



Invasive Ductal Carcinoma of the Breast with Metastasis to the Uterine Cervix

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Abstract

Hematogenous metastasis of breast cancer tumors frequently occur at the lung, bones, liver and brain. However, presence in the cervix remains rare, since the majorities of tumors in this organ are primary carcinomas or result from the direct extension of primary pelvic tumors. The number of reported metastases to the uterus and cervix remains low. Invasive lobular carcinoma spreads to gynecologic organs more frequently than invasive ductal carcinoma. We report a rare clinical case, as well as discuss its implications and peculiarities. A 64-year-old postmenopausal woman with invasive ductal carcinoma metastatic to the cervix more than 15 years after the termination of bilateral breast cancer treatment. A literature analysis confirmed that most cases presented with vaginal bleeding or abdominal discomfort, but many were asymptomatic. Common characteristics between the cases were the patient's age, the time period between primary tumor diagnosis and the emergence of metastatic lesions, treatment, medication, and signs/symptoms. Although rare, metastasis should be considered in women with a history of breast cancer, particularly with abnormal vaginal bleeding as a symptom.

Keywords: Breast cancer; Cervix; Metastasis; Histopathology; Immunohistochemistry

Introduction

Breast cancer is the most common malignancy in women. More than one million breast cancer cases are diagnosed per year, and it is one of the major causes of cancer death [1]. The female genital tract is rarely affected by metastatic tumors. The most common anatomic locations for metastases to the female genital tract are the ovaries and the vagina. Among extragenital cancers metastasizing to the female genital tract, breast is the most common primary site, followed by the gastrointestinal tract, lung, kidney and skin (melanoma) [1,2]. Literature reports the incidence of breast cancer metastasizing to the uterus is between 3.8% to 8% [3,4]. As to breast cancer metastasizing to the cervix, lobular carcinoma is the most common type with about 60% of patients has metastases at the time of diagnosis [5-7]. We present a case of invasive ductal breast carcinoma metastasized to the cervix more than 15 years after the end of breast cancer treatment.

Case Presentation

A 64-year-old at the time of writing postmenopausal woman, (gravid 5, para 5) without significant past medical or family history, was diagnosed with grade-2 invasive ductal carcinoma of the right breast 15 years ago (January 2004), measuring 2 cm at the largest tumor diameter, with edema of the skin, and clinically positive axilla. There was no blood or lymphatic invasion (T1N1M0-stage IIA). Immunohistochemistry (IHC) revealed that the tumor was estrogen-receptor positive, progesterone-receptor positive, and human epidermal growth factor receptor-2 (HER-2-receptor) negative. The patient was treated initially by a right modified radical mastectomy and axillary clearance surgery followed by adjuvant chemotherapy with 4 cycles of Adriamycin Cytosol and 4 cycles of Taxol. No radiotherapy or hormonal therapies were given. Six months later (July 2004), the patient was kept on follow up and developed a left breast mass (3 cm). A mammogram and biopsy confirmed invasive ductal carcinoma (T2N0M0). IHC revealed that the tumor was estrogen-receptor positive, progesterone-receptor negative, and HER-2-receptor negative. Similarly, the patient was treated initially by a left modified radical mastectomy and axillary clearance surgery followed by adjuvant chemotherapy with 4 cycles of Taxotere. Hormonal therapy (tamoxifen and Zoladex then Arimidex) and follow up continued until 2011. In May 2011, the patient had abnormal uterine bleeding; diagnostic work-up was initiated to detect possible causes of the vaginal bleeding.

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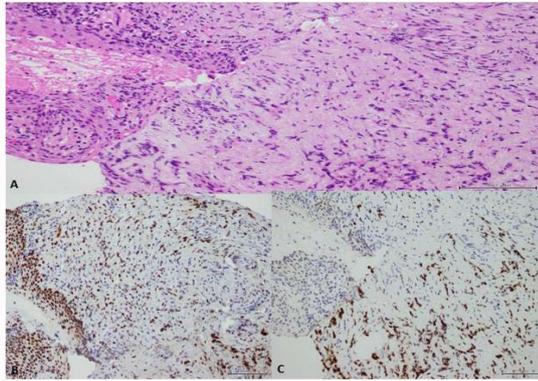


Figure 1: The subtle microscopic evidence of involvement of the cervical biopsy by metastatic carcinoma. A: There are individual cells arranged in cords infiltrating the submucosa (H&E, x40). B: The cells are immunoreactive for GATA-3 (x40). C: the cells are immunoreactive for Estrogen Receptor (ER) immunostain (x40). Sections examined show tumor cells arranged in an Indian-file pattern, dissecting in between the fibrous tissue in the submucosa. The overlying squamous epithelium of the vagina is unremarkable with no evidence of dysplasia. The cells are arranged individually with a deceiving bland appearance (Figure 1A). Individually, the tumor cells show eccentric hyper-chromatic nuclei, with abundant cytoplasm. Some of the tumor cells contain intra-cytoplasmic mucin. Immunostains are positive for GATA-3 (Figure 1B) and Estrogen Receptors (ER) (Figure 1C). In view of the history of breast carcinoma, this would be consistent with metastatic breast carcinoma rather than a primary female genital track malignancy.

