Isolated metastasis to the uterine cervix from primary breast carcinoma: A case report*

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ABSTRACT

Metastasis of malignancy to the uterine cervix is a rare event in itself. Breast cancer is a commonly diagnosed malignancy in women that has been extensively studied, and it has been known that common areas of metastasis are the lungs, skin, liver and brain. Since the 1980s, there have been a handful of reported cases of metastasis to the uterine cervix. We present the case of a 64-year-old Gravida 4 Para 1 (1031) who developed postmenopausal bleeding 9 years after treatment of the primary breast cancer, which after work-up, turns out to be an isolated metastatic lesion to the cervix. In cases such as this one, surgery is a reasonable treatment option that is sufficient in itself without the need for chemotherapy or radiation. Our patient was offered a different treatment option, which is chemotherapy, instead of proceeding straight to the treatment option presented by most case reports, which is surgery. This paper aims to highlight a possible route of metastasis, to emphasize the need for regular gynecological examination in patients with breast cancer, as well as the importance of aggressive treatment in the form of surgery in cases of isolated cervical metastasis.

Keywords: Breast cancer, Cervical metastasis

INTRODUCTION

Breast cancer is one the most frequently diagnosed malignancies in women worldwide. Over the last few decades more women have been diagnosed during early stages of the disease, presumably due to increased awareness and knowledge of the disease, for which curative approaches are still available at early stages. Nevertheless, 20-85% of these patients will develop distant metastasis within 5 years of their initial diagnosis.[1]

In 2011, Langballe et al investigated the risk of developing a second non-breast malignancy in pre and post menopausal women, and found that women diagnosed in the postmenopausal period had no overall excess risk of developing a second primary, compared to 18% in those women diagnosed in the premenopausal period.[2] The study by Karrison et al in 1999 showed that risk of recurrence of stage 1 disease such as in our patient is 3.5% up to the third year and 1-1.5% every year thereafter.[3] In 1950, Abrams et al analyzed 1000 autopsied cases of malignancies of epithelial origin for the incidence of metastases. Overall, metastasis to the cervix was only 0.3%, and out of 167 cases of carcinoma of the breast, 23% metastasized to the ovary, 8.4% to the uterus and 1.2% to the vagina.[4] There were no cases of cervical metastasis noted from a breast primary in this analysis.

The first objective of this case report is to discuss a possible route of metastasis from a breast primary to the uterine cervix. For cases of isolated cervical metastasis such as our patient, surgical removal of the uterus, ovaries and the uterine cervix may prove to be beneficial or even curative. Lastly, this paper aims to emphasize the need for a regular gynecologic examination especially after diagnosis and treatment of breast carcinomas.

THE CASE

S.R. is a 64-year-old Gravida 4 Para 1 (1031) who presented with a firm, tender, non-movable mass approximately 1x1 cm at the 11 o'clock position of the left breast 9 years ago. She is a known diabetic, maintained on insulin, and surgical history reveals that patient has had a previous cesarean section in 1987, and an appendectomy in the 1980s. Patient had menarche at 11 years old and had subsequent regular menses. She was menopause at 50 years old. Family history was negative for any malignancies. Patient has no history of intake of oral contraceptive pills. She had one sexual partner.

Nine years prior to admission, during an annual physical examination at the office, bilateral mammography showed an irregular focal area suggestive of spiculations in the left breast, seen only in the upper posterior and mediolateral oblique view. A breast ultrasound was then done, and the left breast shows a mass with ill-defined slightly irregular margins and shows post-acoustic

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shadowing at the 11 o'clock position, about 7cm from the nipple. This was said to be suggestive of malignancy, hence was advised surgery. Patient underwent a modified radical mastectomy of the left breast with frozen section and axillary lymph node dissection. Histopathology revealed invasive ductal carcinoma, histologic grade 1, nuclear grade 1, lymph nodes were all negative for metastasis. Patient was asymptomatic after her surgery and was on regular follow up every 3-6 months with her surgeon for the next 5 years. During these five years, she was maintained on tamoxifen.

