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# METASTATIC CARCINOMA TO UTERINE CERVIX FROM BREAST PRIMARY - AN INCIDENTAL FINDING: A RARE CASE REPORT WITH REVIEW OF LITERATURE

Pathology

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## ABSTRACT

Involvement of uterine cervix as the exclusive site of metastasis is very unusual. Carcinoma arising from ovary, breast, stomach, gallbladder, pancreas and lung has been reported to metastasize to the uterine cervix by hematogenous spread. However in majority of the cases, metastasis to cervix is from uterine malignancies. We describe a case of 40 years woman diagnosed with breast carcinoma 7 years ago. She underwent chemoradiotherapy and modified radical mastectomy. Histopathology revealed infiltrating ductal carcinoma with axillary lymph node metastasis. Immunostaining with hormonal receptors was positive for Estrogen Receptor, Progesterone Receptor and negative for Her2neu. On follow up, ultrasound showed thickened endometrium. Hysterectomy was done which incidentally revealed a tiny focus of carcinoma in the cervix. Immunohistochemistry confirmed metastasis from breast primary. Incidentally detected isolated metastatic carcinoma to uterine cervix from breast primary though not common, must be considered in the differential diagnosis.

## KEYWORDS

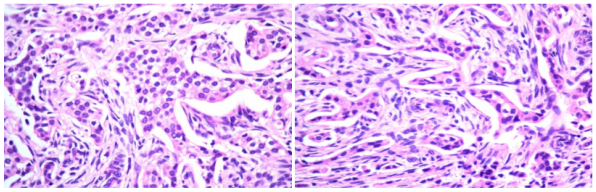
Cervix, breast, metastasis, carcinoma.

**Introduction:**

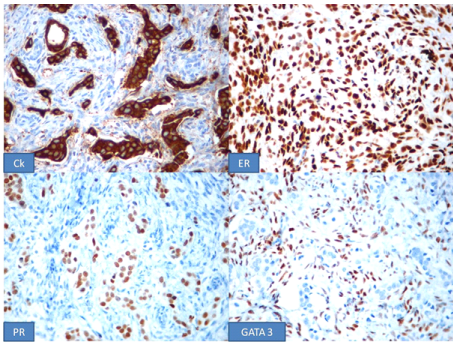
Metastasis to female genital tract from extra genital primary is unusual. Metastatic carcinoma to the cervix usually arises from other genital organs, most commonly from the uterus. [1] Metastasis from breast is very uncommon. Breast carcinoma usually metastasizes to lung, bone, liver and brain. The most common presenting symptom is abnormal vaginal bleeding. For an accurate diagnosis, careful scrutiny of the histomorphologic features and appropriate selection of the immunohistochemical stains is essential to recognize the nature of the cervical malignancy as secondary and to evaluate the site of primary malignancy. To our knowledge, only a few cases of secondary involvement of the uterine cervix from breast primary have been described. Here, we report a single case of secondary malignancy of the uterine cervix from Infiltrating Ductal Carcinoma (IDC) of the breast to emphasize the importance of immunohistochemistry to arrive at a correct diagnosis.

**Case report:**

A 40 years woman was diagnosed with IDC of the breast 7 years ago. She underwent 4 cycles of neoadjuvant therapy with 5 fluorouracil, epirubicin and cyclophosphomide followed by modified radical mastectomy. Pathological examination of the tumor revealed residual IDC grade 2 with metastatic carcinoma in 11 of 31 axillary lymph nodes (Stage III C). Immunohistochemical staining showed strong positivity for Estrogen Receptor(ER), Progesterone receptor (PR) and negative for HER-2neu. Later 4 cycles of chemotherapy with Docetaxel followed by external beam radiotherapy with a total dose of 50.4 gray in 28 fractions was delivered. She was on Tamoxifen 10 mg twice daily till 6 months before the surgery when she was changed to Luteinizing Hormone Releasing Hormone analogue along with Letrozole. The patient was on regular follow up for 7 years. On routine regular examination, transvaginal ultrasound showed thickened endometrium with tiny cystic spaces. Hysterectomy and bilateral salpingo-oophorectomy was performed in view of abnormal vaginal bleeding. Gross examination of the cervix was unremarkable. Microscopic examination showed an epithelial neoplasm arranged in nests, cords and trabeculae within the cervical stroma measuring 0.8 cm in maximum dimension. The neoplastic cells were large, round to polygonal with moderate eosinophilic cytoplasm and large nuclei. The rest of the uterus was unremarkable.

