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Cutaneous metastasis as a first sign of adenocarcinoma of the cervix

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Abstract

Cervical cancer remains one of the most common malignancies diagnosed in women as well as a leading cause of cancer related deaths in women worldwide. Cutaneous metastasis associated with cervical malignancy is a remarkably rare phenomenon. We present a patient whose cutaneous signs led to the diagnosis of metastatic adenocarcinoma of the cervix.

Keywords: adenocarcinoma, cervical, cervix, malignancy, metastasis, skin

Introduction

Cervical cancer is the fourth most common cancer diagnosed in women worldwide. It is estimated that in the year 2020, 604,000 new cases of cervical cancer were diagnosed and 342,000 women died of the disease worldwide, making it also the fourth most common cause of cancer death in women [1]. Cutaneous metastasis from cervical malignancy is a rare phenomenon. We report a patient whose cutaneous signs led to the diagnosis of metastatic adenocarcinoma of the cervix.

Case Synopsis

A 36-year-old woman was referred to our dermatology department for a painful rash on her right thigh which was previously treated as cellulitis but was unresponsive to antibiotics. She first noticed the skin lesions two months prior to presentation

and reported worsening over time. On examination, the patient had red-to-purple-colored nodules and papules, coalescing into plaques which were studded with pustules and honey-colored crust (**Figure 1**). She also had significant edema involving the entire right lower extremity. Punch biopsy of a nodule revealed aggregates of epithelioid cells with clear ductal differentiation that were CK7+, CK20-, PAX8+ (**Figure 2**). Histopathology and immunostaining of the skin biopsy were consistent with metastatic carcinoma favoring a primary gynecological malignancy. The patient was referred to the oncology department and a whole-body PET CT was performed. This revealed extensive widespread hypermetabolic lymphadenopathy



Figure 1. Clinical morphology: red-to-purple painful nodules and papules coalescing into plaques studded with pustules and overlying honey-colored crust.

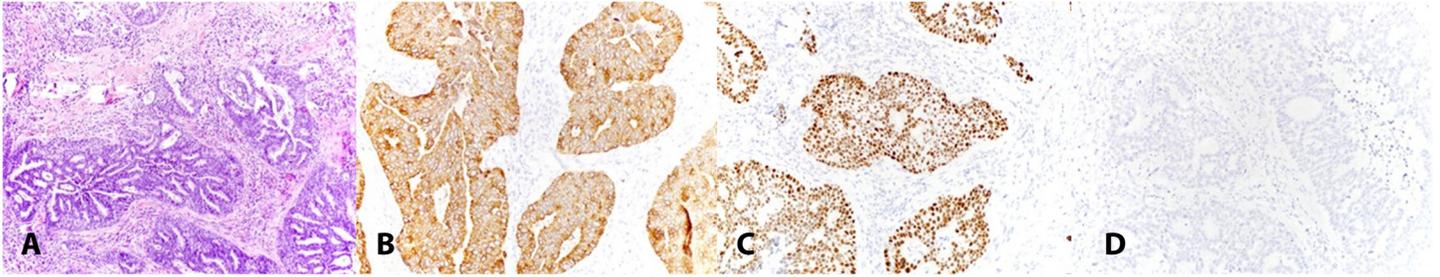


Figure 2. Histopathology of skin biopsy showing **A)** glandular structures non-native to the skin, H&E, 100 \times , which are **B)** positive for CK7, 200 \times , **C)** positive for PAX8, 200 \times , and **D)** negative for CK20, 200 \times .

involving the supraclavicular region, thorax, abdomen/pelvis, and right lower extremity suspicious for metastatic disease as well as a hypermetabolic mass in the uterine cervix suspicious for being the site of primary malignancy. The patient was ultimately diagnosed with stage IV adenocarcinoma of the cervix and palliative chemotherapy (paclitaxel-cisplatin-bevacizumab) was initiated with initial improvement in skin lesions and right lower extremity edema. Restaging scans initially showed partial response to treatment but subsequent scans revealed progression of disease. The patient's condition continued to deteriorate and required admission to the intensive care unit; she died two months later. The period between the date of her presentation in our clinic with skin metastasis, to the date of her death was 15 months.

Case Discussion

Cutaneous metastasis of uterine cervical malignancy is rare; in a retrospective analysis of 1190 patients with cervical cancer, the reported incidence of cutaneous metastases was only 1.3% [2]. It has been reported in patients with cervical adenocarcinoma, mixed adenosquamous carcinoma, squamous cell carcinoma, and poorly differentiated carcinoma, with recent data showing a higher incidence of cutaneous metastasis in patients with squamous cell cervical cancer [3]. The most common reported anatomic sites of cutaneous metastasis of cervical malignancy include the abdominal wall, followed by the vulva and the anterior chest wall [2]. Other described sites include the scalp, thighs, back, and hands [3]. The most common presenting morphologies are nodules, plaques, and inflammatory telangiectatic lesions, although cases

of diffuse inflammatory rashes and patches of alopecia have also been described [2,3]. The mechanisms of skin metastasis includes direct local extension, distal retrograde spread via lymphatic obstruction, and hematogenous dissemination [4]. Cutaneous metastasis of cervical malignancy has also been described at the site of a hysterectomy abdominal incision scar a year after the surgical procedure, suggesting direct tumor cell implantation [5].

Cutaneous metastasis of cervical carcinoma usually presents as a sign of recurrence of disease and it is rarely the first sign of malignancy. In a review by Agrawal et al., 47 reported cases of cervical cancer with cutaneous metastasis in a 12-year period were reviewed [3]. Of these, three presented with cutaneous metastasis which preceded the diagnosis of cervical malignancy, specifically metastatic cervical squamous cell carcinoma and poorly differentiated carcinoma [2-4,6]. On review of the literature, four other reported cases have described cutaneous metastasis leading to a diagnosis of cervical cancer since then [7-10]. All four of these cases described metastatic cervical squamous cell carcinoma. To the best of our case is unique in that it reports cutaneous metastasis preceding a diagnosis of metastatic adenocarcinoma of the cervix and highlights the importance of prompt cutaneous biopsy of suspicious lesions. Cutaneous metastasis of cervical carcinoma is associated with a very poor prognosis, with an average reported survival of 8.5 months [2]. Treatment remains palliative.

Conclusion

Cutaneous metastasis from cervical malignancy is a remarkably rare phenomenon. When present, it may

indicate recurrence of disease and may also precede the diagnosis of cervical malignancy as demonstrated in this case. The clinical presentation of cutaneous metastasis from cervical carcinoma can be variable, posing a diagnostic challenge. Tissue histology and immunohistochemistry studies are essential for the proper identification of disease. It is important to include this entity in the differential

diagnosis of non-healing skin lesions with early biopsy being imperative for its diagnosis and timely institution of treatment.

Potential conflicts of interest

The authors declare no conflicts of interest.

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