EJGO European Journal of Gynaecological Oncology

Case Report

Clear cell carcinoma of the vagina followed by breast cancer in a patient without prenatal diethylstilbestrol exposure

Isao Otsuka[1]

[1]*Department of Obstetrics and Gynecology, Kameda Medical Center, 929 Higashi-cho, Kamogawa, Japan*

Summary

Clear cell carcinoma of the vagina or cervix and breast cancer are the only malignancies associated with prenatal diethylstilbestrol (DES) exposure. Clear cell carcinoma of the vagina develops mainly in young women, and rarely develops in elderly women without DES exposure. A 68-year-old woman, who had not experienced prenatal DES exposure or received hormone replacement therapy, presented with vaginal bleeding. Pelvic examination revealed a 3-cm polypoid solid mass in the posterior fornix. Biopsy showed clear cell carcinoma. She underwent radical hysterectomy with posterior vaginal wall resection. Thirty-four months after the surgery, she developed pulmonary metastasis and underwent video-assisted tumor resection. Forty-nine months after the initial surgery, screening mammography revealed an abnormal breast mass. Biopsy revealed invasive lobular carcinoma, and she underwent breast resection followed by radiation therapy. She remained well with no evidence of disease 89 months after the initial surgery.

Key words: Clear cell carcinoma; Vagina; Pulmonary metastasis; Breast cancer.

Introduction

Clear cell carcinoma of the vagina is a rare malignancy, which mainly develops in young women who had prenatal exposure to diethylstilbestrol (DES), and less frequently develops in women with congenital anomalies of the genitourinary tract. We present a case of clear cell carcinoma of the vagina in a 68-year-old woman without prenatal DES exposure or congenital anomalies, who subsequently developed breast cancer, which is the only other cancer associated with prenatal DES exposure.[1, 2]

Case Report

A 68-year-old woman, gravida 2, para 2, presented with vaginal bleeding. She had not been exposed to DES prenatally. Her menarche and menopause occurred at 15 and 50 years of age, respectively. She underwent left salpingo-oophorectomy for a benign ovarian cyst at 35 years of age, and did not subsequently receive hormone replacement therapy. Pelvic examination revealed a 3-cm dark red polypoid solid mass in the posterior fornix. Biopsy showed clear cell carcinoma (Figure 1), whereas the results of cytological examination were normal. Pelvic magnetic resonance imaging and whole-body positron emission tomography/computed tomography (PET/CT) revealed no metastatic disease. Her serum CA-125 level was 13 U/mL. She was diagnosed with stage I vaginal carcinoma and underwent radical hysterectomy with posterior vaginal wall resection, right salpingo-oophorectomy, and pelvic lymphadenectomy. Since no paravaginal extension or lymph node metastasis was observed, she was followed up regularly without adjuvant therapy. Thirty-four months after the surgery, her serum CA-125 level was found to be elevated to 47 U/ml. PET/CT revealed a 23-mm mass in the lower lobe of the right lung. As a needle biopsy showed carcinoma, she underwent video-assisted tumor resection with lymphadenectomy. Pathological examination showed a clear cell carcinoma; the tumor was then diagnosed as pulmonary metastasis from vaginal carcinoma. As no lymph node metastasis was observed, she did not receive adjuvant therapy. Forty-nine months after the initial surgery, screening mammography revealed an abnormal breast mass. Biopsy revealed invasive lobular carcinoma. She underwent endoscopic breast resection with sentinel node biopsy, which revealed no lymph node metastasis, followed by radiation therapy. As the breast cancer was positive for estrogen and progesterone receptors, the patient received aromatase inhibitor treatment. She remained well with no evidence of disease 89 months after the initial surgery.

Discussion

Clear cell carcinoma of the vagina or cervix and breast cancer are the only malignancies associated with prenatal DES exposure [1, 2]. Although our patient had not experienced prenatal exposure to synthetic estrogen, it may be possible that she was affected by prenatal environmental estrogens,[3] including phytoestrogens (plant-derived dietary estrogens) and xenoestrogens (industrial chemicals, such as polychlorinated biphenyls and dioxins), which exert similar effects to those of DES. A second peak of clear cell carcinoma has been shown to occur in DES-unexposed women aged 50-80 years, suggesting that this may also be the case

Eur. J. Gynaecol. Oncol. - ISSN: 0392-2936
41, n. 4, 2020
doi: 10.31083/j.ejgo.2020.04.5007

