Breast Cancer Metastatic to Vulva - a Case Report

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Summary

Vulvar cancer is a rare malignancy which accounts 3-5% of all gynecologic tumors. Metastases to the vulva are also rare but can have significant implications for both treatment and prognosis. Here we report a case of vulvar lesion which was the presenting sign of de novo stage IV breast cancer. We describe diagnostic and treatment approach which combined aggressive first-line treatment plus definitive therapy to her vulvar metastasis.

Key words: Breast cancer; Metastases in the vulva; Invasive ductal carcinoma.

Introduction

Primary cancers of the vulva are rare, accounting for less than 5% of all cancers in women [1]. They typically occur in women aged 64 to 69 years. Risk factors includes weakened immune system and previous history of precancerous conditions of the vulva [2]. In addition, the human papilloma virus is considered a possible trigger of the vulvar dryness which is seen as contributing factor in the occurrence of vulvar cancer [3].

Pruritus is the most common and long-lasting reported symptom of vulvar cancer, followed by vulvar bleeding, discharge, dysuria, and pain [4]. The differential diagnosis must take into account whether vulvar lesion represent a primary or metastatic tumor. Although rare, 5-8% of all vulvar tumors are metastatic from another primary site, particularly in postmenopausal women [5]. In 2002, Neto et al. reported on single-institution experience with 66 cases of metastatic disease in the vulva, during the 57-year period, of which 43.9% had a non-gynecological origin. The histological subtypes of these cases included one each of ductal carcinoma, lobular carcinoma, cystosarcoma phylloides and poorly differentiated carcinoma [6]. Differentiation between primary and metastatic lesion is crucial, since vulvar metastasis is usually associated with a wide spread disease [7].

Breast cancer is the most common malignancy in women worldwide with estimated > 2 million cases of breast cancer diagnosed on an annual basis [8]. Most women present with early stage breast cancer. However, between 6% and 7% of them will present with stage IV disease, with metastases involving (in decreasing frequency) axillary lymph nodes, lungs, bone, liver and brain [11]. About 2-3% of them have metastatic spread to the female reproductive system [12]. Since breast cancer patients may have a significant risk of metastatic disease, a full staging work-up, including a complete history, physical examination, laboratory tests and imaging of chest and abdomen (preferably with CT scan) and bone, before initiation of systemic therapy, is highly recommended. PET-CT, if available, may be used (instead of and not in addition to CT scans and bone scan) [13]. Metastatic involvement of the female reproductive tract occurs rarely in breast cancer, the ovaries and uterus being the most common sites [14] while the metastasis to the vulva occurs rarely [15]. However, gynecological lesion, including vulvar site, have to be kept in mind as a possible site of metastatic lesions from breast cancer [16]. Here we report a case of de novo stage IV breast cancer, originally presenting as a large vulvar lesion.

Case

A 66-year-old post-menopausal woman, without significant personal or family medical history, was admitted to our institution in March 2017 due to bleeding, pain, abnormal vaginal excretions and inability to sit. The symptoms had gradually worsened over 9 months prior to her admission. The patient had first noticed an ulcer on her labia majora, which had been increasing in size and eventually started bleeding. Different analgesics were tried with no improvement, which prompted her to seek our medical expertise.

On a physical examination, a 4 × 5 cm ulcer was noted on the left labia major. The ulcer was tender to palpation, and notably hemorrhagic. By ultrasonography of superficial lymph lymphadenopathy nodes was excluded. A subsequent biopsy with histology revealed a Grade 2 adenocarcinoma, indicating likely metastasis from breast cancer (Figure 1). Estrogen (ER) and progesterone (PR) receptors were both positive 8/8 and 7/8, respectively, while Her2/neu was negative and Ki-67 was 15%.

Based on the histology results, the patient underwent a bilateral mammography which revealed a 16 -18mm mass in the upper lateral quadrant of the right breast. Core biopsy of the breast lesion confirmed an invasive ductal carcinoma,
Figure 1. — Biopsy specimen from a vulvar lesion showing grade 2 invasive ductal carcinoma.

Figure 2. — Pelvic MRI revealing a 5 × 6 cm vulvar lesion.

Figure 3. — Post-radiotherapy MRI showing complete resolution of the vulvar lesion.

Grade 2, with both ER (8/8) and PR (7/8) being positive, HER2/neu being negative, and Ki-67 being 17%. Axillary ultrasound demonstrated enlarged axillary and infraclavicular lymph nodes (sized 9.4 × 4.4 mm and 12.4 × 4.5 mm, respectively) although with normal structure. No other disease was noted (by pelvic MRI, Chest and abdominal CT scan with contrast and mammography) beside the vulvar mass (Figure 2). The case was reviewed at our multidisciplinary tumor board and an aggressive treatment approach of both the primary and metastatic lesion was suggested, given that the case was judged as oligometastatic breast cancer.

