CASE REPORT

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Gestational choriocarcinoma after term pregnancy: a case report

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Abstract

Choriocarcinoma coexisting with or after a "normal" pregnancy has an incidence of one per 160 000 pregnancies. In case of choriocarcinoma after term pregnancy, early diagnosis by histopathological examination of the placenta is very important, the precocity of the diagnosis influencing the prognosis and tumor response to chemotherapy. In this paper, we report the case of a 29-year-old woman gravidity 2, parity 2, with metastatic choriocarcinoma after term pregnancy, diagnosed at four months after the delivery of a healthy baby. An episode of abundant vaginal bleeding occurred after four months from delivery. The local exam revealed a vaginal tumor whose pathological examination on biopsy samples was inconclusive. Subsequently, she was admitted in our clinic with abundant vaginal bleeding, severe anemia and fever. Abdominal ultrasonography revealed an intracavitary uterine tumoral mass with signs of myometrial invasion to the uterine serosa, strong Doppler signal and moderate ascites. Pulmonary X-ray and computed tomography scan excluded extrapelvic tumoral masses. The pretreatment human chorionic gonadotropin (HCG) level was 31 030 IU/mL and her FIGO risk factor score was 8 (high-risk group). Total hysterectomy with bilateral salpingo-oophorectomy and omentectomy was performed as an optimal cytoreduction. Postoperative remaining lesions were represented by the metastasis located in the lower two-thirds of the vagina. Histopathological examination revealed uterine choriocarcinoma with ovarian metastasis. Postoperative was initiated four courses of polychemotherapy. Case evolution was favorable, with the normalization of the βHCG value in two months postoperative and complete remission of the vaginal metastasis in six weeks postoperative.

Keywords: choriocarcinoma, metastasis, pregnancy.

Introduction

The term "gestational trophoblastic neoplasia" (GTN) replaces and include hydatidiform mole, metastasizing mole, choriocarcinoma, placental site trophoblastic tumor (PSTT) and epithelioid trophoblastic tumor (ETT). More convincing data have shown that the common trophoblastic stem cell develops along two lines of trophoblastic differentiation: villous and extravillous [1]. Molar pregnancies and choriocarcinoma are derived from villous trophoblast and PSTT and ETT are derived from extravillous trophoblast [2].

Choriocarcinoma is thought to be a more "undifferentiated" trophoblastic tumor compared to PSTT and ETT as the latter two tumors show phenotypic characteristics of extravillous intermediate trophoblast cells either in an implantation site (PSTT) or the migratory intermediate trophoblast (ETT) [3]. Choriocarcinoma coexisting with or after a "normal" pregnancy has an incidence one per 160 000 pregnancies [4], and is associated with an unfavorable outcome especially because of delayed diagnosis. If the interval from index pregnancy to initial treatment is less than four months, the remission rate is 87.5% [5]. Most of the cases reported in the literature known as choriocarcinoma after term pregnancy were diagnosed through macroscopic and histopathological examination of the placenta.

In this paper, we report the case of a 29-year-old woman diagnosed with vaginal metastatic choriocarcinoma after term pregnancy at four months after the delivery of a healthy baby.

Patient, Methods and Results

A 29-year-old Caucasian woman delivered vaginally a healthy normoponderal baby with normal postnatal evolution on February 2010, in a territorial maternity, after a normal labor. The macroscopic aspect of the placenta was apparently normal according to the discharge documents. The histopathological exam was not performed because is not a routine test to be carried out in the territorial hospital, considering the required resources and the rare incidence of this pathology.

The patient was admitted to a territorial department of obstetrics and gynecology on May 2010 because of abundant vaginal bleeding. The obstetrical history showed no abortions and two vaginal births (2003 and February 2010). The clinical examination revealed a vaginal tumor whose pathological assessment on biopsy samples was

inconclusive, showing fibrinohematic clots, necrosis and inflammation.

