Cutaneous metastasis from a vaginal squamous cell carcinoma

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INTRODUCTION

Cutaneous metastases from internal malignancies are uncommon and typically portend a poor prognosis.[1-5] Approximately 0.6% to 4.4% of cancers metastasize to the skin.[1] In men, the most common cancers are lung, colon, and melanoma, whereas in women they are breast, colon, and melanoma. Carcinomas of the cervix and vagina exhibiting skin metastases are rare, and only 4 prior cases of metastatic squamous cell of the vagina are described.[6-9]

CASE REPORT

A 62-year-old white woman presented to the Vanderbilt University Medical Center emergency room with a several-day history of chest and abdominal pain, progressive dyspnea, and vaginal bleeding. Her medical history was significant for a bilateral lung transplant in 2013, and she was taking azathioprine, tacrolimus, and prednisone to prevent rejection. The onset of vaginal bleeding occurred shortly after having an abnormal PAP smear 3 month before admission. A computed tomography scan of her chest, abdomen, and pelvis found lung, skeletal, muscle, and liver lesions and a large, necrotic vaginal mass. Bronchoscopic biopsies and pleural fluid both showed "poorly differentiated carcinoma." A vaginal biopsy under general anesthesia found a "poorly differentiated squamous cell carcinoma." The tumoral cells were Cam 5.2, CK 7, p40, and p16 positive and negative for estrogen receptor, napsin A, thyroid transcription factor 1, and CK 20. A PAX8 stain was moderately positive.

The patient had a history of nonmelanoma skin cancer including squamous cell carcinoma treated with Mohs micrographic surgery with no evidence of recurrence. She presented with an erythematous scalp lesion with overlying alopecia of less than 4 months' duration (Fig 1). A punch biopsy of the dermis exhibited diffuse collections of atypical epithelioid cells (Fig 2) with numerous mitotic figures (Fig 3) but no connection to the overlying epidermis. The immunohistochemistry panel performed on the vaginal tissue was applied to the skin biopsy and exhibited identical staining patterns. In-situ hybridization studies for high- and low-risk human papillomavirus (HPV) were performed but were unremarkable.

She was offered palliative radiotherapy, which she declined and was discharged to her home. She died the next day.

Abbreviations used:

HPV: human papillomavirus
SCCV: squamous cell carcinoma of the vagina

DISCUSSION

Several large series of patients with cutaneous metastases from internal malignancies have been published.[1-5] None have noted a case of squamous cell carcinoma of the vagina (SCCV) including the study containing the largest cohort of women (272) by Brownstein and Helwig.[2]

SCCV is itself a relatively rare cancer, comprising only 1% to 2% all gynecologic malignancies, and typically occurs in the elderly (mean age 68 years) and carries a poor prognosis.[10] Approximately 3000 new cases occur annually in the United States. There is a strong association with HPV infection, and these malignancies are correlated with having several lifetime sexual partners, age at first intercourse, and current cigarette smoking. The most common

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Fig 1. An erythematous nodule with overlying alopecia on the scalp.

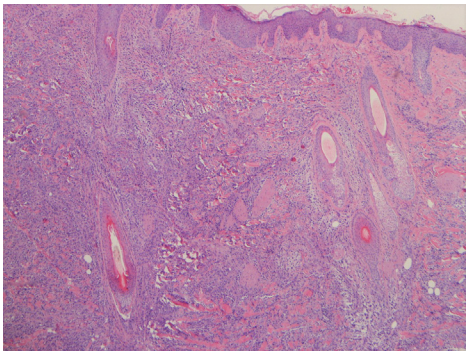

Fig 2. Throughout the dermis are several epithelioid cells. (Hematoxylin-eosin stain; original magnification: ×40.)

symptom at presentation is vaginal bleeding. Standard therapy involves radiation with surgery, and chemotherapy plays a lesser role. The largest series to date included 70 women with an overall 2-year survival rate of 33%.[9,10] Three patients exhibited distant metastases, none to the skin. Early metastatic disease affects the pelvis, peritoneum, and liver with late disease involving the lung and bones.[10] Two smaller patient series of SCCV noted no cutaneous metastases.

Skin metastases from internal malignancies are believed to occur via 3 mechanisms: direct extension from the tumor, hematogenous spread, or lymphatic spread. Given the distance of the metastatic deposit from the site of tumor origin in the patient presented here, a hematogenous form of spread is the only viable consideration.

Table I outlines the 4 previously reported cases of cutaneous SCCV and the one reported here.[6-9] Two patients, the current one and that reported by Sardana et al,[8] presented with contemporaneous cutaneous metastases. Cutaneous disease began 2 and 4 months after diagnosis in 2 other patients, respectively,[6,9] and died 24 months after diagnosis of unrelated causes, but the status of her disease was not mentioned.[7] With so few cases, reported definitive conclusions about this condition are elusive. However, it is interesting that 40% of the patients had cutaneous metastases at the time of their diagnoses of SCCV. In an evaluation of 7316 patients, fewer than 1% exhibited skin metastases before the diagnosis of their internal carcinoma.[4] Additionally, the 4 reported patients with SCCV exhibited locoregional metastases, whereas this woman's lesion was well removed from the site of origin. Skin metastases tend to occur in the general region of the primary neoplasm, with scalp metastases typically originating from lung or kidney in men and breast in women.[1,2]

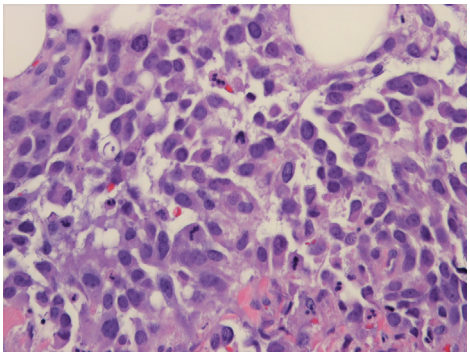

Fig 3. The epithelioid cells exhibit atypia and mitotic figures. (Hematoxylin-eosin stain; original magnification: ×400.)

Table I. Clinical features of patients with vaginal squamous cell carcinoma with skin metastases

Age	Tumor stage	Site of metastasis	Regional nodal metastasis	Therapy	Outcome	Reference
86	IV	Below left knee	NR	RTX	DOD, 8 mos*	Saruk et al[6]
72	NR	Vulva and thigh	Yes	RTX, surgery	NR	Kouvaris et al[7]
60	NR	Labia, mons	NR	NR	NR	Sardana et al[8]
66	II	Thigh, mons	Yes	RTX	NR	van Ruth et al[9]
62	NR	Scalp	NR	None	DOD	Present case

DOD, Dead of disease; *NR*, not reported; *RTX*, radiation therapy.
*Both primary and metastatic tumor demonstrated the presence of HPV 16 and 18.

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