One year prior to admission, patient she noted postmenopausal bleeding, amounting to about 1-2 moderately soaked pads per day, lasting approximately 3 days, occurring intermittently. This was accompanied with hypogastric pain graded 5-6/10 on the visual analogue scale. When she sought consult with a gynecologist, a papsmear was done showing "atypical squamous cells, cannot exclude high grade squamous intraepithelial lesion," hence was referred to a gynecologic oncologist. A cervical biopsy was done, and this showed results consistent with breast metastasis to the cervix. She consulted with a medical oncologist, who requested for a slide review of her cervical biopsy, the following immunohistochemical stains were done: mammoglobin was positive, gross cystic disease fluid protein – 15 (GCDFP-15) was negative and p16 was negative, pointing to a cervical metastasis from the breast. A transvaginal ultrasound was done however no cervical lesion was noted. She was started on Letrozole 2.5 mg/ tablet, 1 tablet once daily however patient took this for only 3-4 months before she decided to seek a second opinion. She consulted with a gynecologist, and was told that there were abnormal findings seen on the cervix on speculum examination so a referral was made to a gynecologic oncologist at our institution. She was seen and examined 5 months prior. On examination, the right breast was grossly normal. There was no skin dimpling, no nipple retraction, no erythema. There was no noted nipple discharge or palpable masses. Mastectomy scar of the left breast was intact, with no palpable masses up to the margins of the clavicle and the sternum. The bilateral axillae were likewise unremarkable. Chest expansion was symmetrical; breath sounds were clear. The precordium was adynamic, no murmurs were appreciated, heart rate and rhythm were regular. On bimanual pelvic examination, the cervix measured 4x4 cm, the uterine corpus was small and both parametria were smooth. A transvaginal ultrasound showed a sonologically unremarkable cervix, small retroverted uterus with myoma nodule and adenomyosis, thin endometrium and atrophic ovaries. PET-scan was also done for metastatic evaluation, and this showed a hypermetabolic focus in the uterine cervical region suspicious for a malignant lesion, as well as bilateral lung nodules. Three months prior, cervical biopsy was repeated, showing poorly differentiated adenocarcinoma, breast primary (Figure 1). Immunohistochemical stains showed the following results: p16 was negative (Figure 2), mammoglobin was positive (Figure 3) and GATA-3 was positive (Figure 4). Based on these results, the diagnosis is a metastatic cancer to the uterine cervix

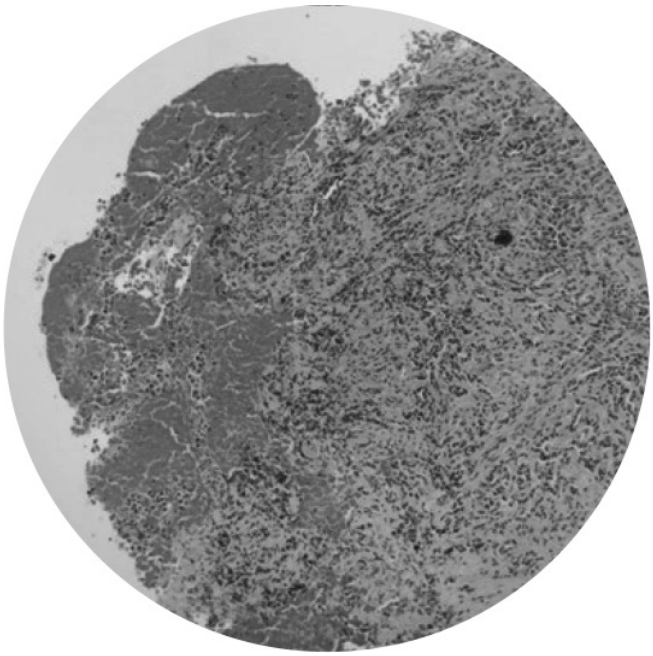

Figure 1. Microsections disclose several invasive clusters and nests of atypical epithelial cells with large hyperchromatic pleomorphic nuclei, prominent nucleoli and ample to fair amount of eosinophilic cytoplasm. Several areas also show atypical epithelial cells with pleomorphic small nuclei arranged in single file.

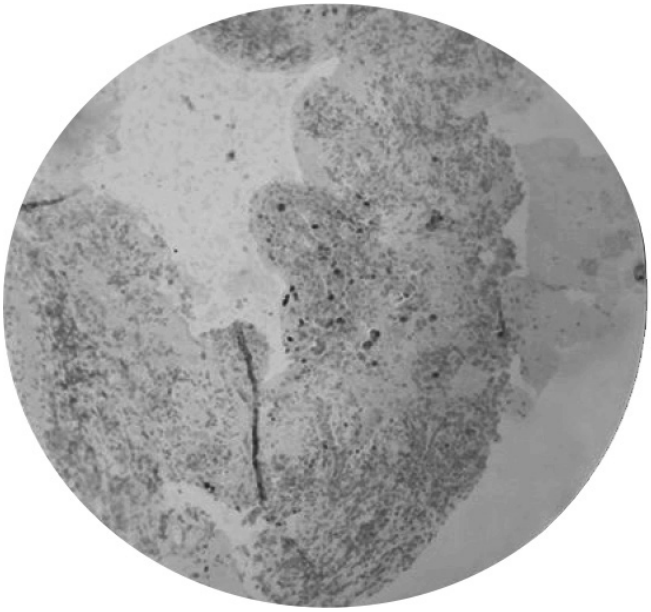

Figure 2. p16 staining negative.