On June 2010 (four months after delivery), she was admitted in our clinic with abundant vaginal bleeding and fever – body temperature measurement of 38–39^{0}C. Paraclinical test results showed severe anemia – hemoglobin 2.9 g/dL. The following tests were performed: βHCG dosage, abdominal ultrasound, computer tomography scan, paracentesis and pulmonary radiograph. βHCG revealed a value of 31 030 IU/mL.

Abdominal ultrasonography revealed intracavitary uterine tumoral mass with signs of myometrial invasion to the uterine serosa, strong Doppler signal and moderate ascites.

Two-dimensional ultrasonographic evaluation (Voluson 730 Pro ultrasound machine, GE Medical Systems) has been performed transabdominal because of the vaginal tumors' presence and the existing severe vaginal bleeding, using the gynecology presets (AB 2-7 probe, Har-low, PRF 4.0 kHz).

Ultrasound findings assessed by conventional B-mode and color Doppler mapping revealed heterogeneous, almost entirely moderately echogenic mass, filling and exceedingly enlarging the uterine cavity, numerous pseudocystic spaces and large areas of hemorrhage. Myometrial invasion has been obviously detected, as the innermost layer, relatively hypovascular and hypoechoic, compared with adjacent endometrium in normal basic conditions, has been disappeared. No subendometrial halo could be identified. Color and spectral Doppler examination demonstrated high velocities and low resistance flow in the uterine arterial circulation and strong Doppler signal, low resistance flow in the echogenic mass enlarging the uterine cavity (Figures 1 and 2).

Pulmonary X-ray and computer tomography scan excluded extrapelvic tumoral masses.

Paraclinical test results along with the clinical examination allowed us to establish the diagnosis of metastatic gestational trophoblastic neoplasia.

In order to evaluate the severity of the disease and the type of post-operative adjuvant chemotherapy, we used WHO (*World Health Organization*) risk factor scoring system along with the FIGO (*International Federation of Gynecology and Obstetrics*) staging system.

At this point, surgery was decided. Intraoperative findings showed perforating metastasis at the level of uterine fundus, where was attached the great omentus. Total hysterectomy with bilateral salpingo-oophorectomy and omentectomy was performed as an optimal cytoreduction and hemostatic method.

Postoperative remaining lesions were represented by the metastasis located in the lower two-thirds of the vagina.

Histopathological examination revealed uterine choriocarcinoma infiltrating the entire uterine wall, including the serosa with right ovarian metastasis. Macroscopic uterine appearance was of a soft, dark red, nodular and hemorrhagic tumor, and right ovarian appearance of a small red soft nodule. Histopatological examination of the uterus reveal clusters of cytotrophoblasts separated by arias of syncytiotrophoblast disposed in a dimorphic plexiform pattern.

Hemorrhage and necrosis were present and the villi aspect was not identified in the tumor (Figures 3–6).

Postoperative staging and histopathological examination established the diagnosis: gestational choriocarcinoma stage IIA (FIGO).

Postoperative polychemotherapy was initiated with four courses of Methotrexate (100 mg/m^2 IV infusion over one hour and then 200 mg/m^2 IV infusion over 12 hours by pump), Actinomycin D (500 micrograms IV push new IV) and Cyclophosphamide (600 mg/m^2 IV).

Case evolution was favorable, with the normalization of the βHCG value in two months postoperative and postchemotherapy, with complete clinical remission of the vaginal metastasis in six weeks postoperative, according to the current guidelines does not require biopsy.

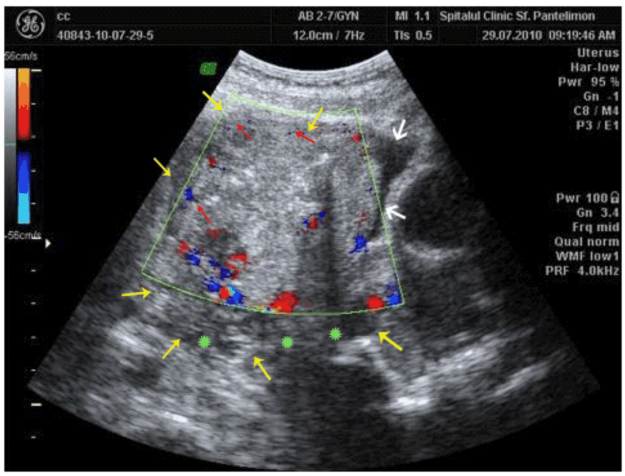

Figure 1 – ***Sagittal sonogram demonstrating severely enlarged uterine cavity, heterogeneous echogenic mass (yellow arrows), absent subendometrial halo (red arrows), myometrial invasion (green stars), large areas of hemorrhage and strong color Doppler signal in the echogenic mass (white arrows).***

