Clear Cell Adenocarcinoma of Vagina During the Pregnancy

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Received 15 January 2007; received in revised form 11 March 2007; accepted 20 March 2007; published online 17 April 2007

Abstract

Vaginal clear cell carcinoma is very rare during the pregnancy. A 31-year-old woman was admitted by persistent vaginal bleeding at 28th weeks of gestation. On pelvic examination, fragile and hemorrhagic mass of 6 by 7 cm mass on the anterior vaginal wall adjacent to bladder trigone was detected. Biopsy of the lesion demonstrated clear cell adenocarcinoma of vagina. She had no history for prenatal exposure to DES. Treatment was postponed to 31 week's of gestation to achieve lung maturity of fetus and preoperative work-up. She underwent surgical staging following the delivery by cesarean section at 31 week's of gestation. Preoperative diagnosis was confirmed postoperatively and two metastatic pelvic lymph nodes were also detected. She refused postoperative adjuvant radiotherapy. She died at postoperative 6th month due to distant metastasis. However majority of antenatal bleedings are related to obstetrical causes, lower genital tract malignancies should be excluded by basic gynecological examination and cervical smear screening.

Keywords: pregnancy, vaginal cancer, clear cell adenocarcinoma, antenatal bleeding

Özet

Gebelikte Vajenin Berrak Hücreli Adenokarsinomu

Gebelik sırasında vajinal berrak hücreli kanser çok nadirdir. İntrauterin DES maruziyeti olmayan, 31 yaşında, 28 haftalık gebe olan hasta, inatçı vajinal kanama şikâyeti ile başvurdu. Yapılan pelvik muayenede; mesane trigonuna komşu, 6x7 cm çapında, frajil, kanamalı kitle saptandı. Biyopsi sonucu berrak hücreli vajinal adenokarsinom olarak bildirildi. Fetusun akciğer matürasyonunun ve yenidoğan yoğun bakım koşullarının sağlanması için tedavi 31. gebelik haftasına kadar ertelendi. Otuz birinci gebelik haftasında, olgunun sezaryenle doğumunun gerçekleştirilmesini takiben cerrahi evreleme yapıldı. Preoperatif tanı, operasyon spesmeninde onaylandı ve 2 adet pelvik lenf nodunda metastaz saptandı. Adjuvan radyoterapiyi reddeden hasta, postoperatif 6. ayda metastatik hastalık nedeni ile kaybedildi. Antenatal kanamaların büyük bir kısmı obstetrik nedenlere bağlı olarak ortaya çıksa da, basit bir pelvik muayene ve servikal smear ile aşağı genital kanal maligniteleri kolaylıkla dışlanabilir.

Anahtar sözcükler: gebelik, vajinal kanser, berrak hücreli adenokarsinom, antenatal kanama

Introduction

Vaginal cancer during the pregnancy is very rare (1). Ninety percent of these cancers have been squamous carcinomas (2). Only 10% of vaginal cancers are adenocarcinoma. Clear cell adenocarcinoma of vagina is a well-known type of adenocancer which has causal relationship with intrauterine DES (Diethylstilbestrol) exposure (3). Optimal management in the pregnancy is unclear due to very rare occurrence of vaginal clear cell cancer.

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Case

A 31-year-old primigravida was admitted by vaginal bleeding at 28 week's of gestation to obstetrics and gynecology department. She had had vaginal spotting since 6th weeks of gestation without history for postcoital bleeding or spotting before the pregnancy. Vaginal bleeding had been considered to be a result of abnormal placental localization. She was referred for regular uterine contractions and persistent vaginal bleeding at 28th weeks of gestation.

During the pelvic examination a fragile and hemorrhagic mass was seen on anterior vaginal wall adjacent to bladder trigone. The pelvic examination revealed fixed vaginal mass which had infiltrated the whole vagina. Ultrasonographic examination revealed a posteriorly located placenta which did not cover cervical ostium. Also, a heterogeneous solid

mass of 77x63 mm in diameter located in the vagina was seen by ultrasound. We detected regular and low amplitude uterine contractions. Ritodrin HCl infusion (Pre-Par, Eczacıbaşı, Istanbul) was started to stop regular contractions and to gain time to corticosteroid administration. Also, to enhance lung maturation, bethametasone (Celestone Ampul, Schering-Plough, Germany) was given two times intramuscularly with 24- hour interval. Pelvic MRI (Magnetic Resonance Imaging) revealed a vaginal mass adjacent to bladder base. The vaginal mass extended to the level of external cervical ostium. Pathologically enlarged lymph node was not detected by pelvic MR scan. Histopathological diagnosis was clear cell adenocarcinoma of vagina. She had no history for the prenatal exposure to DES. Extrapelvic dissemination was not detected by metastasis work-up (including, abdominal ultrasound and chest X-ray). After the initial evaluation, she underwent surgery.

A female infant of 1610 g birth weight was delivered by cesarean section at 31 week's of gestation. Following the delivery, total abdominal hysterectomy, bilateral salpingo-oopherectomy, bilateral pelvic lymphadenectomy, infracolic omentectomy, appendectomy, total vaginectomy, bladder repair and ureteroneocystostomy and vaginal reconstruction by myocutaneous flap was performed. During the postoperative period, vaginal flap was infected and abdominal incision breakdown had occurred at postoperative 8th days. Secondary repair was performed at postoperative 18th days. During the hospital stay, citalopram was prescribed due to symptoms of depression (Sleep disturbances, loss of appetite, mood disturbances).

