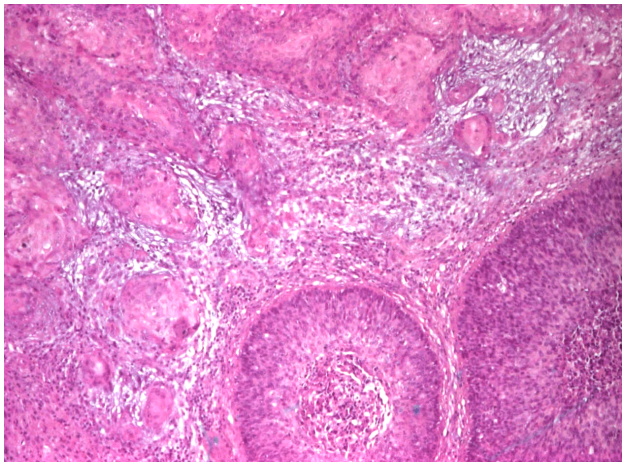

Figure 5 – ***Cervical intraepithelial neoplasia (CIN) III developed on the squamous metaplastic epithelium and moderately differentiated squamous cell carcinoma (G2) (HE staining, ×100).***

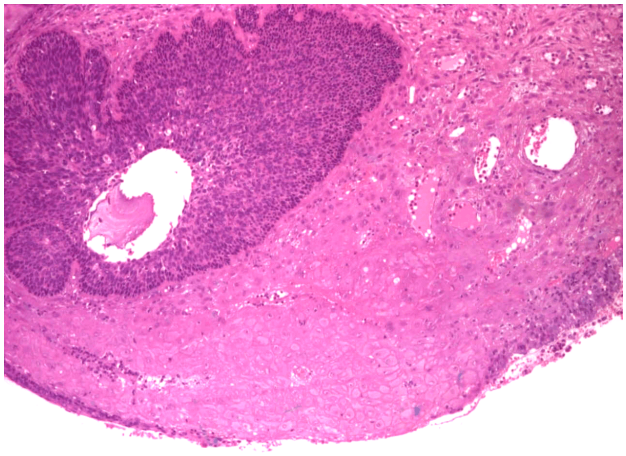

Figure 6 – ***CIN III developed on the squamous metaplastic and decidualization subepithelial area (HE staining, ×100).***

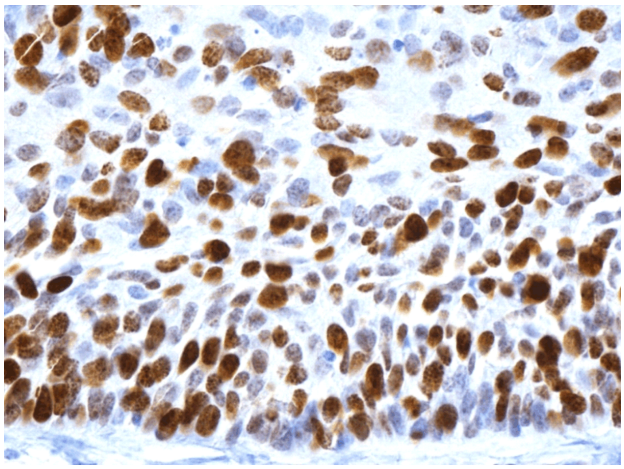

Figure 7 – ***Cervical squamous epithelial, high grade, CIN III (Anti-Ki67 antibody immunostaining, ×400).***

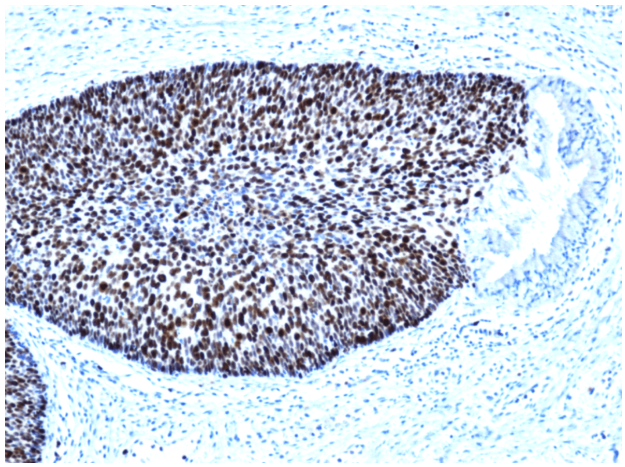

Figure 8 – ***Endocervical gland with glandular epithelial metaplasia and aggravated dysplasia of metaplasic epithelium (Anti-Ki67 antibody immunostaining, ×100).***

