

## Case Report

# Advanced stage cervical carcinoma diagnosed one year after pregnancy: the importance of cervical cancer screening

Gayem Inayet Çelik<sup>1</sup>, Yasam Kemal Akpak<sup>2</sup>, Sercan Kantarci<sup>2\*</sup>,  
Alaattin Karabulut<sup>2</sup>, Serkan Oral<sup>3</sup>

<sup>1</sup>Izmir Medicana International Hospital, Department of Obstetrics and Gynaecology, Izmir, Turkey

<sup>2</sup>Department of Obstetrics and Gynaecology, Tepecik Training and Research Hospital, Izmir, Turkey

<sup>3</sup>Halic University, Department of Obstetrics and Gynaecology, Istanbul, Turkey

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### \*Correspondence:

Dr. Sercan Kantarci,

E-mail: [sercan.kntrc@gmail.com](mailto:sercan.kntrc@gmail.com)

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### ABSTRACT

Cervical cancer is the most common gynecological malignancy during pregnancy. The incidence of cervical cancer during pregnancy is 0.004-0.1%. Cervical cancer accompanied by pregnancy may have severe maternal and fetal consequences. In our case, our patient died approximately 1 year after giving birth and 2 months after being diagnosed with cervical cancer. Among the treatment options, chemotherapy, radiotherapy and surgical treatment options were available alone or in combination. Type of treatment needed to be individualized and depended on stage, type of histology and gestational age. The aim of our study was to emphasize the importance of vaginal examination and its method during pregnancy in the diagnosis of cervical cancer, which was among the preventable cancers in pregnancy.

**Keywords:** Cervical cancer, Pregnancy, Infertility treatment, Vaginal examination, Human papilloma virus

### INTRODUCTION

Along with melanoma and breast cancer, cervical cancer is common for cancer during pregnancy.<sup>1</sup> Although the advancements in the cervical cancer screening programs of the countries affect decreasing this rate, the incidence of cervical cancer during pregnancy is 0.004-0.1%.<sup>2</sup> 20-30% of malignant tumors seen in women are seen under the age of 45.<sup>2</sup> Due to advances in assisted reproductive techniques and women's roles in society and business life, the average age at conception has improved. This situation has increased the coexistence of pregnancy and cancer. The main reason for this is the frequent examination of the cervix at the beginning of pregnancy and following weeks and the smear test at the first examination of the pregnancy.<sup>3</sup> Increased blood flow and lymphatic circulation, weakened immune response due to pregnancy, cervical dilatation and many other factors

facilitate the metastasis of possible cervical cancer during pregnancy.<sup>4</sup>

Approach to cervical cancer during pregnancy depends on tumor size, presence of lymph node involvement, gestational age, histological subtype and the patient's expectation from the continuation of the pregnancy.<sup>3,5</sup> Surgical treatment and chemoradiotherapy, the methods used in treating cervical cancer, affect the fetus negatively.<sup>6</sup> The patient should be evaluated with a multidisciplinary team consisting of a neonatologist, medical oncologist, gynecological oncologist and perinatologist with a personalized treatment.<sup>7</sup> Our case report emphasized the importance of cervical cancer screening and vaginal examination in early diagnosis and treatment during pregnancy.

## CASE REPORT

The patient, who was 30 years old, gravida 1 parity 1, university graduate was referred from an external center to our urology department with difficulty in urinating, which gradually increased in the last month. The patient was admitted to the urology department of our hospital in October 2020 with a urinary catheter inserted a week ago. The urology department evaluated the patient and she was admitted to the neurology service to investigate centrally originated pathology. Gynecology consultation was requested due to the complaint of bloody vaginal discharge. The patient had in vitro fertilization (IVF) attempts two times due to unexplained infertility in 4 years and became pregnant in the second trial. She had a live birth with cesarean delivery in November 2019. The patient's menstruation was regular, the last menstruation occurred three weeks ago and the last coital activity was described one month ago. She stated that she last had a smear test 2 years ago and the result was normal. She complained of occasional bloody vaginal discharge and a burning sensation in the vaginal area. She also reported that she recently used treatments for her complaints without a vaginal examination. It was understood that the patient had a sociocultural structure that did not accept vaginal examination.