On gross examination, whole vaginal wall was infiltrated by a fragile, yellowish colored mass. The final histopathological diagnosis was clear cell adenocarcinoma of vagina (Figure 1). Tumor was seen along the surgical margin with stromal invasion. Also, pelvic lymph node metastases were detected. Final tumor stage was FIGO stage III disease. Adjuvant radiotherapy was postponed due to wound complications. Two months later, computed tomography (CT) scan revealed pelvic mass in 4x5 cm located on urinary bladder. Beside this, hepatic metastasis and bilateral dilated collecting system of kidneys were observed. Patient refused systemic chemotherapy and pelvic irradiation due to traditional and religious beliefs. Written informed consent was obtained from patient. She died 6 months after the operation.

Discussion

Nine percent of primary vaginal cancers are adenocarcinomas and they affect the younger age group. Causal relationship between the vaginal clear cell adenocarcinoma and intrauterine DES (Diethylstilbestrol) exposure is well-known (4). Adenocarcinoma of vagina may arise from Wolffian rest elements, peri-urethral glands and foci of endometriosis (5).

Vaginal cancer is one of the rarest malignancies diagnosed during pregnancy (3,6,7). Major diagnostic signs are lower genital tract malignancy during pregnancy with persistent vaginal spotting. In this case, vaginal bleeding began as early as 6th week's of gestation. Usually, genital bleeding during the

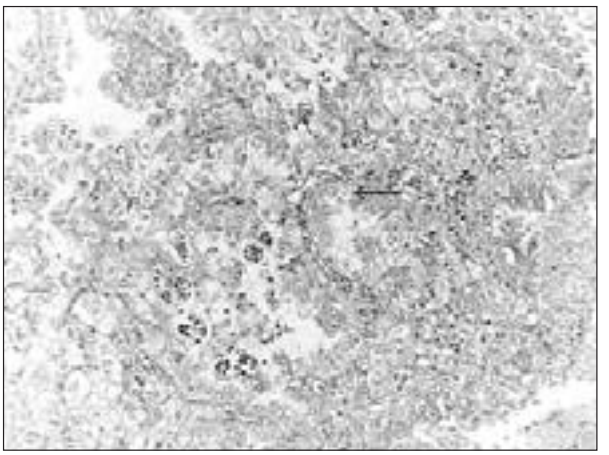

Figure 1. Nests of clear cells with abundant vacuolated cytoplasm and highly atypical nuclei (Arrow) (HE, x200).

pregnancy links to obstetrical causes. Vaginal examination and cervical screening by Pap-smear might be neglected especially in underdeveloped countries due to traditional beliefs. Vaginal spotting or bleeding could be evaluated as a result of pregnancy-induced cervical ectropion, cervical decidualisation or exaggerated changes of pregnancy. Following the diagnosis of clear cell adenocarcinoma of vagina at 28th weeks of pregnancy, surgery was postponed to 31st weeks of pregnancy to achieve lung maturation and preoperative work-up. Three weeks delay allowed for an additional 380 g fetal weight gain. Birthweight is an important factor which affects the neonatal survival of preterm delivered baby. Neonatal mortality was less than 10%, when the birthweight of prematurely delivered baby was above the 1600 g. Also, approximate improvement in neonatal survival per week is 5% and 3% at 28th and 29th weeks of gestation, respectively (8).

Local extension of tumor could be determined by pelvic MRI scan. Also, pelvic MRI can discriminate involvement of cervix as a primary site or secondary extension to vaginal primer (9).

We performed vaginectomy as a part of surgical staging. Radiotherapy may be an alternative to extirpation of vagina. However, vagina was filled by tumor 70% of total length and vaginal involvement did not permit endocavitary radiotherapy. Therefore, vaginectomy was performed for reduction of central tumor bulk.

Prognosis of clear cell adenocarcinoma of vagina is related to the stafe of the primary disease, with 68% survival rate for stage I disease (10). Other prognostic factors are tubulocystic growth pattern, tumor size less than 3 cm^3, and less than 3 mm of stromal invasion. Relatively short survival period might be related with locally advanced disease when the diagnosis was done.

Lymphatic involvement is a bad prognostic sign. Nordqvist et al. (11) reported that patients who had lymphatic spread, died from carcinoma. Metastatic lymph nodes were not

detected by MR examination due to small size of involved lymph nodes (widest diameter was less than 10 mm). However, evaluation of pelvis by MR is useful to detect local invasion, although the role of MRI for preoperative assessment of lymph node status is controversial (12). Majority of pelvic and para-aortic lymph node metastasis are smaller than 10 mm. In a prospective analysis of the 1.0 cm criterion for diagnosis of a positive pelvic lymph node, MRI had a 72% accuracy, a 68% sensitivity, and a 78% specificity (13). Choi et al. (14), reported that, CT/PET (Positrone Emmision Tomography) had better sensitivity (57.6% vs 30.3%) than MRI to detect positive pelvis and para-aortic lymph nodes. Major handicap of this study was limited sample size. Recently, a new lymph node-specific contrast agent, ferumoxtran-10, composed of ultrasmall particles of iron oxide (USPIO) has been used to enhance the detection of lymph node metastases independent of node size (15).

Major concern is the gestational age at the diagnosis. In the first half of pregnancy, optimal surgical approach or radiotherapy must be performed regardless of fetal survival. During the late 2nd trimester (especially beyond the 22 week's of gestation) and early 3rd trimester, the fetal survival expectancy increases and treatment delay until the achievement of lung maturation is another option (8,16). Squamous cancers of vagina may have similar clinical progression like cervical cancers. Because of the rarity of vaginal cancer during the pregnancy, to assess optimal management is very difficult.

In conclusion, despite the linking of majority of antenatal bleedings to obstetrical causes, complete pelvic examination and Pap-smear evaluation is necessary to exclude gynecological causes especially in lower genital tract malignancies. Gynecologic examination and Pap-smear test at first antenatal visit is a good opportunity to detect lower genital tract malignancies and must be a part of routine antenatal follow-up.

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