Case Reports in Women's Health 42 (2024) e00607

Contents lists available at ScienceDirect

Case Reports in Women's Health

journal homepage: www.elsevier.com/locate/crwh

Recurrent invasive ductal carcinoma of the breast with metastasis to the uterine cervix: A case report

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ARTICLE INFO

Keywords:
Cervical cancer
Breast cancer
Cervical cancer treatment
Gynecologic oncology
Breast cancer recurrence
Chemotherapy

ABSTRACT

This article presents a case of cervical metastasis from recurrence of invasive ductal carcinoma of the breast >20 years after initial diagnosis. The diagnosis was made after the patient presented with three months of intermittent post-menopausal vaginal spotting. She underwent palliative radiotherapy combined with chemotherapy and was disease free at the time of writing. Cervical metastasis of a primary breast cancer is extremely rare and can present with a variety of symptoms. This case report highlights the importance of life-long gynecologic care and surveillance in patients with a history of breast cancer.

1. Introduction

Cervical metastasis from primary breast cancer is rare, with the majority of its documentation in the literature in the form of case reports. Common sites of breast cancer metastasis include the lungs, bone, liver, and brain. It is estimated that the frequency of cervical metastasis from a primary breast cancer is between 0.8% and 1.7% [1]. Symptoms of cervical metastasis can vary from being asymptomatic to more commonly presenting as abnormal vaginal bleeding, dyspareunia, and pain [1]. While most cases arise from a primary invasive lobular carcinoma (ILC) pathology, there are a few cases reported in the literature of an invasive ductal carcinoma (IDC) pathology [1–3]. Treatment focuses on palliative measures and a combination of hormone therapy, chemotherapy, radiotherapy, and surgery, as there is currently no standardized treatment [4].

2. Case Presentation

A 72-year-old woman with a history of IDC of the left breast presented to the emergency room with a one-day history of heavy post-menopausal bleeding and crampy pelvic pain. In the preceding three months, she had experienced two episodes of vaginal bleeding. She was otherwise in good health and denied fatigue, lightheadedness, nausea, vomiting or weight loss. Her past medical history included IDC of the left breast, diagnosed >20 years previously. In addition, her medical history was notable for hypertension, obstructive sleep apnea, and chronic gout. She had been treated with a left-sided radical mastectomy and lymph node dissection. She received adjuvant chemotherapy with adriamycin and cyclophosphamide followed by radiation therapy. She was then on maintenance therapy with tamoxifen for seven years. She also had an autologous bone marrow transplantation and was under surveillance. Her last Papanicolaou smear, performed at age sixty-four, was negative for intraepithelial cervical lesions and concurrent HPV. She had no history of abnormal pap smears or cervical dysplasia. She had been monogamous (one male partner throughout adult life) and had no reported history of a sexually transmitted infection. She also denied use of tobacco, alcohol, and recreational drugs.

The patient presented to the emergency room with complaints of post-menopausal bleeding consisting of vaginal spotting, passage of blood clots, and new-onset crampy abdominal pain. Her last menstrual period was 25 years prior to presentation. The vaginal spotting had begun three months prior to presentation and had been intermittent and light. She was now experiencing passage of large blood clots and new-onset abdominal cramping.

Transvaginal ultrasound showed a 9.7 × 6.4 × 6.6 cm uterus with a 0.3 cm endometrial stripe. At a prompt gynecology follow-up

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https://doi.org/10.1016/j.crwh.2024.e00607
Received 29 February 2024; Received in revised form 1 April 2024; Accepted 3 April 2024
Available online 6 April 2024

