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Robot-Assisted Hysterectomy for Primary Choriocarcinoma of the Cervix – A Novel Approach

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Rezumat

Histerectomie asistată robotic pentru coriocarcinom primar al colului uterin – o nouă abordare

Incidența coriocarcinomului ectopic cu localizare primară în colul uterin este extrem de scăzută, cu mai puțin de o sută de cazuri raportate în literatura de limba engleză până în acest moment. Prezentăm un caz de coriocarcinom cervical primar la o femeie de 41 de ani, la suspiciunea inițială a fost de cancer de col uterin. După verificarea histologică, s-a decis tratamentul chirurgical primar din cauza hemoragiei extinse, planificarea familială încheiată şi localizarea tumorii. În prezent, după şase luni de urmărire, pacienta este considerată vindecată din punct de vedere chirurgical, şi nu prezintă semne de recidivă sau metastaze. Acest caz demonstrează o utilizare inovatoare a intervenției chirurgicale asistate robotic, fezabilitatea şi eficacitatea acestei abordări pentru tratamentul primar al coriocarcinomului ectopic.

Cuvinte cheie: primar, cervical, coriocarcinom, histerectomie, robotic

Abstract

The incidence of ectopic choriocarcinoma with primary localization in the uterine cervix is extremely low, with less than hundred cases reported in the English language literature to date. We present a case of primary cervical choriocarcinoma in a 41-year-old woman, originally suspected for cancer of the cervix. After histological investigation, the decision was made for primary surgical

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treatment due to extensive hemorrhage, finished family planning, and the localization of the tumor. Currently, after six months of follow-up, the patient is disease-free without evidence of recurrence or metastasis. Our case demonstrates an innovative use of the robot-assisted technique, the feasibility and the efficacy of this approach for primary treatment of ectopic choriocarcinoma.

Key words: primary, cervical, choriocarcinoma, hysterectomy, robotic

Introduction

Choriocarcinoma is a rare gynecological entity classified as gestational trophoblastic neoplasia (GTN) or as germ cell tumor. Differentiation between the two can be achieved through DNA analysis or HLA typing, by identifying a paternal component in the tumor and proving a prior pregnancy-related event. Premenarchal status, clinical history and molecular genotyping can further help the differential diagnosis. Determination of the origin has a clinical and prognostic value as non-gestational choriocarcinoma can develop from pluripotent germ cell, or after a metaplastic cancer differentiation, behaving as germ cell tumor with poorer prognosis. Gestational choriocarcinoma arises following a normal or ectopic pregnancy, spontaneous abortion or hydatidiform mole (1). Most commonly it develops within the uterine cavity, while extrauterine localization is a characteristic feature of the non-gestational type. In 1965, Saito et al. outlined diagnostic guidelines for extrauterine choriocarcinoma consisting of four criteria: no evidence of disease in the uterus, pathological sample confirmation of the disease, and the exclusion of extrauterine choriocarcinoma coexisting with hydatidiform mole or normal intrauterine pregnancy, while intramural choriocarcinoma in the uterine corpus not to be considered as ectopic choriocarcinoma (2). We present a case of a radical minimally invasive approach for a primary gestational choriocarcinoma of the uterine cervix.

Case Report

A 41-year-old woman, gravida 3, para 1 presented to the hospital with abnormal uterine bleeding, following an induced abortion due to fetal malformation in 16th week of pregnancy 12 months before. Prior to hospitalization, the patient visited a specialist because of an intermittent vaginal bleeding in the last three months. A cervical biopsy was obtained after a diagnostic ultrasound, suggestive of neoplasia of the uterine cervix. The histology report was highly suspicious of choriocarcinoma, and the initial serum level of human chorionic gonadotropin (ß-hCG) was 7018 mIU/L.

Upon admission to the hospital, a pelvic examination revealed a cervical tumor with diameter of 3 cm, bleeding at contact, without parametrial invasion or extension to the vaginal fornices (*Fig. 1*). The uterus was slightly enlarged, no adnexal mass was palpable. Transvaginal ultrasonography found a heterogeneous mass in the cervix with no extension into the bladder or rectum, enlarged uterus with well-defined, solid, concentric, hypoechoic mass with diameter up to 2 cm, located on the anterior wall, suspicious of a fibroid, without signs of adnexal pathology. Abdominal sonography excluded metastatic lesions on abdominal organs. MRI of the pelvis revealed a 2.4 x 3.1 cm hypervascular tumor occupying the uterine cervix. T2-weighted imaging showed poorly defined oval area with variable signal intensities, including hyperintensity (*Fig. 2, 3*). The mass did not appear to extend to the parametrium. On the anterior uterine wall, a well-defined hypointensive lesion with a diameter of 1.9 cm was found – an intramural