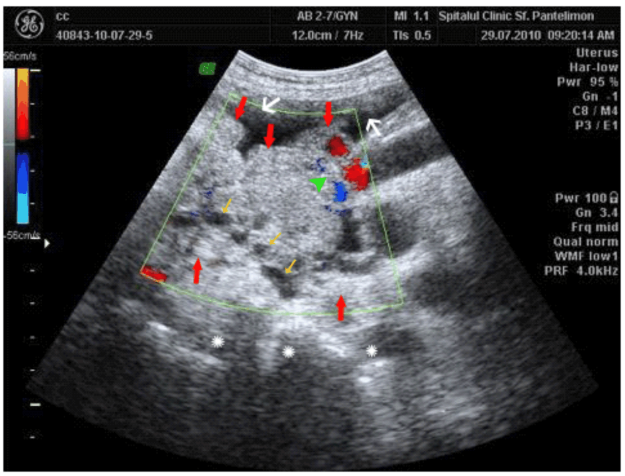

Figure 2 – ***Sagittal sonogram demonstrating heterogeneous moderately echogenic mass (red arrows), pseudo cystic spaces (yellow arrows), myometrial invasion (white stars), large areas of hemorrhage (white arrows), strong color Doppler signal (green arrow).***

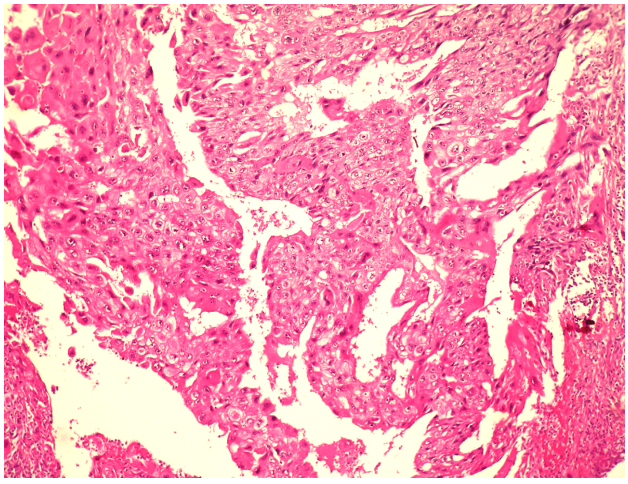

Figure 3 – ***Choriocarcinoma: cellular infiltrates in the uterine wall syncytiotrophoblast and cytotrophoblast, biphasic pattern. HE staining, ×100.***

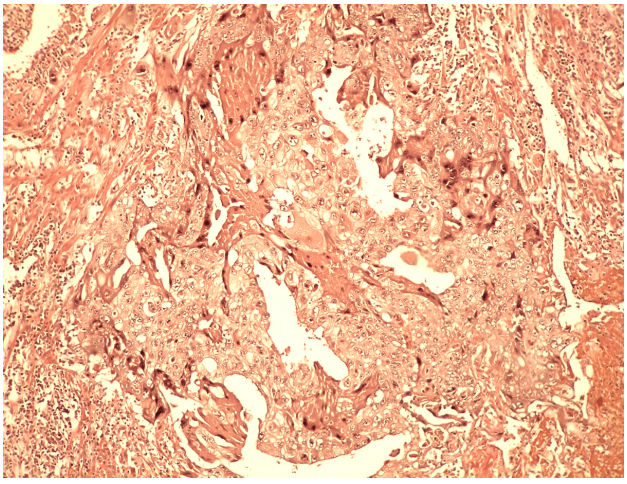

Figure 4 – ***Choriocarcinoma: outbreaks of syncytiotrophoblast and cytotrophoblast surrounded by hemorrhagic areas. Van Gieson staining, ×200.***