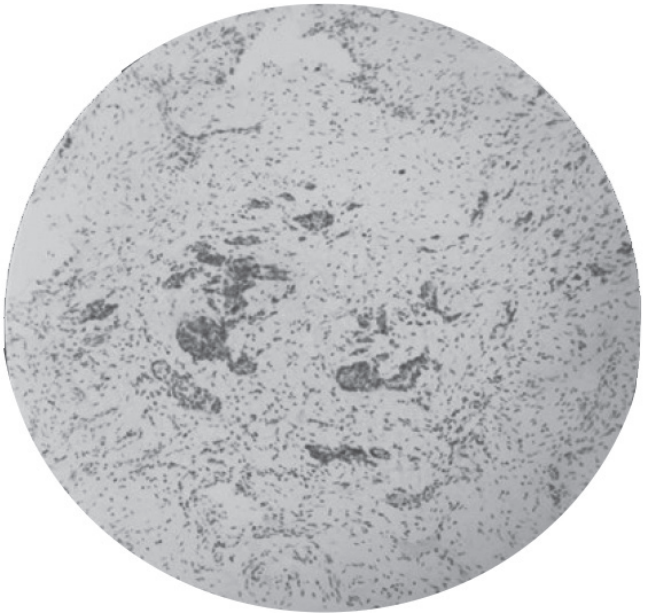

Figure 3. Mammoglobin staining positive.

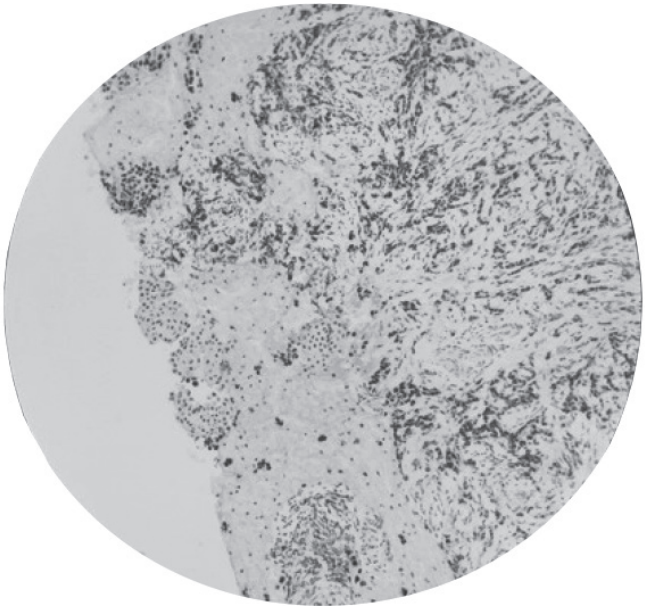

Figure 4. GATA-3 staining positive.

from primary carcinoma of the breast. Initially, the plan was to do a total abdominal hysterectomy with bilateral salpingo-oophorectomy, however the patient was not yet amenable at that time and opted to do chemotherapy with carboplatin and docetaxel instead. After 6 cycles of chemotherapy, a bimanual pelvic examination was done, the cervix measured 3x4 cm compared to the last examination done 3 months prior to commencing chemotherapy. At this time, imaging was repeated. Transvaginal ultrasound showed that the cervix measured 1.6 x 2.8 x 3.1 cm, with a distinct canal and homogenous stroma. The endometrial cavity was dilated to 1.9 cm, with anechoic intracavitary fluid (10 milliliters). The anterior endometrium was 0.27 cm, and the posterior endometrium was 0.36 cm, a total thickness of 0.73 cm, with regular endomyometrial junction, with minimal color flow. The corpus was 5.5 x 4.9 x 5.7 cm, retroverted, atrophic, with an intramural myoma measuring 1.52 x 1.51 x 1.27 cm at the anterior lower uterine segment. Both ovaries were atrophic. Whole abdominal CT scan only showed dilated and fluid filled endometrial cavity, and chest CT scan were unremarkable. Since we did not see a favorable response in the patient after the chemotherapy, she was again offered surgery, to which she now consented to. A total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed, and intraoperatively, noted that there was no ascites, and that the liver edge and subdiaphragmatic surfaces were smooth. The uterus was symmetric with a reddish smooth serosal surface, measuring 5 x 6 x 3.5 cm (Figure 5). The cervix measured 2 x 1.5 cm, and was nodular with a firm indistinct mass at the 3-4 o'clock position (Figure 6). On cut section, the endometrial canal measured 0.5cm. The myometrium was 3 cm. The endometrium was 0.4 cm with no areas of necrosis. The endocervical canal was 1 cm long (Figure 7). Both ovaries were atrophic and grossly unremarkable. Histopathologic diagnosis was as follows: adenocarcinoma involving the endometrium and cervix, compatible with breast carcinoma origin, intramural myoma, and unremarkable ovaries and fallopian tubes.

