



Case Report

# Distant Metastasis to Genital Organs in Infiltrating Ductal Carcinoma of the Breast in a Young Patient

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## Abstract

A case of metastatic involvement of uterus including cervix in a 37-year old patient with invasive ductal breast carcinoma, ER/PR positive but HER-2 negative and managed on tamoxifen for 2 years is reported. The patient presented with post-coital spotting. Importance of pelvic examination during follow-up of pre-menopausal patients on tamoxifen is emphasized. All patients of breast cancer presenting with vaginal bleeding and/or an enlarged uterus must be evaluated for metastatic involvement of the female genital tract.

**Keywords:** Uterus; Cervix; Metastasis; Ductal carcinoma; Breast

## Introduction

Breast cancer is the most common cancer in women. Current treatments of patients have significantly improved survival, bringing into focus the delayed effects of treatment and effects on quality of life. Even though only 12% of young women between 20-34 years represent a minority of breast cancer patients, but they have distinct concerns and issues compared to older women, including queries related to fertility and pregnancy. We present a case of metastasis to uterus and cervix in a young patient with invasive ductal breast cancer seeking medical attention for post-coital spotting. Metastasis to the uterus in breast cancer patients is often overlooked due to its rare incidence.

## Case Presentation

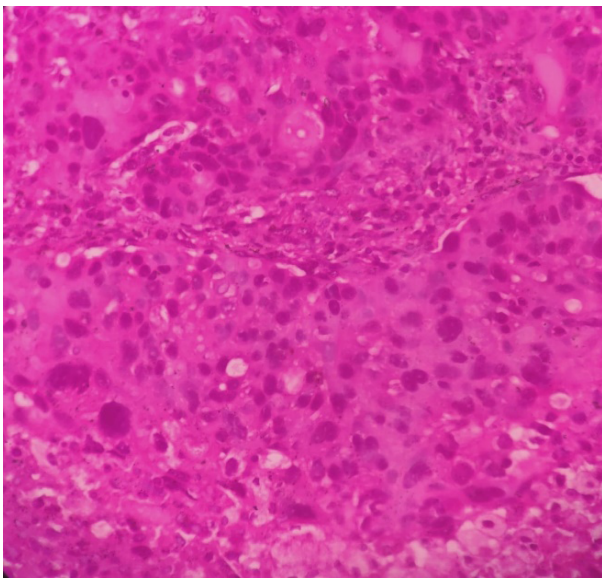
A 37-year-old female patient reported at the Gynecology Clinic with profuse bleeding per vagina for 3 days. The patient

had two episodes of post-coital spotting 4 months and 3 months back, which stopped spontaneously like light menstrual flow. The patient was P2L2, last child born 8 years ago and had no history of hormonal contraceptive intake. In presence of continuous bleeding, a speculum examination revealed a friable growth on the anterior wall of the cervix partially obliterating the os. Internal examination revealed a bulky uterus. The bleeding originated from the friable tissue of the cervix and a biopsy sample was obtained from the same. USG found a uterus with endometrial thickness of 15 mm, hyperechoic content in the uterine cavity and cervical canal (5.5cm x 2.8cm), a multi loculated cystic lesion 4.6 cm x 3.6cm mass seen in left adnexa with no solid component. The right ovary, liver, gall bladder, spleen and both kidneys were normal.

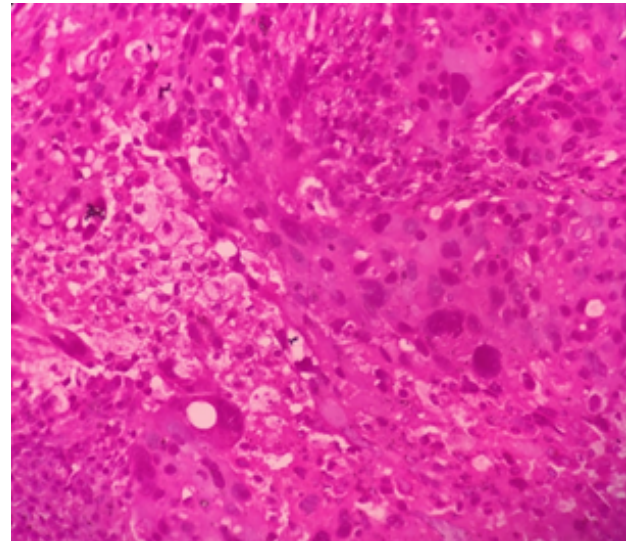
Past history revealed that the patient had a breast lump at 34 years of age. The tumour was 2 cm x 2.5 cm, firm and located in the upper outer quadrant (UOQ), with a mobile node palpable in axilla (1.5 cm x 1.5 cm). Patient disclosed that her mother had also suffered from breast carcinoma. According to her bilateral mammogram, there was a highly suspicious mass in the left axillary