In the first examination, the vaginal introitus was edematous, there was an appearance of a fragile mass that narrowed the vaginal entrance and having full-thickness vaginal involvement. Only one finger could be inserted into the vagina and the only area without involvement on palpation was the posterior fornix (Figure 1). On pelvic magnetic resonance imaging (MRI), a gross nonhomogeneous mass lesion was observed in the uterus, involving the whole myometrium except a focal area in the corpus anterior, protruding the endometrium and extending to the parametrium, especially at the level of the cervix. In the 2/3 lower part of the vagina, a similar solid mass lesion reached up to 5.5 cm in its widest axial diameter, extending to the periurethral area and compressing the urethra. Although the described gross mass lesion extended anterolaterally to the paravaginal area, the fatty planes between the rectum and the rectum were preserved; the posterior wall was intact at the level of the vaginal fornix, the lesion had not invaded the bladder and ischiorectal fossae are open (Figure 2).

Punch biopsy was performed on the palpable tumor tissue at 3, 7 and 9 o'clock, just behind the hymenal ring, under general anesthesia. The pathological examination resulted in poorly differentiated carcinoma. Tumor cells were stained CK7 and p16 focal positive and p40 negative in the immunohistochemical examination. These findings were considered in favor of cervical adenocarcinoma (Figure 3).

## Positron emission tomography/computed tomography (PET/CT) of the patient after pathological examination

Hypermetabolic nodular lesions with diffuse infiltration in both lungs, varying in size from a few millimeters to 15 mm and occupying almost the entire lung parenchyma were observed (maximum standardized uptake value) ( $SUV_{max}$ ): 5.8-14.6). No manifest pleural fluid was detected. The described lesions were evaluated in favor of lymphangitic metastatic spread. A hypermetabolic mass lesion with its widest dimension 102×97 mm was observed, forming hypodense contour lobulations and extending to the cervix ( $SUV$ : 13.1). After a short interval at the cervical level, the lesion continued as a separate component in the vagina surrounding the urethra. The size of this lesion was measured as 62×62 mm ( $SUV$ : 12.2). Pelvic and inguinal multiple hypermetabolic lymph nodes were observed. The rectum and sigmoid colon were in normal calibration. A nodular lesion with a diameter of 2.5 cm ( $SUV$ : 6.5) on the presacral fascia on the right was noticeable and was evaluated in favor of lymphadenopathy or metastatic implant. In the evaluation of bone structures, hypermetabolic metastatic lesions were noted in the ischium bone on the left, the iliac bone on the right and medially adjacent to the sacroiliac joint ( $SUV$ : 5.4-8).



Figure 1: Cervical appearance in vaginal examination.

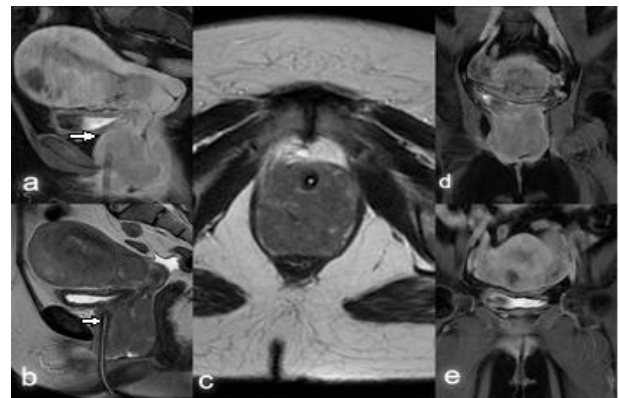
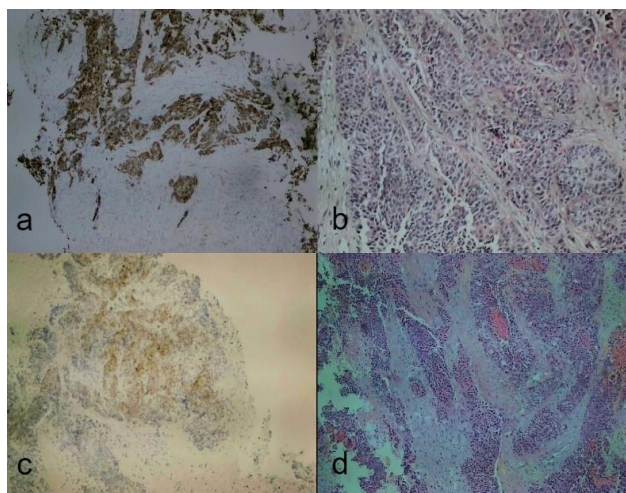


Figure 2: (a-d) Tumoral metastasis in different sequence (White arrow). (e) Anterior myometrial metastasis.