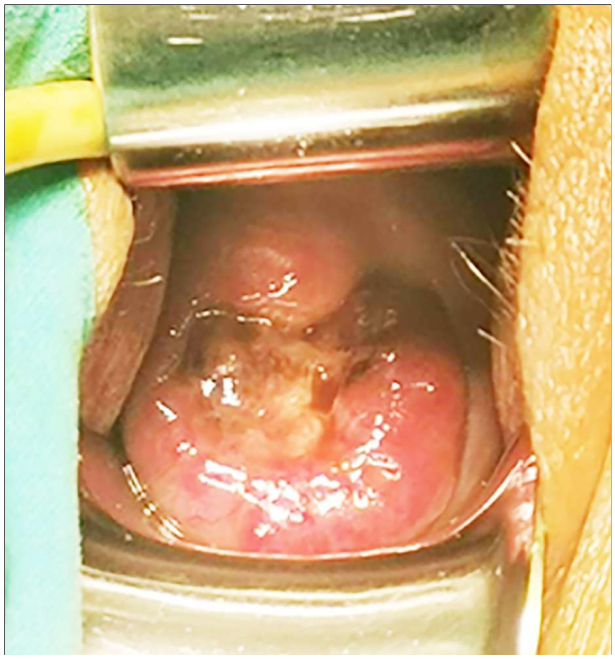


Figure 1. The image shows cervical tumor with diameter of 3 cm with friable structure.

fibroid. The radiologist's impression was probable choriocarcinoma of the uterine cervix. The patient was accepted as low-risk stage I, according to the FIGO scoring system for gestational trophoblastic disease (GTD). Chest X-Ray showed clear lungs with visible lung markings, normal heart size, and a clear diaphragm with no signs of fluid accumulation, mass, or pulmonary nodules. The blood test showed secondary hypochromic anemia and an elevated serum level of ß-hCG - 13820 mIU/L.

After multidisciplinary institutional and state Tumor Board approval the patient was taken to the operating room by a board-certified gynecologic oncologist for a robotic-assisted radical hysterectomy type II with bilateral adnexectomy and bilateral selective pelvic lymphadenectomy. Exploration of the abdominal cavity was performed after placement of the trocars and no macroscopic abnormalities were observed. The uterus, ovaries, and tubes were grossly normal and no enlarged lymph nodes were identified. The avascular vesicovaginal and rectovaginal spaces were developed. The ureters were separated and freed from the surrounding tissues and the uterine arteries were clipped near the internal iliac arteries. The bladder and rectum were dissected inferiorly from the vagina near the cervicovaginal junction. Placement of a uterine manipulator was not feasible due to the friable structure of the tumor. Given the aggressive potential of the malignancy and the patient's young age, a bilateral selective lymph node dissection was performed removing a total of eight lymph nodes. The surgery lasted 180 minutes with an estimated blood loss of 150 ml.

The final histology report revealed an infiltration by choriocarcinoma of the cervix, free surgical margins and eight lymph nodes with sinus histiocytosis. Multiple sections of

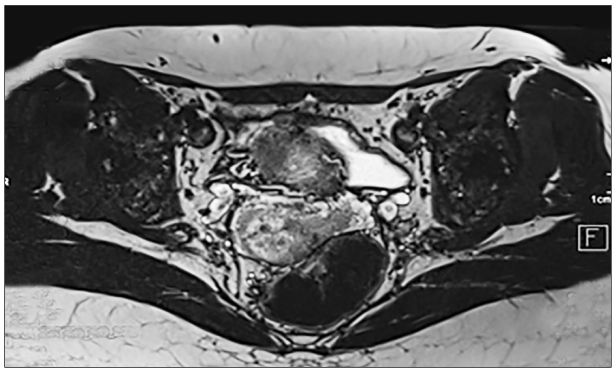


Figure 2. MRI depiction a 2.4 x 3.1 cm hyperintense lesion occupying the uterine cervix

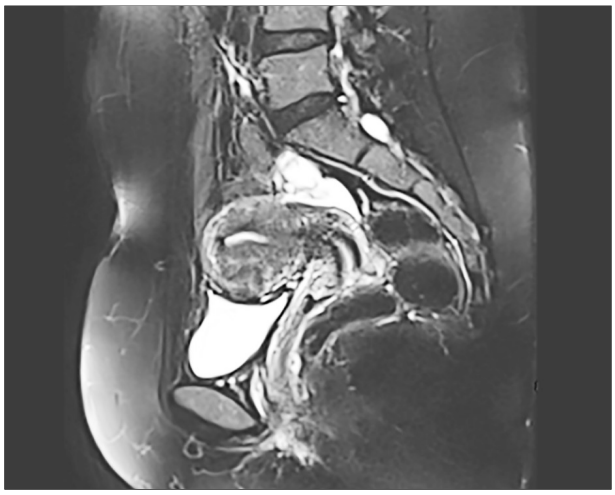


Figure 3. MRI depiction a 2.4 x 3.1 cm hyperintense lesion occupying the uterine cervix

the uterine corpus and bilateral ovaries failed to show any focus of trophoblastic cells. Microscopic examination revealed vascular, hemorrhagic, and necrotic tissues composed of abnormal, bizarre cytotrophoblastic cells and syncytiotrophoblastic cells. No chorionic villi were identified (*Fig. 4, 5*). The pathological specimen was evaluated by immunohistochemistry (IHC) together with ß-hCG and were found to be diffusely positive stained in tumor tissue (*Fig. 6*).