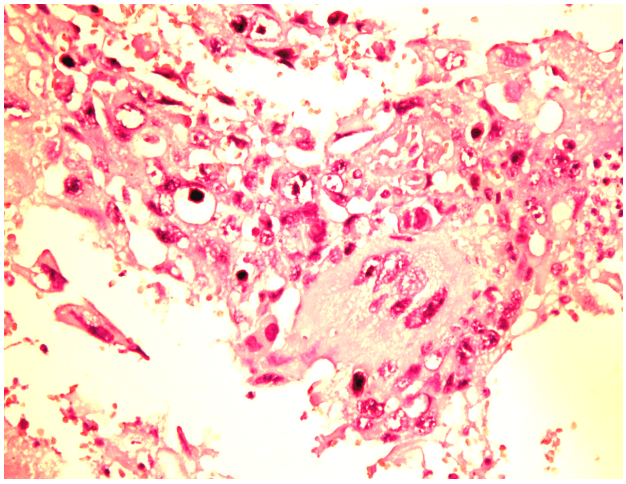

Figure 5 – ***Choriocarcinoma, syncytiotrophoblast: multinucleated giant cells with dense cytoplasm. HE staining, ×400.***

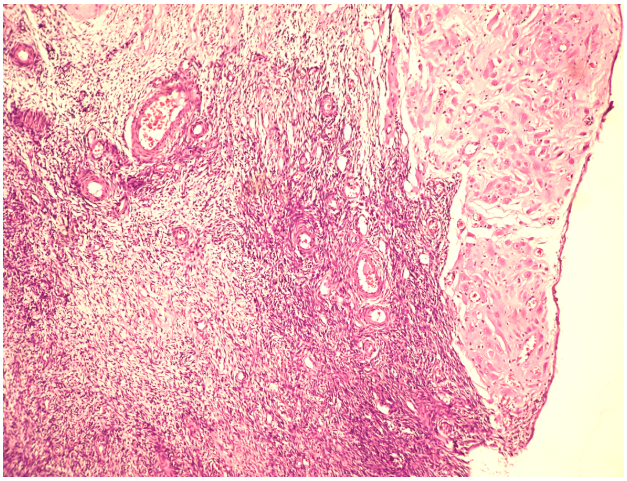

Figure 6 – ***Ovarian metastasis of the uterine choriocarcinoma. HE staining, ×100.***

Discussion

Choriocarcinoma is a highly malignant epithelial tumor. It can arise from any type of trophoblastic tissue (molar pregnancy, abortion, ectopic pregnancy) but occurs only rarely after a partial mole and after normal term pregnancy [6, 7]. Choriocarcinoma is a curable malignancy with a poor prognosis. Maternal choriocarcinoma is usually diagnosed in symptomatic patients with metastases.

Histologically, choriocarcinoma consists of sheets of anaplastic cytotrophoblast and syncytiotrophoblast tissue without chorionic villi. While some trophoblasts, which are intermediate in appearance, may also be seen, the biphasic pattern of obviously malignant appearing mononuclear (cytotrophoblast) and multinuclear cells (syncytiotrophoblast) is essentially pathognomonic of choriocarcinoma. Extensive necrosis, hemorrhage, and vascular invasion are common.

Diagnosis of gestational choriocarcinoma after a term pregnancy is difficult to determine without a histopathological examination of the placenta. Rare incidence of this disease after a term pregnancy did not result in routine histopathological examination of the placenta after birth in all obstetric centers, such as delayed diagnosis of choriocarcinoma. Simple macroscopic examination of the placenta after delivery can identify suspicious placental areas. Macroscopically, choriocarcinoma appears like white nodules and infracted areas in the placental mass [8]. The histopathological type of gestational trophoblastic neoplasia after a normal term pregnancy is always choriocarcinoma and the important aspect is prompt moment of diagnosis [9].