DISCUSSION

Breast Cancer

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in women worldwide.[5] Most breast malignancies arise from epithelial elements hence are characterized as carcinomas. Invasive breast carcinomas are of several diverse histologic subtypes, the most common of which are invasive ductal (76%) and invasive lobular (8%) types; mixed ductal-lobular types account for 7%.[6]

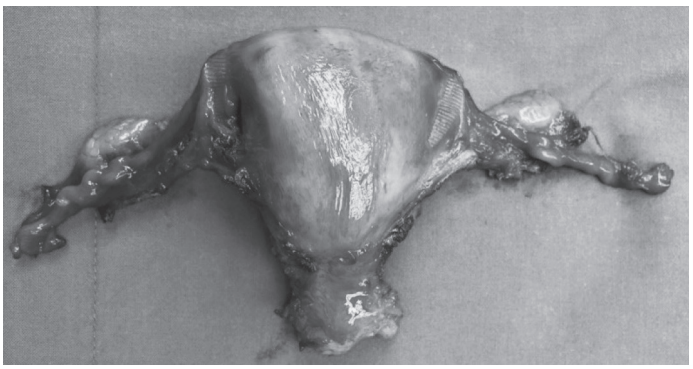

Figure 5. The uterus was symmetric with a reddish smooth serosal surface, measuring 5 x 6 x 3.5cm.

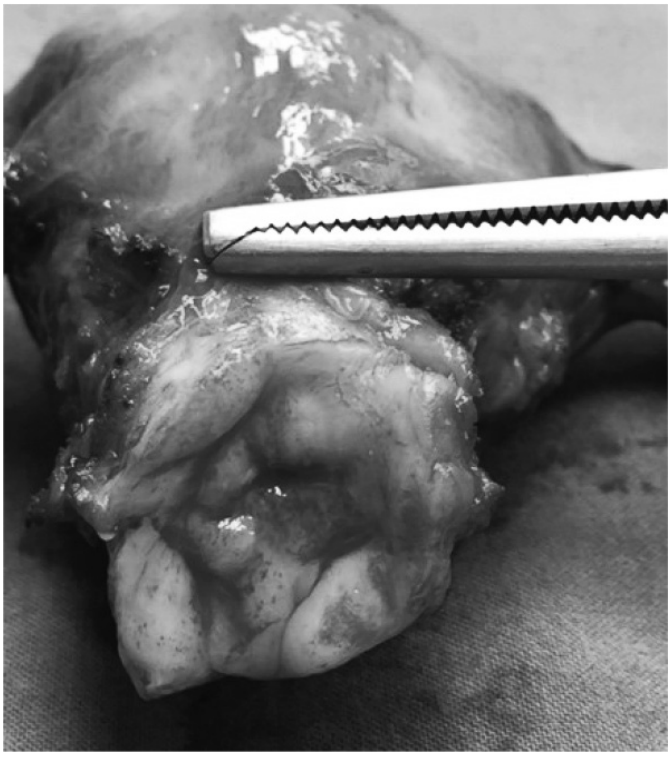

Figure 6. The cervix measured 2 x 1.5cm, and was nodular with a firm indistinct mass at the 3-4 o'clock position.

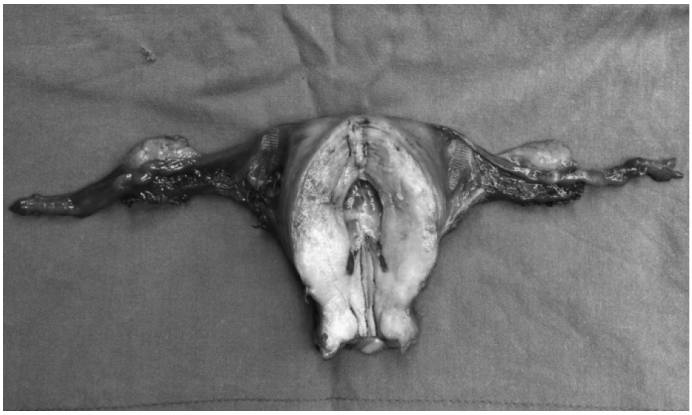

Figure 7. On cut section, the endometrial canal measured 0.5cm. The myometrium was 3cm. The endometrium was 0.4cm with no areas of necrosis. The endocervical canal was 1cm long.