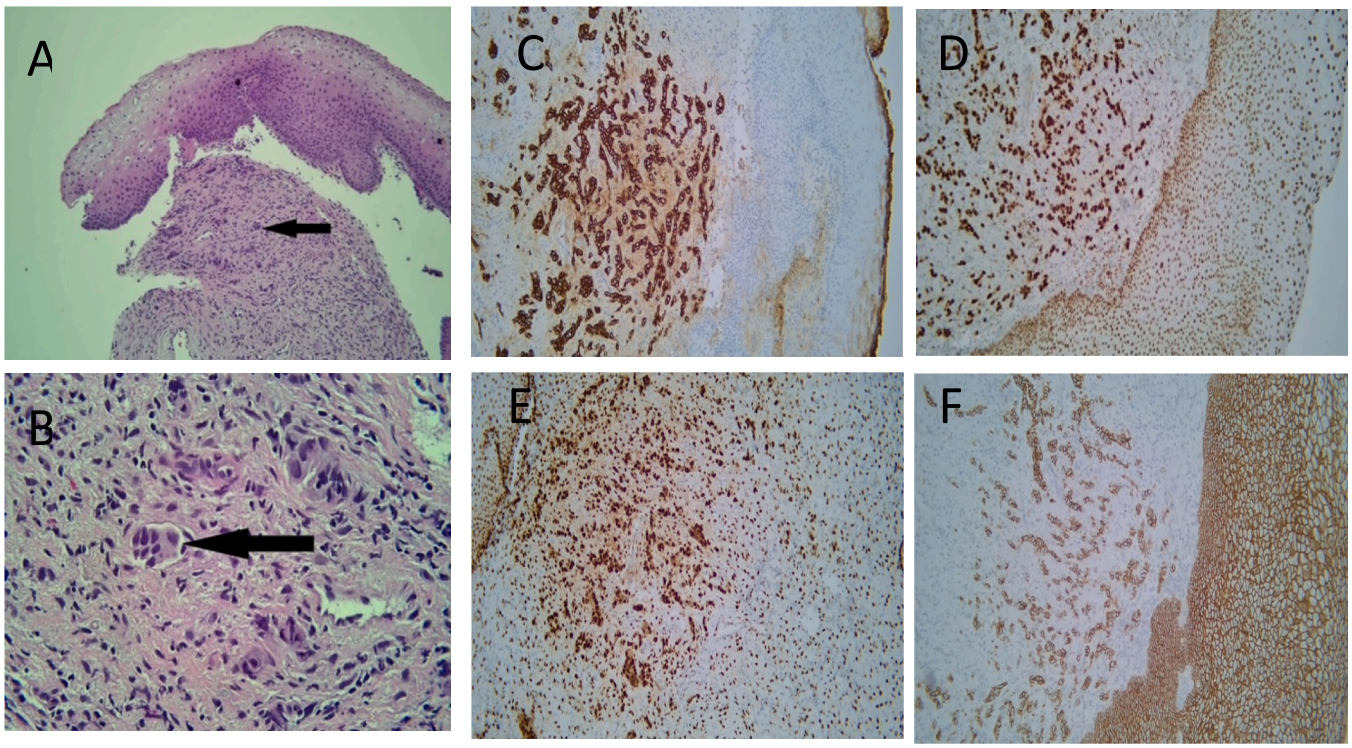

Fig. 1. Histopathological sections and immunochemistry demonstrating the phenotype compatible with mammary origin. (A) Histologic sections show unremarkable ectocervical squamous epithelium, and there are infiltrative tumor cells in the cervical stroma (arrow head, H&E stain at 10×). (B) On higher magnification, the tumor cells are large with hyperchromatic nuclei (arrow head, H&E stain at 40×). (C) The tumor cells are immunoreactive for CK7 (image 2, immunohistochemical stain with brown chromogen, 10×), (D) GATA-3 (image 3, immunohistochemical stain with brown chromogen, 10×), (E) ER (image 4, immunohistochemical stain with brown chromogen, 10×), (F) E-cadherin (image 5, immunohistochemical stain with brown chromogen, 10×). Mammaglobin immunohistochemistry immunoreactive but unable to be imaged due to tissue folds present. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

appointment, two ectocervical biopsies were obtained, which revealed that the lesions were poorly differentiated carcinoma, which showed immunoreactivity for CK7, GATA-3, ER (>70% cells) (Fig. 1), PR (40% of cells), and mammaglobin. The specimen did not have reactivity for P63, PAX8, CDX2. P16 staining was focal/rare, beta-catenin showed membranous staining, and E-cadherin expression was retained (Fig. 1). Together, this phenotype supported carcinoma of breast origin. Her subsequent scan revealed increased metabolic uptake within the inferior aspect of the uterus (Fig. 2A), consistent with carcinoma of the cervix. Her initial PET scan was also notable for multiple sclerotic bone lesions. Brain CT showed sclerotic osseous metastases in the calvarium, skull base, but no metastases in the brain.