On the fourth postoperative day, serum ß-hCG level was measured to be 2829 mIU/L and the patient was discharged. A month and a half after the surgical treatment a PET/CT was performed, revealing no residual tumor or distant metastasis. At the time, serum ß-hCG level reached normal range – 1.42 mIU/L. The patient was referred for chemotherapy. Six months post-surgical management serum ß-hCG level is 0.552 mIU/.

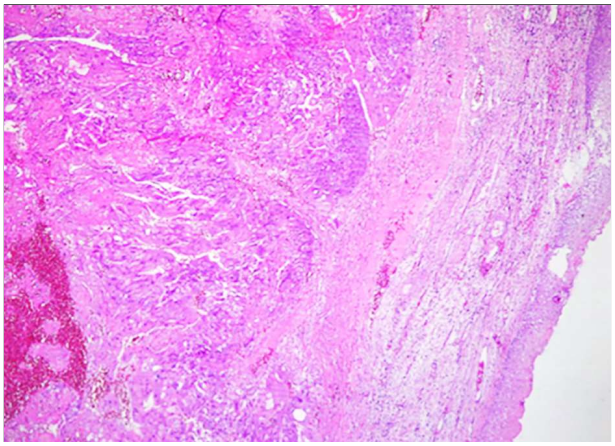


Figure 4. The wall of uterine cervix with choriocarcinoma (HE x10).

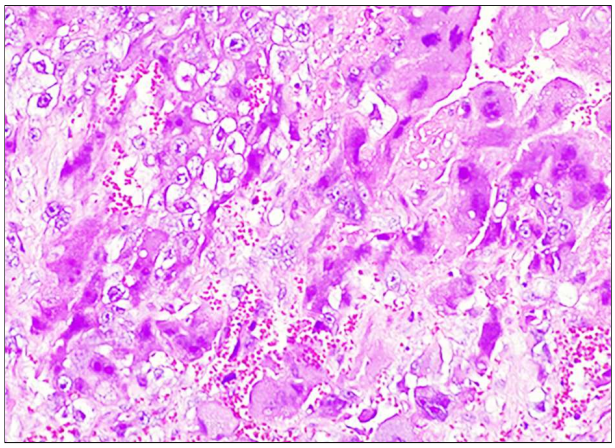


Figure 5. The image shows classic biphasic appearance in a choriocarcinoma consisting of mononucleated cytotrophoblastic cells with clear cytoplasm and multinucleated syncytiotrophoblasts with deeply eosinophilic cytoplasm (HE x40).

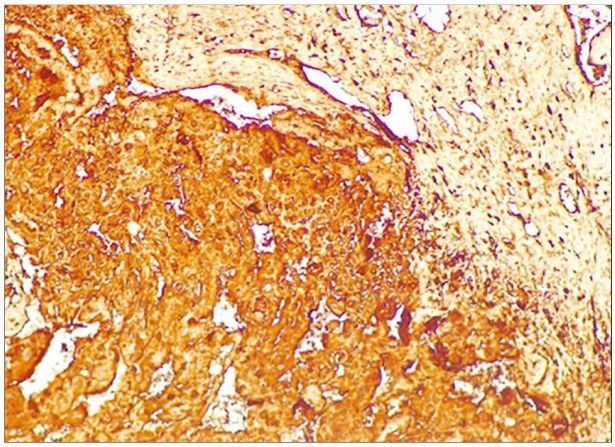


Figure 6. The image shows strong immunoreactivity for hCG (x25).