**Figure 3: (a) Immunohistochemically strong CK7 positive tumor islands (DAB, x40). (b) Carcinoma areas (HE, x100) that tend to form impaired adenoid structures. (c) Weak p16 positivity in tumor areas by immunohistochemically (DAB, x40). (d) It has formed large islands in the vaginal wall, and necrotic carcinoma areas in the middle of places (HE, x40).**

The patient was referred to medical oncology with the diagnosis of stage 4 cervical carcinoma with the results. Paclitaxel+carboplatin chemotherapy was started for the patient. The patient, who received chemotherapy intermittently due to respiratory distress and completed four doses of chemotherapy in total, died two months after the diagnosis due to respiratory failure.

## DISCUSSION

Cervical cancer, which was the most common gynecological malignancy during pregnancy was observed in 1/1200-10000 of pregnancies in western societies.<sup>1</sup> Being the only type of cancer screened during the prenatal period made cervical cancer an important position. The frequency of preinvasive lesions observed in the general population had increased and the expectation for treatment with fertility-sparing treatment methods had also increased.<sup>2</sup> This necessitated special attention to cervical preinvasive lesions in terms of follow up and treatment. The cervicovaginal smear (CVS) test taken during pregnancy should be evaluated carefully as physiological changes in the cervical cells can mimic cervical dysplasia.<sup>5</sup> Because of the suppression of the immune system during pregnancy and the highest levels of cervical squamous metaplasia, preinvasive lesions regress after pregnancy. Therefore, conservative approaches to lesions observed during pregnancy were seen as the first choice.<sup>5</sup>

The most frequently diagnosed abnormal cervical cytology during pregnancy was low-grade intraepithelial lesion (LSIL) and atypical squamous cells of undetermined significance (ASCUS). High-grade intraepithelial lesion (HSIL) was observed less

frequently. Malignancy potential in high-grade lesions had been reported as 5%.<sup>8</sup> Although preinvasive lesions of the cervix were high-grade lesions, they can be postponed to the postpartum period.<sup>9</sup> Post pregnancy regression was often expected in these lesions. In preinvasive lesions of the cervix, the delivery method depended on obstetric indications.<sup>4</sup> Although the colposcopy procedure applied for diagnostic purposes in cervical smear abnormalities was technically not easily applicable due to physiological cervical changes and increased metaplasia during pregnancy, it was the method that should be preferred due to the high false-negative rates of randomly performed four-quadrant biopsies.

Chemosensitivity in cervical cancers had been reported at a rate of 78-95%, therefore, neoadjuvant chemotherapy can be applied as another treatment method in pregnancies older than 20 weeks and radiotherapy can be postponed after delivery.<sup>10</sup> Cisplatin was considered a relatively safe chemotherapy option during pregnancy.<sup>11</sup> Cisplatin and etoposide were the most commonly used agents. Chemotherapy protocols with cisplatin and etoposide (PE) or vincristine, adriamycin and cyclophosphamide (VAC) have been shown to prolong the estimated survival time.<sup>12</sup> Conization was sufficient in the treatment of stage 1A1 patient group. It should be kept in mind that if the surgical margin was negative due to pathology, it can be accepted as the final treatment, but if it was positive, recognition may be required.<sup>13</sup> In stage 1A1-1B1 tumors, large conization or trachelectomy may be sufficient in patients with a tumor diameter of <2 cm. However, it should be considered that these procedures increased the risk of pregnancy complications such as preterm labor and premature rupture of membranes. In addition, the presence of positive lymph nodes in this stage 1B1 patient group required the patient to start definitive treatment as soon as possible.<sup>14</sup> Conservative surgical treatments were not possible during pregnancy in patients with stage 1B1, tumor diameter >2 cm and more advanced stage. Until the maturation of the fetus was completed, the neoadjuvant chemotherapy option should be considered. The pregnancy should be terminated at the first opportunity when the maturation was thought to be completed. Then the radical postpartum hysterectomy should be applied to the patient after birth.<sup>5</sup> According to current guidelines, the preterm delivery option can be considered acceptable to complete the mother's oncological treatment.<sup>15</sup>

Pregnancy-related admissions of women who do not undergo routine health screening enable many women in this period to get an early diagnosis. Cesar et al asked women about the CVS test performed during pregnancy in their study involving 2288 women. They found that 33% of the women did not take the CVS test during pregnancy, 2/3 did not know about the test's necessity, and 18% did not take the test because of feelings of fear and embarrassment. They stated that not taking the CVS test at the reproductive ages, when the frequency of cervical cancer was at its peak, might increase the

morbidity and mortality rate of cervical cancer.<sup>16</sup> Likewise, in this case, it was understood that the sociocultural background caused disruptions in CVS follow up.