Invasive ductal carcinoma is the most common type of invasive breast cancer and is characterized by cords and nests of tumor cells with varying amounts of gland formation, and cytologic features that range from bland to highly malignant. The malignant cells induce a fibrous response as they infiltrate the breast parenchyma, and this reaction is responsible for the clinically and grossly palpable mass, the radiologic density and solid sonographic characteristics. Grading is based on architectural and cytologic features. [5]

Invasive lobular carcinoma is the second most common type of invasive breast cancer. In many cases, no mass lesion is grossly seen, and the excised specimen may only look normal or be slightly firm. Microscopically, lobular carcinomas are characterized by small cells that infiltrate the stroma and adipose tissue individually and in single file pattern, growing in a target-like configuration around normal breast ducts, and frequently inducing only minimal fibrous reaction.[5]

According to a study in 2000 by Caplan et al on the time to diagnosis and treatment of breast cancer, it was said that regardless of mammogram or clinical breast examination result, median treatment intervals were within 2 weeks – nearly 80% of the women began treatment within 30 days after the diagnosis.[7] For this patient, the interval from diagnosis to treatment was 34 days. She presented with a small breast lump that was small and non-tender, for which she wouldn't have sought consult for, if not for an annual physical examination. The diagnosis was only made incidentally, so to speak. From the time of a suspicious mammogram and breast ultrasound, it took her 34 days before a modified radical mastectomy with lymph node dissection was performed.

The longest interval between primary treatment of breast cancer and tumor recurrence defines the appropriate length of follow up, the effectiveness of treatment, and curability of disease. Karrison, et al (1999) studied the recurrences and deaths, hazard rate for first recurrence or death and excess mortality rate of 1547 patients from 1945 to 1987 and determined that in this population, the limit of breast cancer dormancy appears to be 20-25 years. Most recurrences were noted to occur within the first ten years after mastectomy. In this study, they found that for stage 1 cases such as in our patient, the rate of recurrence or death was low at about 3.5% per year in the third year, but generally remaining within 1% to 1.5% per year thereafter. As expected for more advanced stages, hazard rates were much higher: in stage II, 14% per year in the second year after mastectomy; in stage III, 28% per year in the first 2 years after mastectomy.[3] A more recent update on this concept was reviewed by Brackstone et al in 2007, bringing into light the fact that due to more advanced ideas and new discoveries over the years in the diagnosis and treatment of breast cancer, many more factors should be considered in tumor dormancy such as sensitivity to hormone receptors. In patients with hormonally sensitive tumors, recurrence frequently occurs after completion of the 5 years of hormone therapy.[8] Probably, during those 5 years, the changes in the host were not favorable for the tumor cells. Our patient was only given hormone therapy but was never started on chemoradiation and it seems that in her very early stage of diagnosis of stage 1 node negative cancer, it was deemed sufficient for her to only

have undergone a mastectomy. She was diagnosed with stage IV metastatic breast cancer to the uterine cervix, 8 years after her mastectomy.

Breast Metastasis

In this case, the question is, is this a second primary, or a metastatic disease from the earlier diagnosed breast malignancy? And, if it is metastatic, what is the possible route of spread? The majority of cancer mortalities are due to the metastasis of tumor cells to other organs. The most common route of spread of breast metastasis is the lymphatic system. Invasive ductal carcinoma metastasizes more commonly to the liver, lung and brain, while lobular carcinomas metastasize more commonly to the bones, peritoneum, retroperitoneum, gastrointestinal tract and the genitourinary tract. Although no direct lymphatic routes to these target organs have actually been identified, one possible mechanism is that when tumor cells seed into the lymphatic system, these eventually exit via efferent vessels and utilize the venous system to merge with the systemic circulation.[9] The concept of tumor dormancy says that breast cancer metastasis can manifest years after successful treatment of the primary tumor. During the protracted asymptomatic phase, tumor cells can undergo intermittent growth and quiescence and attain malignant potential in the new microenvironment of the target organ, as postulated by the "seed and soil" hypothesis.[8]

The postulated mechanism for the metastatic pattern of lobular carcinoma is the loss of E-cadherin expression, which leads to loss of cell to cell adhesion and signaling, which may be the reason for the unusual sites of spread for lobular type carcinomas.[10] The reason for a different metastatic pattern for lobular and ductal carcinoma is not clear yet.

In 2008, Sanuki-Fujimoto et al retrospectively analyzed 3783 patients treated for invasive breast cancer, for frequency of usual and unusual metastases. Unusual metastasis is defined as systemic failure with a frequency of less than 1% at each site, of which gynecologic organs are included. Overall, unusual metastasis is observed in 2.2% of patients, and of this number, the unusual metastasis was the first event in only 15 patients.[10]

Metastasis to cervix

In general, metastasis to the cervix from non-gynecological primaries are rare. When present, these non-gynecologic malignancies usually metastasize to the ovaries, presumably due to its abundant blood supply, especially in premenopausal women. In a study by Mazur et al in 1988, out of 325 cases of metastasis to the female genital tract, only 3.7% have involvement of the uterine cervix, and out of this number, none were from the breast.[11] Abnormal uterine bleeding is often the first sign in patients with metastatic disease to the cervix. Our patient presented with postmenopausal bleeding, which may at first seem like a probable endometrial or cervical pathology. Since she did not have regular gynecologic follow-up, a Pap smear done during her initial consult for this new symptom showed a high probability for cervical malignancy. If further work-up had not been done the patient would have been treated inappropriately for a primary cervical carcinoma.