The patient underwent neoadjuvant chemotherapy with four cycles of Doxorubicin (60 mg/m²) and Cyclophosphamide (600 mg/m²) followed by four cycles of Paclitaxel (175 mg/m²) every 3 week. Repeated imaging (pelvic MRI, Chest and abdominal CT scan with contrast and mammography) showed a complete clinical response in her breast and a partial response in her vulva. The patient underwent lumpectomy with axillary node dissection. There was no evidence of residual carcinoma on final pathology, and she was staged as ypT0N0M1. After surgery the patient underwent concurrent RT to the breast (50 Gy) and RT to the vulva (40 Gy) and was then placed on Letrozole. Eight months following RT there was no evidence of residual disease in the vulva (Figure 3). She was followed with pelvic MRI and abdominal and chest CT scan every three months.

Eighteen months following completion of therapy the patient was readmitted to our hospital due to cough and dyspnea. Chest/abdominal/pelvic CT was performed and revealed right-sided pleural effusion with multiple metastases in the right lung. No signs of vulvar recurrence were found on gynecological examination. Given her symptoms, we treated her with docetaxel (75 mg/m²) and after 3 cycles she achieved the partial response to metastases in the lungs and pleural effusion was disappeared. Due to absence of disease-related symptoms and organ failure she was subsequently placed on Fulvestrant. The patient remains with stable disease for 3 years from the time of initial diagnosis. By last (FEB 2020) chest and abdominal CT the patient has several metastases in both lungs, which are not changed in size. There is no any evidence of disease recurrence in her breast or vulva by mammography and pelvic MRI accordingly.

Discussion

The embryological development of the female reproductive tract is associated with the formation and regression of the milk ridge (bilateral thickened ectodermic strips where the primary breast tissue develops) along the primitive “milk line” stretching from the axilla to the groin.
area. Remnants of ectopic breast tissue have been identified along this tract, including the vulva [8]. This pear-shaped tissue of the vulva reacts to the hormonal effects of the menstrual cycle, pregnancy and lactation, and is also susceptible to the same benign and/or malignant processes of the breast, which likely explains the de novo stage IV presentation of breast cancer in this patient [10, 11]. Ectopic primary breast cancer of the vulva is particularly rare [17]. About 30 cases have been published in the English-language literature until 2020.

Primary breast carcinoma metastatic to the vulva was first described in 1964 by Convington et al. [19], and several criteria have subsequently been proposed to distinguish the primary from the metastatic lesions of the vulva [20, 21]. Both Perrone [20] and Sheen [21] favor the diagnosis of a metastatic breast cancer in women presenting with a vulvar cancer provided that: (a) identical histological or immunohistochemical data between both lesions; (b) identical hormone receptor status data; (c) absence of in situ and/or normal mammary gland cells in the vulvar sample; and (d) the presence of a positive history of primary breast cancer.

The two most common histologic subtypes of invasive breast cancer are ductal and lobular. Invasive ductal carcinoma (IDC) accounts for 60 – 75% of all tumors, while invasive lobular carcinoma (ILC) accounts for 10 – 15% of all tumors. Cancer of the vulva, by contrast, is relatively uncommon, accounting for less than one percent of all cancers in women [21]. Our pathology report confirmed that metastasis was from hormone receptor-positive invasive ductal breast carcinoma.

Unlike the cases in the medical literature, our patient’s vulvar cancer heralded the diagnosis of stage IV breast cancer, and notably, it was the only site of metastatic disease at presentation. This is in contrast to the series from MD Anderson [6], in which over 90% of cases had multiple metastases in the organs. Most data suggest that patients were diagnosed with vulvar metastasis more than 12 months after the diagnosis of breast cancer (range, 0 to 168 months), although other authors stated that in most cases it observed of up to 1-6 years [19]. In contrast to these, metachronous cases, in our patient it was a synchronous occurrence of breast cancer, an important finding clinicians need to be aware of.

Conclusions

We herewith report of a case of breast cancer with a single metastasis in the vulva. Patient with no medical or family history of breast cancer was treated with radical treatment approach targeting both the primary and metastasis and initially experienced clinically complete response for approximately 12 month. After relapsing, the patient have been treated with chemotherapy and achieved prolonged remission of her lung metastases and complete resolution of her pleural effusion. Since there are only a few reports about invasive ductal carcinoma of the breast with a solitary metastasis in the vulva, we call for careful and thorough investigation of an isolated vulvar lesion due to rarity of breast cancer being diagnosed as the primary tumor entity. In addition and whenever possible, aggressive local/regional and systemic treatment may be a gratifying approach in patients with oligometastatic disease.

Ethics Approval and Consent to Participate

Written informed consent was obtained from the patient for the publication of this case report.

The study was conducted in accordance with the Declaration of Helsinki, and was approved by the Ethics Committee of the Research Institute of Clinical Medicine (approval number:10.09.19-1).

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Conflict of Interest

The authors declare no conflict of interest.

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