Discussion

Gestational choriocarcinoma is a rare aggressive form of epithelial malignancy that arises from the trophoblastic cells of the placenta in about 1 out of 20,000-40,000 pregnancies. Half of the cases are found in women who have completed a pregnancy, 25% develop after molar pregnancies, and the rest occur following other types of pregnancy events (3). Appropriate theory for the development of this tumor is either that the cervical choriocarcinoma might be a metastasis from primary tumor of the corpus, which later disappears, or emboli of chorionic cells from a preceding pregnancy that stay dormant in the cervix and later become malignant (1). Choriocarcinoma typically presents as irregular vaginal bleeding. With cervical localization the incidence of uncontrolled massive vaginal bleeding is higher, owing to the anatomical position of the lesion. Other signs that suggest postmolar GTN include an enlarged and irregular uterus, persistent enlargement of both ovaries, and occasionally, a visible metastatic vaginal lesion that may cause uncontrolled bleeding (4). Because of its non-characteristic

presentation and rarity, choriocarcinoma is not the first diagnosis that is considered. It is easily mistaken for cervical pregnancy, a threatened abortion, a cervical polyp or other cervical neoplasia as becomes obvious form reported cases in literature (5,6). However, cervical choriocarcinoma should be considered in every woman in reproductive years with unclear cervical mass.

Ultrasonography is a useful tool in the diagnosis of choriocarcinoma, as it allows the observation of a specific visual pattern that is indicative of the disease. This pattern typically consists of multiple echoes or hypoechogenic zones and high diastolic blood flow and low impedance on color Doppler due to angiogenesis and neovascularization (7). MRI is a gold standard for female pelvic tumors and is informative of the structure of the lesion - abundance of blood vessels and presence of central necrosis (8).

Human chorionic gonadotropin, a placental glycoprotein consisting of a unique beta subunit, is a disease-specific tumor marker for gestational trophoblastic neoplasms. It can be easily measured in both urine and blood and its levels have been found to be directly proportional to the burden of the disease. Moreover, it is used for monitoring the response to therapy.

In 1965 Saito et al. reported 18 cases of cervical choriocarcinoma in a series of 119 ectopic choriocarcinomas, in which they observed site-specific features for the cervical localization such as better prognosis and lower incidence of metastasis (2). A retrospective study by Wang et al., encompassing a period of 32 years, reported 13 cases of cervical GTN, of which 12 were diagnosed as choriocarcinoma and one as invasive mola. Hysterectomy was performed in 11 of the patients - 4 with tumor larger than 3 cm in diameter and failure of multi-agent chemotherapy, 3 with plateaued β-hCG levels, 2 with no childbearing plans after chemotherapy, and 2 as initial surgery. The authors addressed that the high rate of surgery of large-sized tumors and the excessive amount of necrotic tissue lead to chemoresistance as the amorphous mass is not easily penetrated by chemotherapy drugs (9). Typical for choriocarcinoma is early hematogenous spread, most commonly in lungs, brain, and liver. However, side-specific ways of spreading should be considered when managing cervical choriocarcinoma. Prognosis of GTN is based on age, antedecedent pregnancy, serum levels of β-hCG pretreatment, tumor size, and the presence and number of metastases. Low-risk GTN (FIGO Stages I-III: score <7), which score 5-6 points, are associated with a higher drug resistance, although overall survival approaches 100% (10). Significant prognostic factors for the most common cervical malignancy - cervical carcinoma are pelvic lymph node metastasis, parametrial involvement, lymphovascular space invasion, tumor size, depth of invasion, and histology. Recent studies report that radical hysterectomy followed by tailored adjuvant therapy for bulky early–stage cancer leads to better survival outcomes and lower morbidity rates, than primary chemoradiation therapy (11). Even though choriocarcinoma is known to be a highly chemosensitive tumor, due to cervical localization, surgical treatment is often required. Literature review shows that in selected cases primary hysterectomy leads to more than satisfactory outcomes (2, 5, 9) with most of the previously reported cases utilizing an open surgical approach for primary tumor resection. Minimally invasive technique is an important tool in complex pelvic surgery and the limits of its utility continue to expand. The robotic-assisted technique has not been investigated in cervical choriocarcinoma and the limited number of cases prevent meaningful survival analysis based on surgical approach. Given the need for enhanced deep pelvic visualization, as well as a desire to minimize post-operative complications, robotic surgery was utilized in our case.

The rarity of primary cervical choriocarcinoma has contributed to the paucity of information regarding the appropriate management and prognosis of these patients. The diagnosis is challenging and often overlooked and should be considered in cases

of unclear tumor of the cervix in women of reproductive age. Immunohistochemical analysis along with patient history, pregnancy-related events, serum levels of ß-hCG and MRI of the pelvis are important for optimal treatment. Robotic-assisted surgery is feasible in carefully evaluated low-risk cases of cervical choriocarcinoma. Compared to laparotomy the minimally invasive approach demonstrates equivalent clinical outcomes, less blood loss, faster patient recovery and shorter hospital stay, due to higher rate of chemoresistance in ectopic choriocarcinoma. The treatment options must be individualized and tailored to the needs of each individual patient and each case must be reported in the literature to add more to our understanding of this rare disease.

Declaration of Competing Interest

None of the authors has any financial support or relationships that may pose a conflict of interest.

Ethics Approval

All procedures performed were in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments.

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