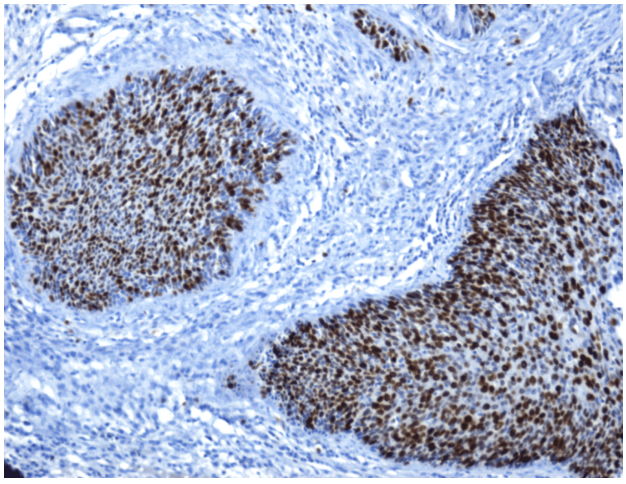

Figure 9 – ***Endocervical epithelial squamous metaplasia presenting aggravated dysplasia, with nuclei of various forms and sizes, with variable chromatic affinity for Ki67 (Anti-Ki67 antibody immunostaining, ×100).***

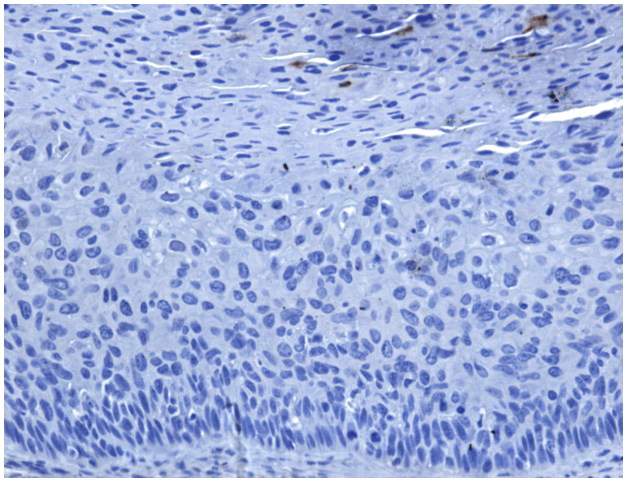

Figure 10 – ***Cervical squamous epithelial cell with human papillomavirus (HPV) negative cell (Anti-HPV antibody immunostaining, ×200).***

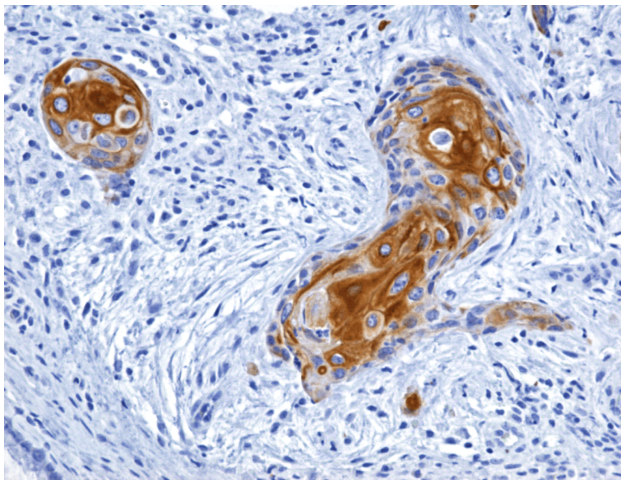

Figure 11 – ***Two cell groups are observed in which the fraction 6 of the cytokeratin 7 (CK7) is expressed positively, especially in the atypical cell cytoplasm, the stroma being negative for CK7 (Anti-CK7 antibody immunostaining, ×200).***