## CONCLUSION

These studies on the reliability and applicability of the CVS test evaluated during pregnancy draw attention to the importance of taking the CVS test following the routine cervical cancer screening algorithm during antenatal evaluation. Pap smear tests taken during antenatal follow up will reduce morbidity and mortality caused by cervical cancer by detecting preinvasive lesions in women who are not accessible within the scope of the screening program and have limited access to health services. In this case, although the patient had undergone IVF treatments and pregnancy in the last two years, the cervical examination was unfortunately missed and the patient was diagnosed with stage 4 cervical cancer within one year after delivery. Regardless of the reason for applying to the gynecology and obstetrics outpatient clinic in young patients, CVS test history should be questioned and if necessary, a test should be applied according to the screening program. The increase in the last decade in cervical cancer cases, which have an aggressive course at early ages, suggests that screening programs should be reviewed again. The need for more effective screening of patients under IVF treatment may come to the fore.

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## REFERENCES

- Eibye S, Kjær SK, Mellemkjær L. Incidence of pregnancy-associated cancer in Denmark, 1977-2006. *Obstet Gynecol.* 2013;122(3):608-17.
- Pentheroudakis G, Pavlidis N. Cancer and pregnancy: poena magna, not anymore. *Eur J Cancer.* 2006;42(2):126-40.
- Sood AK, Sorosky JI, Mayr N, Anderson B, Buller RE, Niebyl J. Cervical cancer diagnosed shortly after pregnancy: prognostic variables and delivery routes. *Obstet Gynecol.* 2000;95:832-8.
- Beharee N, Shi Z, Wu D, Wang J. Diagnosis and treatment of cervical cancer in pregnant women. *Cancer Med.* 2019;8(12):5425-30.
- Han SN, Gziri M, Calsteren KV, Amant F. Cervical cancer in pregnant women: treat, wait or interrupt? Assessment of current clinical guidelines, innovations and controversies. *Ther Adv Med Oncol.* 2013;5(4):211-9.
- Korenaga TK, Tewari KS. Gynecologic cancer in pregnancy. *Gynecol Oncol.* 2020;157(3):799-809.
- Han J, Hu X, He X, Wang J, Mueller MD, Papadia A, et al. Cervical cancer in pregnancy: one case report and a review of current treatment recommendations. *Gynecol Pelvic Med.* 2019;2:10.
- Ackermann S, Gehrsitz C, Mehlhorn G, Beckmann MW. Management and course of histologically verified cervical carcinoma in situ during pregnancy. *Acta Obstet Gynecol Scand.* 2006;85(9):1134-7.
- Paraskevaidis E, Koliopoulos G, Kalantaridou S, Pappa L, Navrozoglou I, Zikopoulos K, et al. Management and evolution of cervical intraepithelial neoplasia during pregnancy and postpartum. *Eur J Obstet Gynecol Reprod Biol.* 2002;104(1):67-9.
- Karam A, Feldman N, Holschneider CH. Neoadjuvant cisplatin and radical cesarean hysterectomy for cervical cancer in pregnancy. *Nat Clin Pract Oncol.* 2007;4(6):375-80.
- Zagouri F, Sergentanis TN, Chrysikos D, Bartsch R. Platinum derivatives during pregnancy in cervical cancer: a systematic review and meta-analysis. *Obstet Gynecol.* 2013;121:337-43.
- Akpak YK, Gun I. Advance stage small cell neuroendocrine carcinoma of cervix: a case report. *East J Med.* 2013;18(1):41-4.
- National Health Commission Of The People's Republic Of China. Chinese guidelines for diagnosis and treatment of cervical cancer 2018 (English version). *Chin J Cancer Res.* 2019;31(2):295-305.
- Hecking T, Abramian A, Domröse C, Engeln T, Thiesler T, Leutner, et al. Individual management of cervical cancer in pregnancy. *Arch Gynecol Obstet.* 2016;293(5):931-9.
- Amant F, Calsteren KV, Halaska MJ, Beijnen J, Lagae L, Hanssens M, et al. Gynecologic cancers in pregnancy: guidelines of an international consensus meeting. *Int J Gynecol Cancer.* 2009;19(1):1-12.
- Cesar JA, Santos GB, Sutil AT, Cunha CF, Sde CD. Pap smears among pregnant women in Southern Brazil: a representative cross-sectional survey. *Rev Bras Ginecol Obstet.* 2012;34(11):518-23.

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