In cases where the diagnosis of choriocarcinoma is not established immediately postpartum by histopathological examination of the placenta, at more than a month after delivery only clinical and laboratory exam (very high levels of βHCG) can suspect the diagnosis of choriocarcinoma [10, 11]. Persistent elevation of serum βHCG following any non-molar pregnancy, miscarriage, ectopic, or preterm/term pregnancy, may be due to development of choriocarcinoma or PSTT [12]. If there the clinical suspicion of GTN (gestational trophoblastic neoplasia) is raised obtaining fragments of tumor biopsy for histopathological examination may be insufficient for diagnosis, due to the presence of large areas of bleeding and tumor necrosis. In our case, histopathological

examination of tumor fragments from the vaginal metastasis was inconclusive. In this case, the diagnosis was established by postoperatory histopathological examination of the uterus, ovaries and omentum, and usually in this pathology is necessary to have enough tissue samples for histopathological diagnosis [11].

Delay of the diagnosis by the lack of histopathological exam of the placenta affect the outcome of the case by increasing the risk of metastasis and increased resistance to monochemotherapy [13]. Low-risk GTN are cases with FIGO stages I, II or III with a WHO score less than 6; these cases have good prognosis with monochemotherapy. High-risk GTN are cases with FIGO stages I, II or III with a WHO score of 7 or greater, and stage IV; these cases needs polychemoterapy. In our case, the risk factor score that influenced the therapeutic approach was 8.

Prognosis of metastatic choriocarcinoma after term pregnancy is poor due to: larger tumor size including uterus (greater than 5 cm), pretreatment βHCG values greater than 30 000 IU/mL, changes in the host's immune response, a delayed diagnosis (six months) [14, 15]. From the prognosis point of view, the presented case is a high risk case due to ovarian metastasis and high level of βHCG (31 030 IU/mL). The evolution of the case was favorable after the combined surgical treatment and polychemotherapy administered immediately postoperative. Polychemotherapy was preferred as first therapeutic line, to the detriment of monochemotherapy, based on the results of the risk scoring.

Serial testing of βHCG serum concentrations is essential in monitoring treatment and confirming remission. Monitoring of human chorionic gonadotrophin concentrations should be continued for life as late recurrences may occur [16].

In 2008, Chung *et al.* described an incidental placental choriocarcinoma in a term pregnancy, diagnosed by performing a histopathological exam of the grossly normal macroscopically placenta because of the patient's history of gestational hypertension. The patient's serum βHCG dropped from 3070 mIU/mL to less than 2 mIU/mL six weeks postpartum, and in this case no chemotherapy was initiated. Multiple chest X-ray and computed tomography scan all ruled out metastasis during the one year postpartum period. The infant was followed by the pediatric service and found to be normal. To date, both mother and baby have been disease free for eight years [17].

We performed a MEDLINE search (1980 to 2014) using the keywords placenta, choriocarcinoma, and trophoblastic disease. We found 26 articles with 39 cases of placental choriocarcinoma in the English literature. Fourteen cases of choriocarcinoma were limited to the placenta with no evidence of dissemination to mother or infant; six of these 14 cases were incidentally identified in patients with normal pregnancies.

Conclusions

The presented case emphasizes the importance of the microscopic analysis of all placentas postpartum, because even if the incidence of gestational choriocarcinoma after a normal pregnancy is low, the prompt diagnosis significantly improves the patient's prognosis. It is our belief that the incidence of placental choriocarcinoma may actually be higher than reported. By reporting this case and review of the literature, we support the opinion of early diagnosis of gestational choriocarcinoma by routine histopathological examination of the placenta after birth. At more than six weeks after delivery, the suspicion of gestational choriocarcinoma occurs after clinic exam combined with βHCG levels and transvaginal ultrasound examination. For the diagnosis of gestational choriocarcinoma the pathologist needs sufficient tumor sample due to large areas of bleeding and tumor necrosis specific to this tumor. The use of WHO risk factor scoring together with FIGO staging allows us to control the therapy and to choose the type of chemotherapy depending on the associated risk.

Conflict of interests

The authors declare that they have no conflict of interests.

Acknowledgments

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