She underwent palliative radiation to the uterus/cervix with 3000 cGy in 10 fractions and chemotherapy with abemaciclib and fulvestrant. Following her therapy, a positron emission tomography (PET) scan revealed an increased number of sclerotic metastases involving the axial and appendicular skeleton, but FDG uptake in the cervix previously seen was not appreciated (Fig. 2B). The patient developed osteomyelitis of the left shoulder and required debridement. Bone biopsy taken at the time of debridement was negative for metastasis in the infected shoulder. Abemaciclib was discontinued due to the diagnosis of osteomyelitis, and she was started on denosumab.

At the time of writing, the patient was free of metastasis to the uterine cervix and continued to be treated by her medical oncologist for bone metastasis.

3. Discussion

From the current literature, it is apparent that IDC with metastasis to the cervix has not been well studied due to its rarity. Cervical cancer arising from ILC is well known to have a distinct metastatic pattern, favoring bone, gastrointestinal tract, and the ovaries. For metastasis to be isolated to the cervix is extremely rare. The small size, dense fibromuscular composition, and sole afferent lymphatic drainage of the cervix makes it a less likely target of a metastatic cancer [5]. Recurrence in the first 5–10 years following initial treatment is the highest. In a cohort of premenopausal women initially diagnosed with non-metastatic breast cancer, the median time to recurrence was 45 months or approximately 5 years [6]. Approximately 35 cases of metastatic breast cancer to the cervix are reported in the literature. Of those, ductal carcinoma was reported by Proença et al. [3], Mousavi et al. [2], and Green et al. [1]. Metastasis of breast cancer to the uterus has been reported in >200 cases [7]. However, isolated metastases to the cervix from primary breast cancer was reported in a case series to have occurred in only 2 out of 26 cases examined [1]. The other 24 cases had metastatic disease from primary breast cancer present elsewhere in the body in addition to cervical involvement.

This case report highlights the rarity of cervical metastasis from IDC with recurrence after >20 years. In addition, this case is even more unusual because of the isolated cervical involvement. While abnormal vaginal bleeding or cervical abnormalities may initiate gynecological evaluation, some patients may be asymptomatic and/or have a normal-appearing cervix. Cochrane et al. [8] describe a patient who presented 10 years following treatment for IDC with purulent vaginal discharge. Her pelvic exam was unremarkable and endometrial sampling was negative for malignancy. Objectively, she exhibited all signs of an evolving infectious process, including leukocytosis, fevers, and continued purulent vaginal discharge. After she had undergone a total abdominal hysterectomy she was found to have metastatic breast cancer to the cervix. This case is in stark contrast to the one presented here, with an obvious mass on the patient's cervix. The variable presentation of cervical metastasis from primary breast cancer should prompt timely

