



## Case report

## Invasive ductal breast carcinoma metastasis to the cervix: A case review and clinical correlation

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## 1. Introduction

Breast cancer is the most common cancer in women in the United States, with the lifetime risk of breast cancer being 1:8, and it is the second leading cause of cancer death in women in the US (ACOG Committee on Practice Bulletins - Gynecology, 2012; Breast Disease). The two most common types of breast cancer are invasive ductal carcinoma (IDC) and invasive lobular carcinoma (ILC), representing about 80% and 15% of cases, respectively (Breast Disease). Prognostic factors and survival rates are primarily based on tumor stage, hormone receptor status, nuclear grade, and Her-2/neu expression (Breast Disease).

The common sites of metastatic breast cancer include bone, lung, liver, and brain (Breast Disease). Breast cancer metastasis to the uterine cervix is rare, occurring more commonly in patients with ILC. The metastatic patterns of lobular and ductal invasive breast cancer demonstrate some differences, although it is not explicitly known why that is so. ILC accounts for increased metastasis to the peritoneum, gastrointestinal tract and the ovaries, whereas IDC more commonly involves the lungs and the pleura (Mathew et al., 2017). Prior studies based on tumor registry data have demonstrated ILC metastasizes to the gynecologic organs in approximately 4.5% of cases, compared to IDC, which metastasizes in 0.8% of cases (Waks et al., 2015). There is minimal data on cervical metastasis from breast cancer, and a review of literature estimates that only 35 cases have been described thus far (Cervical Cancer; Fontainebleau et al., 2019).

Due to the infrequent occurrence of invasive ductal breast cancer metastasis to the cervix or uterus, prior research is mainly limited to case reports. In this case, we present a patient with metastatic invasive ductal breast cancer to the cervix in the setting of completion of

chemotherapy and radiation in March 2011.

## 2. Case

A 62-year-old G3P3 postmenopausal patient with a history of a Stage IIIA Grade 2, ER/PR positive, Her2/neu amplified, IDC of the right breast diagnosed in 2010 was referred to the gynecologic oncology service for further evaluation and treatment recommendations of purulent vaginal discharge.

The patient initially underwent a right mastectomy and right axillary lymph node dissection on January 10, 2010, when she was premenopausal. The final pathology demonstrated: estrogen receptor 95% nuclear staining with strong intensity, progesterone receptor 70% of nuclear staining with moderate intensity. Her2/neu performed by IHC was 2+, FISH for HER2/neu performed with HER2 and CEP 17 ratio 2.4. She underwent six cycles of chemotherapy, with Trastuzumab, Docetaxel, and Carboplatin from March 2010 until June 2010. She then completed a total of one-year treatment of Trastuzumab in March 2011. From July 2010 until September 2010, she completed postmastectomy radiotherapy. She was started on tamoxifen for approximately one year, but it was discontinued due to patient intolerance of therapy. She did not tolerate Leuprolide, either. She received a bilateral salpingo-oophorectomy for estrogen reduction approximately two years after diagnosis. No cancer predisposition genetic testing was performed. She was followed in the outpatient setting with surveillance mammograms and ultrasounds.

The patient had remained disease-free for ten years when she presented to her gynecologist for purulent dark vaginal discharge intermittently mixed with dark-red blood over a span of one month. She was

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prescribed clindamycin for a likely infection. Despite the clindamycin, the patient's discharge continued, and she reported low-grade fevers. Her gynecologist subsequently ordered blood work and imaging. Her WBC was elevated to 17. An MRI revealed an anteverted and anteflexed uterus, measuring  $3.8 \times 9.7 \times 11$  cm, and a moderately enhancing intramural left anterior fundal fibroid with submucosal extension, measuring  $3.17 \times 3.1 \times 4.1$  cm. The uterine cavity was distended and fluid-filled. The MRI revealed no evidence of a cervical mass.

With concern for malignancy in the setting of persistent pyometra, she was referred to the gynecologic oncology service. At the initial visit, her physical exam was significant for a normal-appearing cervix but an enlarged 10–12 cm uterus. An endometrial biopsy was performed, at which time significant purulent discharge was noted. The plan was made for a total abdominal hysterectomy and possible endometrial cancer staging. The patient was prescribed doxycycline and metronidazole to take until her surgery. Endometrial biopsy resulted as predominantly aggregates of neutrophils with rare strips of glandular and squamous epithelium.

The patient subsequently underwent a total abdominal hysterectomy. Intraoperative findings were significant for an 8–10 cm uterus, absent fallopian tubes and ovaries, and an otherwise normal pelvis and upper abdomen. On gross inspection after specimen removal, pyometra was noted. There were no endometrial masses. A small submucosal myoma was appreciated, as well as a firm, but normal appearing cervix. The patient did well postoperatively and was discharged on postoperative day one. Final pathology demonstrated adenocarcinoma with micropapillary features of the cervix, most compatible with metastatic carcinoma of the breast. The tumor was positive for GATA3, ER, and PR and was negative for PAX8. Metastatic workup with a CT scan of the chest, abdomen, and pelvis, and a bone scan was negative for disease. Initially, the patient was to undergo four weekly applications of intravaginal brachytherapy via vaginal cylinder using high dose rate radioactive iridium-192; however, the patient elected to postpone this due to the COVID-19 pandemic. She was then started on letrozole 2.5 mg daily.