A reason for the rarity of a cervical metastasis could be due to its small organ size and minimal blood supply as well as its fibromuscular structure. In the face of an inflammatory reaction, cervical tissue undergoes fibrous proliferation, hence, on physical examination, the finding is usually an enlarged bulky cervix.[12,13] When the anatomy of the cervix is reviewed, the arterial supply of the uterine cervix is derived from a branch of the uterine artery. These run lateral to the cervix and encircle it. Venous drainage accompanies these arteries. We can also note that there are only efferent lymphatic vessels of the cervix, so circulating tumor cells do not readily find their way to the cervix through lymphatic vessels. Extravasated plasma and proteins from blood are collected in the interstitial space, which then form lymph fluid. These fluids will then be reabsorbed into small veins, thus making their way back into blood circulation. Perhaps in this case, after the modified radical mastectomy, there were tumor cells that seeded into the lymphatic system. The lymphatic vessels, being highly permeable and having a slow flow rate, may have harbored dormant tumor cells which eventually was absorbed back into the veins and back to the blood circulation of the pelvis.

In 2012, Bereza et al aimed to describe the architecture of the vaginal and supravaginal parts of the human uterine cervix by collecting uteri at autopsy and creating vascular casts of the vasculature after perfusing the uteri with resin. In so doing, they found four distinct zones – an outer zone containing large arteries and veins, an arteriole and venule zone, the endocervival mucosal capillaries zone and the pericanalar zone containing small veins and capillaries. This study was the first to suggest that there may be the existence of a countercurrent transport between adjoining veins and arteries.[14] With this information we figured that a lymphatic and hematogenous route of metastasis is easier to understand – from the breast, tumor cells seed into the lymphatic system (in our case the patient had a lesion on the left breast, so we assume that the lymph has drained into the thoracic duct). All lymph drains back into the venous system, and the venous system flows back into the heart, which then pumps blood into the arteries of the entire system. Now since it was found

that there may be adjoining venules and arterioles in the cervix, dormant tumor cells finding its way to this microvasculature is not so far a possibility.

Another possible route is through a lymphatic network in the cervix. What has been widely accepted is that in the uterine cervix, only efferent lymphatics were present, and this was one of the basis of other case reports on their hypotheses about the rarity of cervical metastasis from the breast and other organs. The concept of a blood brain barrier has been widely accepted and the existence of lymphatic vessels in the brain was proposed but evidence was lacking. Recently in 2015, Dissing-Olesen et al published an article that identifies a network of lymphatic vessels in the brain, as studied in two laboratories. What they found was an expression of lymphatic vessel endothelial hyaluronan receptor 1 (Lyve-1) and vascular endothelial growth factor receptor 3 (VEGFR-3), just like in peripheral lymphatic vessels.[15] This mechanism may perhaps be present in the cervix as well. As we have learned of a possible countercurrent transport between arteries and veins of the cervix, an afferent and efferent lymphatic system may very well be present, accounted for by signaling transduction by proteins similar to VEGF-3 and Lyve-1.[15]

We postulate that the metastasis of breast carcinoma to the uterine cervix may be through drop metastasis – a term commonly used in neurology to mean the spread of an intracranial tumor through cerebrospinal fluid to the spinal cord. Rare as it may be, a drop metastasis in this case could seem more improbable than easily explainable by our knowledge of anatomy, but we propose the hypothesis of drop metastasis as a possible mechanism of spread. The efferent lymphatic vessels of the cervix drain into the external iliac, internal iliac and sacral lymph nodes, which drain into the common iliac nodes. Lateral aortic nodes receive lymph from the common iliac node and drains into the lumbar trunk, which then drains into the cisterna chyli. From the breast, axillary lymph nodes drain into the thoracic duct. Extra-axillary nodes such as the internal mammary group of nodes also drain into the thoracic duct. Based on a foundational knowledge of the lymphatic system and Starling's forces, the cisterna chyli is a dilated sac that marks the distal end of the thoracic duct, which is the major lymphatic vessel that drains from the entire body except the right upper extremity and the right thorax. From the cisterna chyli, an interplay between the osmotic and hydrostatic forces may have allowed dormant tumor cells to seed into peritoneal fluid and settle in the cul de sac. These same forces may also be responsible to a possible seeding of tumor cells through the very absorbable lymphatics or veins in the cervix, causing it to later be clinically evident, as hypothesized by the tumor dormancy theory.