On clinical examination, the cervix was indurated but lacked any visible tumor, on Transvaginal ultrasound measured the endometrial thickness at 5.0 mm, and Magnetic Resonance Imaging (MRI) revealed a thickened endometrial myometrium. A hysteroscopic examination revealed a cervical mass, and cervical cytology samples were collected. On pathology analysis (Figure 1), it was shown that the sample was compatible with metastatic breast carcinoma, which was confirmed by IHC (H and E staining). The tumor was positive for GATA-3 (Figure 1B) and estrogen receptors (Figure 1C). The morphology, the IHC findings, and the clinical history supported the diagnosis of ductal breast carcinoma metastatic to the cervix. The patient underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy for local control due to transvaginal bleeding. Pathology results demonstrated that the cervix shared the same histopathological features as those presented by the primary ductal breast carcinoma. Computed Tomography (CT) scans of the breast, pelvic organs, and uterine cervix showed no lesions or alterations and no evidence of extensive disease and no other distant metastasis. Bone scintigraphy was normal. Aromasin at 25 mg daily was initiated. She remained disease free until she had vaginal vault recurrence in July 2019 when images showed severe left-sided hydronephrosis due to a 4 cm enhancing mass in relation to the left side of the vaginal vault, this likely represented a metastatic deposit. An elective cystoscopy and a left double-J stent insertion were done. Three months later, positron emission tomography CT examination showed heterogeneous hypermetabolic activity likely within the cervix. A pelvic MRI showed a mass lesion with malignant features of the vaginal cuff/residual uterine cervix representing either a recurrence of the previously resected metastasis from the known breast cancer or a uterine cervix primary (Figure 2). A CT guided biopsy from the vaginal mass revealed a metastatic mammary carcinoma from the original breast carcinoma after a 15-year interval. Pelvic MRI in January 2020 showed a 2.6 cm vaginal cuff mass and no lymph node enlargement. At the time of this report, the patient is alive and receiving aromatase inhibitor therapy,

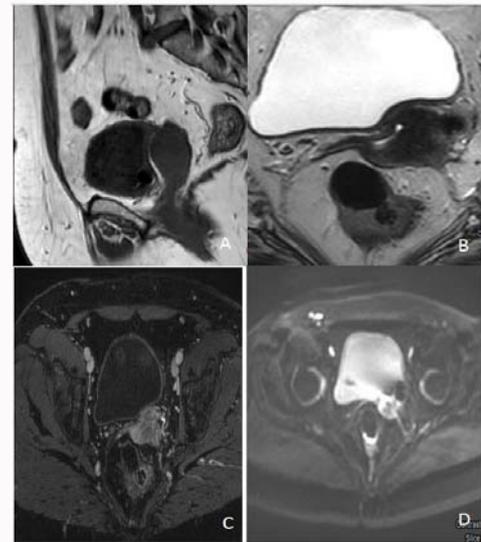


Figure 2: Pelvic magnetic resonance imaging examination. (A) Sagittal T1-weighted MRI. (B) Coronal T2-weighted MRI. (C) Axial mDIXON-W_HR MRI. (D) DWI. Enhancing mass lesion at the vaginal cuff, originating from the residual cervix and it measured about 3 cm × 3.4 cm × 3.6 cm in maximum diameters. Separate from the posterior wall of the urinary bladder, the mass shows significant water diffusion restriction on the DWI and ADC maps.

and is currently on fulvestrant cycle 4 as of 12th January 2020. Planned and received external beam radiotherapy for the vaginal vault mass is 45 Gy in 25 fractions, followed by brachytherapy boost to residual to bring the total dose to 75 Gy. The patient finished her sessions in February 2020, informed consent form was signed by the patient and she agreed to publish the case.

Discussion

There are few reports of breast cancer cases with cervical metastases. Here, we report a metastatic ductal carcinoma to the cervix presenting as abnormal uterine bleeding. Diagnosis was based on previous ductal breast carcinoma and IHC. When uterus is infiltrated, abnormal uterine bleeding is usually the most common manifestation, however, most of the uterine metastases are found on autopsy [8,9]. Mazur et al. [1] reported 325 cases of patients with metastasis to the female genital tract, the ovary and vagina were the most commonly affected sites; breast cancer had metastasized to ovaries in 88.5% of breast cancer cases. Metastasis to the vagina occurred in 5.8%, the endometrium in 3.8%, and the vulva in 1.9%. The uterine cervix was not affected in any of the cases [1]. Another study conducted in women with metastasis to the uterine cervix showed that the breast carcinoma metastatic to the uterine cervix occurred in 0.8% to 1.7% of case [10]. There are approximately 35 cases of breast cancer metastatic to the uterine cervix reported in the literature, most of them lobular carcinomas, ductal carcinoma was reported by Proença et al. [10] Mousavi et al. [11] and Green et al. [12] Metastases of lobular carcinoma is more common than in invasive ductal carcinoma, accounting for over 80% of breast cancers that spread to the female genital organs. Nevertheless, the prognosis is the same for both types of breast cancer [13]. In the majority of cases, the metastatic disease manifests itself as vaginal bleeding and abdominal discomfort. However, patients can be frequently asymptomatic, and the tumor is only found during an autopsy [14,15]. In our reported case, presentation was similar to other reports in the literature. In general, patients have a poor prognosis. A low-grade invasive lobular

carcinoma with estrogen-positive receptors at the time of diagnosis is considered to have a more favorable prognosis. Some may still obtain a complete response, as in this case, and remain disease-free for prolonged periods of time, even exceeding 20 years [13].

Conclusion

Although uterine cervix metastasis from breast carcinoma is rare, its association with a poor prognosis emphasizes the importance of maintaining a regular gynecological surveillance. Metastasis to the uterine cervix should be considered in women with a history of breast cancer, especially when they exhibit abnormal vaginal bleeding.

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