### 3. Discussion

This case presents a rare and not well-studied entity: IDC with metastasis to the cervix. The most common locations for breast cancer to metastasize include the bones, lung, liver, and brain. While it is poorly understood, IDC and ILC both have different metastatic profiles. As referenced above, it is estimated that IDC metastasize to the gynecologic organs in less than 1 percent of the cases (Waks et al., 2015). Furthermore, metastasis to the cervix from non-gynecologic cancers is an uncommon occurrence. Given the rarity of metastatic disease to the cervix, it was important to first confirm that our patient's disease was metastatic breast cancer as opposed to a primary cervical cancer. In this case, the pathology was suggestive of adenocarcinoma with micropapillary features, raising suspicion for a metastatic lesion from breast cancer given that the tumor stained positive for GATA3 (more suggestive of breast cancer) and negative for PAX 8 (suggestive of Müllerian system origins). The cervical tumor was also compared to the patient's original tumor and was consistent with recurrence of her primary breast cancer.

While data is limited on primary cancers metastasizing to the cervix, typically, most cancers in the cervix (primary or metastatic) that are symptomatic, present in a similar way with persistent abnormal bleeding and/or discharge (Cervical Cancer). Other times, a hard mass or visible tumor is present. This patient presented in an atypical fashion with persistent pyometra and occasional dark brown/red discharge, more suggestive of an ongoing infection, or possible uterine cancer. Furthermore, recent cervical cytology was normal, and her MRI, completed two weeks prior to her scheduled hysterectomy, was significant for only a distended endometrial cavity containing fluid. The cervix was noted to be normal with no masses. Interestingly, the endometrial

biopsy performed as well as repeat cytology, were suggestive of ongoing inflammation and infection. It was not until intraoperatively when a firm cervix was appreciated that any significant cervical pathology was suspected. However, given the normal appearance of the cervix on gross inspection, the surgery was completed without intraoperative assessment of the specimen.

This case is also atypical in that her primary cancer was IDC, not ILC. While breast metastasis to the cervix is rare, the majority of case reports describe ILC, not IDC. Though it is not truly understood why ILC may have a higher propensity to metastasize to the cervix as compared to IDC, it may be due to the molecular composition of the disease (Waks et al., 2015). There are few cases of IDC with metastasis to the cervix that have been reported in the literature, and the outcomes vary between patients. Proenca et al describe a patient who was had cervical metastasis from her IDC and was subsequently treated with chemotherapy (Proenca et al., 2016). This patient, unfortunately, was found to have progression of her disease and discovery of additional widespread metastasis. Thouvenot et al describe a case of a deteriorating 86 year old with a cervical metastatic lesion from her IDC (Thouvenot et al., 2018). This patient declined further intervention given her clinical status. Unlike the cases described by Proenca and Thouvenot, Green et al describe a case where the patient had a cervical metastasis from her IDC, underwent a laparoscopic-assisted vaginal hysterectomy and continued on to complete her adjuvant chemotherapy (Green et al., 2004). The patient achieved clinical remission and reported to be alive and well at the time of the case report submission.

In summary, this case presents an atypical presentation of a rare and not well-researched phenomenon: primary breast invasive ductal carcinoma metastasizing to the cervix. The presentation reiterates and emphasizes the importance of performing a full and thorough gynecologic workup when abnormalities are present in the setting of a history of breast cancer. Though another case report, we hope to add to the limited literature with a goal of raising suspicion of the potential of rare metastatic lesions to the gynecologic structures in patients who present with atypical symptoms. We also aim to contribute to the literature that exists on the workup, treatment, and outcomes of metastatic invasive ductal carcinoma of the breast.

### Author contribution

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### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### References

- ACOG Committee on Practice Bulletins – Gynecology, 2012, reaffirmed 2016. Practice Bulletin No. 126: Management of gynecological issues in women with breast cancer. *Obstet. Gynecol.* 119, 666–682.

- Breast Disease. In: Hoffman, B.L., Schorge, J.O., Bradshaw, K.D., Halvorson, L.M., Schaffer, J.I., Corton, M.M. (Eds.), *Williams Gynecology*, 3e. McGraw-Hill, New York, NY.
- Cervical Cancer. In: Hoffman, B.L., Schorge, J.O., Bradshaw, K.D., Halvorson, L.M., Schaffer, J.I., Corton, M.M. (Eds.), *Williams Gynecology*, 3e. McGraw-Hill, New York, NY.
- Fontainebleau, D.R.S., Vieriera, S.C., Junior, R.G.S., Rodrigues, T.S., 2019. Lobular carcinoma of the breast with metastasis to the uterine cervix. *J. Cancer Res. Ther.* 15 (6), 1411–1414.
- Green, A.E., Biscotti, C., Michener, C., Belinson, J., 2004. Isolated Cervical metastasis of breast cancer: a case report and review of the literature. *Gynecol. Oncol.* 95 (1), 267–269.
- Mathew, A., Rajagopal, P., Villgran, V., Sandhu, G., Jankowitz, R., Jacob, M., Rosenzweig, M., Oesterreich, S., Brufsky, A., 2017. Distinct pattern of metastases in patients with invasive lobular carcinoma of the breast. *Geburtshilfe Frauenheilkd* 77 (6), 660–666.
- Proenca, S., Reis, M.I., Cominho, J., Conde, P.C., Pererira, H.S., Ribeiro, F.C., 2016. Metastatic breast cancer in uterine cervix: a rare presentation. *J. Lower Genital Tract Disease* 20 (1), e1–e3.
- Thouvenot, A., Bizet, Y., Baccar, L.S., Lamuraglia, M., 2018. Primary breast cancer relapse as metastasis to the cervix uteri: a case report. *Mol. Clin. Oncol.* 9 (1).
- Waks, A.G., Lennon, J., Yadav, B.S., Huang, H., Carmen, M.D., Johnson, N.B., Reynolds, K., Schapira, L., Gilman, P.B., Overmoyer, B., 2015. Metastasis to the cervix uteri 15 years after treatment of lobular carcinoma of the breast. *Semin. Oncol.* 42 (4), e81–e94.