Role of Immunohistochemical Stains in Diagnosis

There is an undeniable need to accurately distinguish between a metastatic disease versus a second primary carcinoma because of the difference that will matter in management and prognosis. Our patient presented with postmenopausal bleeding, a sign that may be indicative of a gynecologic disease, either endometrial or cervical. Through physical examination, we find a bulky cervix, and on transvaginal ultrasound, there is a thin endometrial stripe, which then leads us to think that this is more of a cervical than an endometrial pathology. After this, the Pap smear that was done was suggestive of a cervical abnormality. At this time, we have to take into consideration the possibility of a metastasis aside from a primary carcinoma because of her medical history. To aid in this, immunohistochemical stains may be used to identify the origin of the tumor. Our patient underwent cervical biopsy twice, and both times immunohistochemical stains were used to confirm whether the tumor was a primary cervical carcinoma or metastasis from the initial breast primary. The following stains were requested: mammoglobin, GCDFP-15, GATA-3 and p16.

In the study of Wang et al in 2009, the expression profile of mammoglobin was tested among primary breast carcinoma, matched ipsilateral axillary lymph node metastasis, non-breast neoplasms and normal human tissues and concluded that sensitivity was 76% with a specificity of 90% in detection of breast carcinoma. This study recommends caution in the detection of a metastatic breast carcinoma since expression was also noted in some samples of endometrial carcinoma, probably since both tissues are similarly affected by estrogen.[16] In 2007, Bhargava et al compared mammoglobin to GCDFP-15 and showed that lobular carcinomas are more strongly stained with mammoglobin than ductal type. The mammoglobin also stained the breast carcinomas more intensely and among the positive cases, the number of cells stained with mammoglobin is higher. Moreover all invasive endocervical adenocarcinomas studied were all negative or had equivocal staining.[17] Miettinen et al examined 2500 epithelial and mesenchymal tumors for GATA-3 and found that GATA-3 was detected in 92% of primary ductal carcinoma, furthermore was retained in 96% of metastatic breast cancer, making it a useful marker for evaluating metastatic carcinomas arising in unusual sites.[18]

Treatment of Metastatic Breast Cancer

Despite breast cancer being one of the most common malignancies worldwide, metastatic breast cancer still has a low median survival time. Patients are usually given endocrine therapy or chemotherapy.

One of the treatments initially started in our patient was letrozole, 2.5 milligrams per tablet taken orally once

daily. She did not comply fully with this medication and stopped after 3-4 months of taking it. Letrozole prevents the conversion of androgens to estrogens by inhibiting the aromatase enzyme which catalyzes this reaction. In the Femara PO25 Trial done in 2007, Mouridsen studied letrozole (Femara) as an effective alternative to the standard first-line treatment, tamoxifen. This study included postmenopausal women with advanced breast cancer which they defined as stage IIIB locally advanced disease, locoregionally recurrent disease that was not amenable to surgery or radiotherapy, or metastatic disease. 907 patients were randomized into the letrozole group and the tamoxifen group until progressive disease was detected, then the patients were allowed to crossover into the other group. The primary endpoint was time to progression, which was significantly longer with letrozole than with tamoxifen. Objective response rate and overall survival rate also showed a significant advantage of letrozole over tamoxifen.[19]

Our patient was given carboplatin-docetaxel combination chemotherapy for metastatic breast cancer to the cervix. Carboplatin is a platinum based chemotherapeutic drug that forms platinum compounds within cells and causes intra- and interstrand cross-linkage of DNA molecules, hence modifying its structure and prevents further synthesis. Its action is available in all phases of the cell cycle. Docetaxel induces mitotic arrest by suppressing microtubule dynamics and causes G2M cell cycle arrest.[20]

Jones et al directly compared the taxanes paclitaxel and docetaxel as monotherapy for advanced breast cancer, and have demonstrated that docetaxel is superior to paclitaxel in time-to-progression, overall survival and response duration. For both groups, the primary reason for discontinuation of the treatment was disease progression, although it was noted that there was a smaller percentage from the docetaxel group than the paclitaxel group. For the adverse reactions such as neuromotor toxicity, peripheral edema and asthenia, there was a higher percentage from the docetaxel group who opted to discontinue therapy. For the intention-to-treat population, the overall response rate was higher for docetaxel, and median response duration was also longer for docetaxel, as well as for overall survival. Overall, docetaxel demonstrated superior efficacy and is expected to be more clinically beneficial compared to paclitaxel, since rates of toxicities are higher but are manageable. [20]