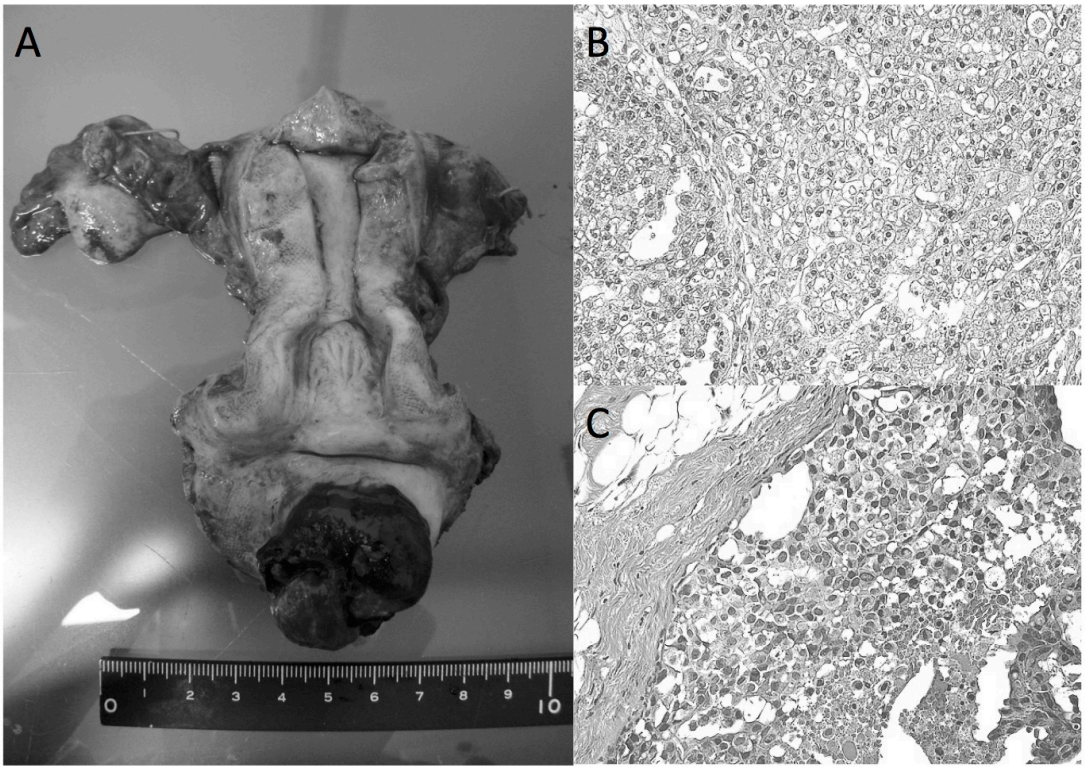

Figure 1. — A. Gross appearance of clear cell carcinoma of the vagina (left adnexa had been previously removed); B. Clear cell carcinoma of the vagina; C. Invasive lobular carcinoma of the breast.

in DES-exposed women.[4] Although breast cancer in our case may have been a chance occurrence, it may be associated with prenatal estrogen exposure, since breast cancer risk is elevated in DES-exposed women aged over 40 years [1]. To our knowledge, this is the first case where a vaginal clear cell carcinoma patient has subsequently developed breast cancer.

Radical surgery appears to be an appropriate method for the management of clear cell carcinoma of the vagina. In stage I vaginal adenocarcinoma, treatment with radical hysterectomy, vaginectomy, and lymph node resection are associated with a lower risk of recurrence compared to local excision via the vaginal route [4]. Stage I tumors have approximately a 16% risk of pelvic node spread [4].

Long-term follow-up appears to be necessary for patients with vaginal clear cell carcinoma, as late recurrences have often been reported. The most frequent sites of metastasis are the pelvis and lungs [4]. Solitary recurrences in these sites should be excised if possible [4]. Radiation treatment can also be an effective alternative.

Ethics Approval and Consent to Participate

The patient gave her informed consent.

Acknowledgments

The author thanks the staff at the Department of Obstetrics and Gynecology and the Department of Pathology at Kameda Medical Center for their help with this study.

Conflict of interest

The author declares no conflict of interest.

Submitted: October 05, 2018
Accepted: December 03, 2018
Published: August 15, 2020

References

[1] Troisi R., Hatch E.E., Titus-Ernstoff L., Hyer M., Palmer J.R., Robboy S.J., *et al.*: "Cancer risk in women prenatally exposed to diethylstilbestrol". *Int. J. Cancer*, 2007, *121*, 356.
[2] Soto A.M., Brisken C., Schaeberle C., Sonnenschein C.: "Does cancer start in the womb? Altered mammary gland development and predisposition to breast cancer due to in utero exposure to endocrine disruptors". *J. Mammary Gland. Biol. Neoplasia*, 2013, *18*, 199.
[3] Newbold R.R.: "Lessons learned from perinatal exposure to diethylstilbestrol". *Toxicol. Appl. Pharmacol.*, 2004, *199*, 142
[4] Herbst AL.: "Behavior of estrogen-associated female genital tract cancer and its relation to neoplasia following intrauterine exposure to diethylstilbestrol (DES)". *Gynecol. Oncol.*, 2000, *76*, 147.

Corresponding Author:
ISAO OTSUKA, M.D., PH.D.
Department of Obstetrics and Gynecology, Kameda Medical Center, 929 Higashi-cho, Kamogawa (Japan)
e-mail: otsuka.isao@kameda.jp