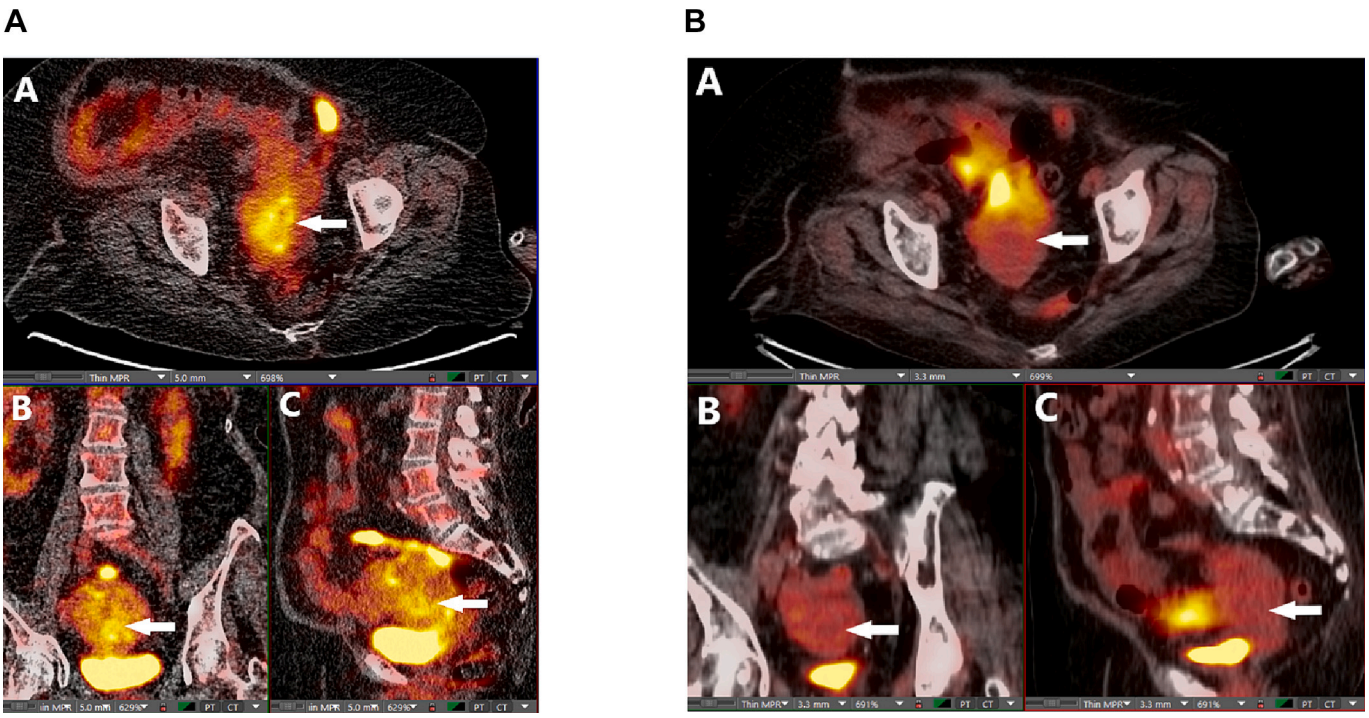

Fig. 2. A: (Cervix pre-radiation 600dpi.tiff): Axial (A), coronal (B) and sagittal (C) fused ^{18}FDG PET/CT images show abnormal increased FDG uptake in the lower uterine segment and cervix (white arrows), consistent with biopsy-proven metastatic invasive ductal carcinoma of the breast. Also noted are multiple sclerotic bone metastasis.
B: (Cervix post radiation 600dpi. tiff): Axial (A), coronal (B) and sagittal (C) fused ^{18}FDG PET/CT images show interval resolution of the previously seen abnormal increased FDG uptake in the lower uterine segment and cervix (white arrows).

workup of women with a history of breast cancer and unusual presenting gynecological symptoms. Additionally, any evidence of postmenopausal bleeding needs to be addressed immediately and any abnormal lesions should be biopsied.

4. Conclusion

Metastases from IDC of the breast to the cervix is rare. This case emphasizes the importance of a prompt and thorough clinical evaluation in patients with post-menopausal bleeding, including biopsies of any abnormal lesions. This case is unusual given that disease recurrence occurred was over 20 years from initial diagnosis and treatment of the primary breast cancer. Additionally, the clinical presentation of the late recurrence was vaginal bleeding, which led to the detection of other, more common metastatic sites, such as the bones, for which she was asymptomatic. This further supports the recommendation of continuing gynecologic care and surveillance for patients with a history of breast cancer.

Contributors

Alexander Dye contributed to conception of the case report, drafting the manuscript, the literature review, and revising the article critically for important intellectual content.

Vasanti Jhaveri contributed to conception of the case report, drafting the manuscript, and the literature review.

Savas Ozdemir contributed to analysis, interpretation, and description of radiological images.

Ahmad Alkhasawneh contributed to analysis, interpretation, and description of pathological specimens.

Karina Hew contributed to patient care, the conception of the case report, drafting the manuscript, the literature review, and revising the article critically for important intellectual content.

All authors approved the final submitted manuscript.

Funding

This work did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Patient consent

Obtained.

Provenance and peer review

This article was not commissioned and was peer reviewed.

Conflict of interest statement

The authors declare that they have no conflict of interest regarding the publication of this case report.

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