Because of the cardiotoxicity caused by anthracycline regimens previously used for metastatic breast cancer, newer nonanthracycline agents are needed for this purpose. Platinum based compounds such as cisplatin and carboplatin have shown activity in breast cancer, but carboplatin has shown to be a more appropriate choice because it causes less severe nonhematologic toxicities. Carboplatin as single agent chemotherapy has elicited 20-35% response in previously untreated patients with metastatic breast cancer, and this has led to the investigation of its combination with a taxane. The rationale for this was their complementary mechanisms of action. It has also been shown that paclitaxel seems to have a platelet sparing action that reduces the thrombocytopenia caused by carboplatin alone. Perez summarized the findings of 2 phase II trials on the use of carboplatin-docetaxel combination and concluded that this showed activity in the first-line setting of metastatic breast cancer, and that the toxicity was deemed acceptable.[21] Our patient was monitored weekly with complete blood count for hematologic toxicities. She has experienced chemotherapy-induced gastroenteritis, occasionally has fatigue but has not complained of neuropathy or mucositis.

Therapeutic Approach in Literature

In most case reports on breast metastasis to the cervix, the breast cancer is already in an advanced stage, and most are synchronous, meaning that both the primary and metastatic lesions were diagnosed almost simultaneously. In 2010, Bogliolo et al reported on a case of synchronous breast cancer with metastasis to the uterine cervix, in a 78-year-old asymptomatic patient who was seen for her mammography and Pap smear. Incidentally she was diagnosed with pT1b/ N2a/ M1 lobular breast carcinoma, and was then treated with radiotherapy on the breast 50 Gy for 5 weeks, and with chemotherapy 5-fluorouracil, epirubicin and cyclophosphamide (FEC-75), then with docetaxel. The patient was alive at 30 months however with note of metastatic lesions in the liver at 19 months.[13]

A case report by Manci et al in 2007 was about a 41 year old with stage 1a breast cancer (pT1/N0/M0) who underwent quadrantectomy with axillary lymph node dissection for an infiltrating lobular breast carcinoma. On histopathology lymphovascular invasion was absent and all 16 lymph nodes were negative for tumor. Postoperatively, the patient received radiotherapy and was maintained on tamoxifen for 5 years. Follow up examinations were all normal until 9 years after, she underwent a routine pelvic exam and found a cervical ectropion. This was confirmed to be metastatic lobular mammary carcinoma to the cervix. She then underwent a laparoscopic total hysterectomy with lymph node dissection. Peritoneal washings and all 14 lymph nodes were negative for tumor. No further therapy was done after the surgery. Patient is reported to have benefited well from the surgery, as she was disease free at 20 months of follow up.[22] This is case is almost similar to our patient, the difference was that our patient had a modified radical mastectomy instead of a

quadrantectomy, and the patient in this report underwent radiotherapy and took tamoxifen. Otherwise, both are similar in that they are very early stage cancers with no lymphovascular spread or lymph node invasion.

In 1999, Bryson et al presented a case of a 47-year-old Para 2 who had been treated for a well differentiated infiltrating ductal carcinoma of the breat with extension to the pectoralis major but not to the lymph nodes. She had been on tamoxifen approximately 2 years. She had a history of 2 abnormal Pap smears and so cervical biopsy was done revealing a metastatic lesion on the uterine cervix from a breast primary. Further metastatic workup turned out negative. She underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy and received chemotherapy and radiotherapy. She was followed until 4 years post-treatment and was found to be well.[12]

There was another case of an isolated cervical metastasis by Mousavi et al in 2005, unfortunately it was not disclosed what stage the primary breast cancer was, or how many years after treatment of the primary breast cancer it has been before developing symptoms of postmenopausal bleeding. They also performed a surgical procedure, a hysterectomy with bilateral salpingo-oophorectomy. On inspection of the abdomen there was no other evidence of disease, and on microscopic examination of the surgical specimen, only the cervix had pathology.[23]

The abovementioned two cases were isolated cervical metastases that benefited from surgery. These are the patients who need to be treated aggressively since they have a very good chance of long term survival because there is no other evidence of metastatic disease.

CONCLUSION

Metastasis to the female genital tract is a rare occurrence, especially to the uterine cervix. We need to emphasize the need for regular gynecologic examination after treatment of breast cancer of any stage, as well as malignancies from other organs such as the gastrointestinal tract. Surveillance for rare conditions is important so that diagnoses are not missed, and treatment, whether surgical or medical, can be started early. Usually with isolated cases, surgery will suffice, compared to a patient with multiple metastases. In our patient, we gave chemotherapy in the hopes of being able to avoid a major surgical procedure, however in this case there was very little to no improvement clinically, and on opening, we even noted that there was already involvement of the endometrium, which, if we had not proceeded with surgery, could have continued to progress further. ■

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