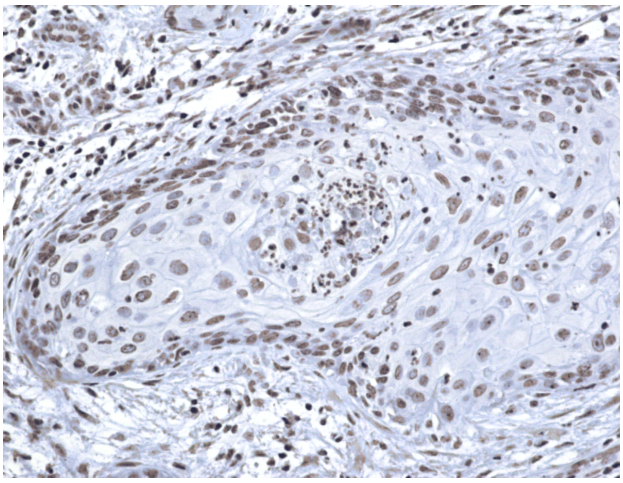

Figure 12 – ***A poor affinity of dysplastic squamous epithelial cells for estrogen receptor (ER) factor is noticed (Anti-ER antibody immunostaining, ×200).***

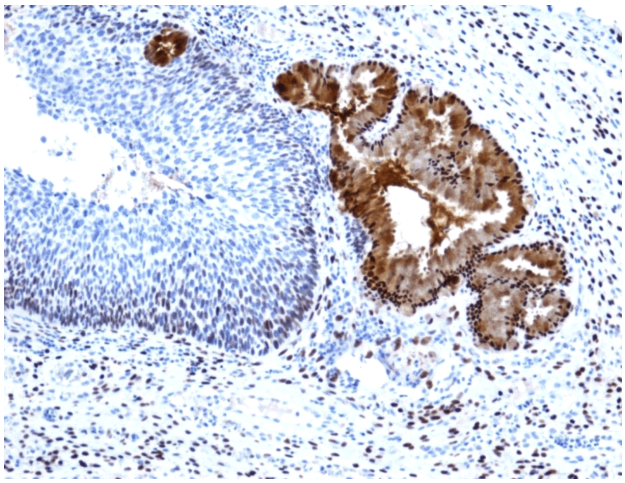

Figure 13 – ***The affinity for progesterone is less pronounced in tumor cells and better evidenced in stromal cells [Anti-progesterone receptor (PR) antibody immunostaining, ×100].***

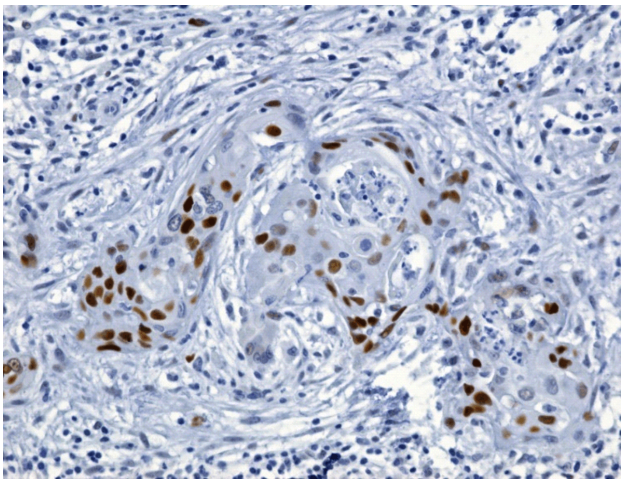

Figure 14 – ***The immunoreaction of p53 is relatively poorly represented in the nuclei and cytoplasm of tumor cells, and absent in stromal and inflammatory elements (Anti-p53 antibody immunostaining, ×200).***