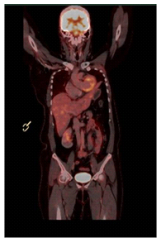


Immunohistochemically, the tumor cells were positive for Pancytokeratin (diffuse and strong cytoplasmic), ER (diffuse and strong nuclear), PR (moderate and strong nuclear), GATA 3 (diffuse and strong nuclear), E-cadherin (diffuse and strong membranous) and negative for Vimentin, HER-2neu, p63, CEA and PAX 8




A diagnosis of metastatic carcinoma from breast primary was rendered based on the histomorphology and immunohistochemical findings. Multiple entities were eliminated including adenocarcinoma of cervix, endometrium, ovary, urinary bladder, appendix, stomach and large intestine as depicted below. Post-operative Positron Emission Tomography (PET CT) scan did not reveal any lesions elsewhere in the body.

| Primary carcinoma | PanCK | ER | PR | Her2neu | Ecadherin | P63 | PAX8 | GATA 3 | CEA |
|---|---|---|---|---|---|---|---|---|---|
| Breast | + | +/- | +/- | +/- | +/- | - | +/- | + | +/- |
| Cervix | + | +/- | +/- | - | + | - | + | - | + |
| Endometrium | + | +/- | +/- | - | +/- | - | + | - | - |
| Ovary | + | +/- | +/- | - | + | - | + | - | +/- |
| Large intestine | + | - | - | - | - | - | - | - | + |
| Appendix | + | - | - | - | + | - | - | - | + |
| Stomach | + | - | - | +/- | + | - | - | - | + |
| Urinary bladder | + | - | - | - | + | +/- | - | + | +/- |



**Discussion:**

Metastasis to the cervix from extragenital sites is very unusual and is probably by hematogenous spread. [2] The common sites of extragenital primaries showing metastasis to female genital tract are gastrointestinal tract and breast. Ovaries are most commonly affected by metastasis (75.8%) followed by vagina (13.4%), uterine corpus (4.7%), cervix (3.4%), vulva (2%) and fallopian tube (0.7%). [1] Despite the differences in the distribution of metastasis, all the sites of female genital tract are at risk of metastasis. Among the gastrointestinal tract primaries, most common sites are colon, appendix and stomach. [3] Metastasis from breast, stomach and appendix are often bilateral. Metastasis from the colon has a worse prognosis compared to the other gastrointestinal tract primaries. Presenting symptoms depend on the site of involvement in the uterus. Abnormal uterine bleeding is the most presenting symptom if endometrium is involved. However if other sites are involved, patient may be asymptomatic. [4] Metastasis to uterine cervix is very rare and in most instances, it is a direct spread from the uterus. However, it can harbor metastasis from ovary, breast, stomach, gallbladder, pancreas and lung. [5,6] Limoine and Hall et al. found 33 cases of cervical metastasis, 4 of them were from breast primary. [7] Mazur et al had reported 325 metastatic female genital tract neoplasms, of which 3.7% had involved the cervix and none of them were from breast primary. [1] Cervix is predominantly a fibromuscular organ with very limited blood supply and has only afferent lymphatics. Hence it is a less common site for metastasis. Only a few cases of cervical metastasis from breast primary have been reported in the literature so far and in most of the cases, the primary tumor was detected before the metastatic site. [7] Differentiation of metastasis from primary is very important as there is difference in the prognosis and treatment. For a correct histopathological diagnosis, careful inspection of the morphology and appropriate immunohistochemistry workup is very crucial to differentiate primary from a metastasis.

Cumming et al [8] found in an autopsy review that young woman are at a higher risk of metastasis to the female genital tract in a large series of 197 woman. The probable reason behind this finding would be an estrogen rich environment of pre menopausal ovary which is a very futile ground for metastasis. There are various histologic sub types of breast cancer, of which the two most common ones are infiltrating ductal carcinoma and infiltrating lobular carcinoma (ILC). The incidence of IDC is 70-75% and ILC represents 5-15%. [9] IDC metastasizes to the female genital tract more frequently that ILC and its incidence is 2-5%. The most common sites of metastasis from ILC include bone, retro peritoneum, gastrointestinal tract and genitourinary tract whereas IDC metastasizes to liver, lung and brain. The exact mechanism for this unusual metastatic pattern is not known. Loss of E-cadherin expression on the tumor cells in ILC results from inactivation of CDH1 gene at 16q 22. This loss results in loosening of cell to cell bonding. Our case was IDC metastasis to the cervix. Harris et al in an autopsy series found that there is a difference in the metastatic pattern also in addition to the metastatic site involved by IDC and ILC. [10] IDC presents as nodular masses however ILC infiltrates either diffusely or as tiny 1-2 mm nodules. Our patient had very focal subcentimetric involvement of the cervix. Presence of koilocytosis and cervical adenocarcinoma in situ in the adjacent cervix strongly suggests a cervical primary. In our case, there was no koilocytosis or adenocarcinoma in situ making a cervical primary unlikely.

The prognosis of ILC was found to be better than IDC in the early years of diagnosis as found in the large series of 12506 breast cancer patients entered in 15 International Breast Cancer Study Group (IBCSG) trials. [11] However after 6 years of diagnosis, relapse rate increased and reached beyond that of IDC. ER positive ILC tends to relapse later than ER positive IDC. [11] In an interesting study by Sanuki – Fujimoto N et al, prognosis of patients with unusual sites of metastasis was found to be similar to that of patients with metastasis at unusual sites. [12] Our patient is disease free and is on medical treatment four months post surgery.

**Conclusion:**

In the case report presented, cervix is the host of IDC of the breast. Absence of specific symptoms, long disease free - interval and misleading histopathological findings posed diagnostic challenges. This distinct lesion, although extremely rare, should be included in the differential diagnosis of tumor that might arise in this location. It is very important to differentiate primary carcinoma from metastasis to the genital tract as there is a huge difference in the management.

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