tail with lymph nodes (LN) [BIRADS 1(R) BIRADS 4c (L)]. The pre-operative staging was T2N1M0 for which modified radical mastectomy had been done. The tumour was an invasive ductal carcinoma of the breast, NST (modified Bloom Richardson grade 2) with infiltrative edges and focal intramural and peri-tumoral lymphocytic infiltrates. Attached left axillary tail tissue yielded metastasis in 12 LNs with perinodal spread. Immunohistochemistry revealed ER+ (Allred score 8/8) PR+ (Allred score 7/8); Her2 – negative. The patient subsequently received 8 cycles of adriamycin + cyclophosphamide within 5 months of surgery. However, soon after skeletal metastases developed (C1, C2 & D7, right Iliac bone, head of right femur and pelvic bone) and had been managed with palliative RT 8 Gy/ 1#, tamoxifen 20 mg OD and monthly injection of zoledronate.

Biopsy of the present friable and bleeding cervical tissue revealed sections composed of sheets of pleomorphic cells displaying high N:C ratio and frequent mitoses, at places forming ill-defined acinar pattern with necrosis & inflammation. Diagnosis of poorly differentiated carcinoma, possibly suggestive of metastatic ductal carcinoma was rendered (Figure 1,2). Following histopathological diagnosis, the patient underwent total hysterectomy. Poorly differentiated metastatic involvement of bilateral ovaries, fallopian tubes, uterus and cervix along with lymphovascular involvement was observed in the histopathologic examination. Immunohistochemistry (IHC) revealed ER+ (Allred score 5/8) PR+ (Allred score 5/8) and Her2 negative while being positive for CK7, CK20 and GATA3 and negative for Pax8 and SOX10.



**Figure 1:** High power microphotograph shows sheets of pleomorphic cells displaying high N:C ratio, hyperchromatic nuclei with irregular margins and eosinophilic cytoplasm.



**Figure 2:** Biopsy of the cervical tissue demonstrated poorly differentiated malignant cells, at places forming ill-defined acinar pattern with adjacent stroma showing necrosis & inflammation.

## Discussion

Invasive ductal carcinoma (IDC) accounts for approximately 70–75% of all breast cancers while invasive lobular carcinoma (ILC) only accounts for 5–20%. Despite of its lower incidence in all breast cancers, ILC metastasizes to the female genital tract in more than 80% of all cases [1,2]. Nevertheless, infrequently IDC also metastasize to the gynecologic organs alone, as was observed in our case.

Abnormal uterine bleeding reported by a patient on tamoxifen therapy raises concern for primary endometrial abnormalities including atypical endometrial hyperplasia, endometrial polyps, and endometrial cancer, while metastatic breast cancer (MBC) is often overlooked as part of the differential diagnoses workup due to its rare occurrence [3].

Distinction between metastatic carcinoma from primary carcinoma of the genital tract is important as it affects clinical decision, treatment, and prognosis. Histological analysis helps in differentiating between primary and metastatic disease. Most metastatic breast carcinomas are positive for GATA3 and negative for Pax-8 which was observed in the present case. Pax-8 and GATA3 immunoreactivity is useful in the distinction between independent primaries and metastatic breast carcinomas as compared to ovarian tumours in the light of clinic-pathological findings [4].

Tamoxifen, a non-steroid anti - estrogen, is considered as standard endocrine therapy for ER - positive breast neoplasms in premenopausal women, resulting in reduction in breast cancer recurrence and improvement in 10 - year survival rate. While

tamoxifen produces antagonistic effect on ER in the breast, its dual agonistic/antagonistic effect in the uterus may increase the risk for development of new leiomyoma, increase the size of existent uterine leiomyomas, and induce cystic and edematous changes as a result of elevated PR expression [3].

Anastrozole, approved later, has been shown to be superior to tamoxifen in cancer treatment. Considering long term use of hormone antagonists and resultant chances of producing endometrial pathologies, anastrozole is expected to be safer and more effective in treatment of breast cancer and in prevention of recurrences and metastases. However, a few reports of gynecologic metastases from breast cancer undergoing anastrozole treatment have also been published [5].

Clinicians should be aware and concerned about isolated uterine metastases that may grow in the patients receiving anti-estrogen therapy and routine gynecological follow-up examination should be carried out in these patients. Additionally, it is important to distinguish the uterine lesions whether primary or metastatic because of the different treatment options.

### **Compliance with Ethical Standards**

Conflict of interest - The authors declare no competing interests.

**Ethical Approval** - Ethical approval was not required for case reports as per the Institutional Ethics Committee guidelines.

**Informed Consent** - Written informed consent was obtained from the patient, and her anonymity was maintained throughout the study.

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