Discussion

The placental abruption, together with the placenta praevia, uterine rupture, hemolysis, elevated liver enzyme levels and low blood platelet count (HELLP) syndrome, eclampsy is indisputably one of the major severe accidents in obstetrics [12–14]. The hemorrhagic shock and the hypovolemia up to collapse, less in eclampsy, always bring immediate danger to the life of the fetus and mother. The common denominator for the cases of placental abruption is "the uteroplacental spiral arterioles fragility", apparently being determined by several factors that create 'the particularly ground': the genetic constellation, over 35 years old, multiparous, gestational hypertension, multiple curettages, leiomyomas, adenomyosis, thrombophilia, collagen diseases, diabetes, trauma and smoking. The shock and the coagulopathy (fibrinogen less than 150 mg/dL) are not reported in minor and intermediate forms of retroplacental hematoma, they are markers of placental abruption. The baby is the first victim. Due to the hypoxia/ anoxia, he dies quickly after the activation of the acute accident.

The higher the number of broken spiral arteries, the more intense becomes the intradecidual bleeding and, more important, is the formed hematoma.

Uterus hypotonia leads to a capital decision: to leave the uterus in place or not. In such circumstances, the only solution is the total hysterectomy to continue the caesarean section, the goal being to stop the disseminated intravascular coagulation and the secondary fibrinolysis, a deadly one if the uterus is left in its place. In many cases, there are authors who consider that subtotal very low hysterectomy is sufficient, given the urgency of the case while the total hysterectomy is prolonging the intervention [15].

Regarding our case report, the parturient presented an asymptomatic cervical neoplasia, the diagnosis was postoperatively decided after performing the hysterectomy and the histopathological examination. Such a case is rare, but it does not mean that we are partisans of subtotal hysterectomy; on the contrary, we prefer total hysterectomy.

Cervical intraepithelial neoplasia and cervical cancer are relatively common injuries diagnosed in pregnant women as a global health problem in the population [16]. Some studies have shown that from 2% to 7% of pregnant patients are diagnosed with an abnormal cytological result [17].

In the uterine cervix, the squamous carcinoma develops frequently at the squamous-cylindrical junction of a pre-existing dysplastic lesion, usually following the HPV infection [18]. The progression from dysplasia to invasive cancer lasts for many years. The HPV oncogene serotypes have the ability to integrate into the human genome. The oncoproteins of early replication E1 and E2 facilitate the viral replication in the cervical cells. These proteins are synthesized in large quantities from the initial stages of HPV infection and induce low-grade squamous intraepithelial lesion (LSIL) type cytological changes as evidenced by the Babeş–Papanicolau test. The amplification of the viral replication results in the transformation of normal cells into tumor cells under the action of the E6 and E7 viral oncoproteins [19]. The E7 protein binds to the suppressor gene protein Rb, and the E6 protein to the p53 suppressor gene, causing degradation of the suppressor proteins [19–22].

In those situations, where it is already known the cervical cancer coexistence with the pregnancy, the surgical attitude is established according to the gestational age and the fetal viability.

The presented case is a complex one from the obstetrical point of view, as well as considering the association of a native land predisposed to arterial hypertension in pregnancy due to a kidney pathology aggravated by gestation. From the obstetrical point of view, it has been observed the association of the severe pre-eclampsia with placenta praevia and with the retroplacental hematoma, a serious form of intrauterine death of the fetus and the imminent threat of the mother's life. The only rescue solution was to perform total hysterectomy with bilateral adnexectomy.

The abundant metrorrhagia was caused by the retroplacental hematoma, which appeared on a lower inserted and outwardly plated placenta and not by the cervical neoplastic pathology subsequently detected after total hysterectomy.

The long-term vital prognosis, in this case, depends on the renal reevaluation performed periodically. From a gynecological point of view, the patient returned regularly to be checked, the vaginal bunt being supple and the pelvis free.

Conclusions

The uteroplacental apoplexy is one of the most dramatic accidents encountered in the pathology and medical practice. The positive diagnosis was eminently a clinical one, being a major emergency. The total hysterectomy performed for the uteroplacental apoplexy and the histopathological examination was of real benefit for the patient by detecting the cervical neoplastic lesions along with the radical surgery.

Conflict of interests

The authors declare that they have no conflict of interests.

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