

## BRIEF ARTICLES

**A case of cutaneous metastatic adenosquamous carcinoma of the cervix**

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**ABSTRACT**

Cutaneous metastases of cervical cancer are very rare among all subtypes with a reported incidence of 0.1 to 2%. A 50-year-old African American female with an eleven-year history of metastatic adenosquamous carcinoma of the cervix presented to the emergency department with a new onset asymptomatic rash in her groin for approximately one-month duration. On physical exam, there were numerous hyperpigmented to violaceous papulonodules across the mons pubis and three ulcerated plaques of the left mons pubis. Punch biopsy was consistent with metastases of adenosquamous carcinoma of the cervix. No disease specific interventions were taken and comfort measures were initiated, and the patient passed away five weeks later. To our knowledge, there have only been few reports of cutaneous metastases of adenosquamous carcinoma of the cervix. Our patient developed cutaneous metastases eleven years after her diagnosis, which is to our knowledge the longest reported interval from initial diagnosis to development of cutaneous metastases. Although rare, it is important to recognize cutaneous metastases of adenosquamous carcinoma of the cervix as it predicts a poor prognosis and treatment has not been shown to improve outcomes.

**INTRODUCTION**

Cervical cancer is the most common gynecologic cancer among women worldwide, and the third most common in the United States.<sup>1</sup> Histologically, cervical cancer is divided into 4 major histologic subtypes: squamous cell carcinoma, adenocarcinoma, undifferentiated and adenosquamous carcinoma.<sup>1,2</sup> Cutaneous metastasis is very rare among all subtypes with a reported incidence of 0.1% to 2%; of note, the adenosquamous carcinoma subtype has been reported the least.<sup>3-5</sup> We present a case

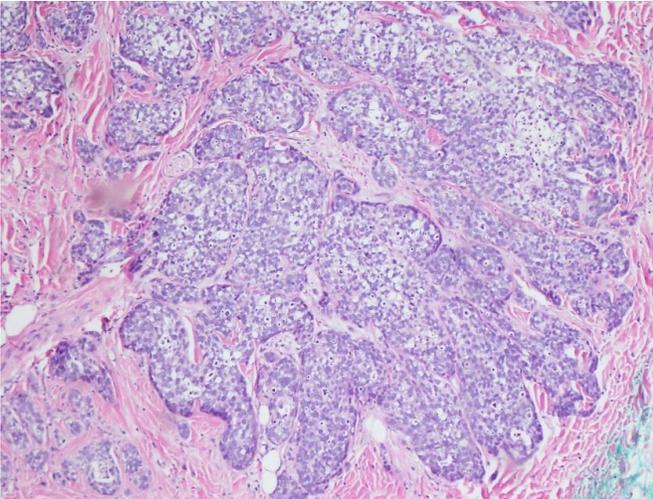
report of ulceronodular cutaneous metastasis of adenosquamous carcinoma of the cervix.

**CASE PRESENTATION**

A 50-year-old African American female with an 11-year history of metastatic adenosquamous carcinoma of the cervix presented to the emergency department with a new onset asymptomatic rash in her groin of approximately one-month duration (Figure 1). The lesions started on her mons pubis and subsequently spread throughout her groin in the coming weeks. She did not try any



**Figure 1:** Grouped violaceous papulonodules and three ulcerated plaques scattered throughout the mons pubis and groin.



**Figure 2:** A punch biopsy with H&E demonstrating atypical, pleomorphic basaloid cells forming nests and cords in the dermis within a fibromucinous stroma.

treatment and had no history of similar cutaneous findings in the past.

Of note, she was initially diagnosed with well-differentiated adenocarcinoma of the cervix in 2006, but declined treatment with radical hysterectomy. In 2014, she presented with recurrent vaginal bleeding and was subsequently diagnosed with metastatic adenocarcinoma of cervix to local lymph nodes. She underwent 7 weeks of radiotherapy with weekly cisplatin infusion, but her disease continued to spread to her lungs and proximal right tibia. Subsequently, in 2016 she completed 15 cycles of a phase 1 trial of pemrolizumab, which was discontinued due to disease progression.

Upon presentation to our emergency department in December 2017, she reported

shortness of breath, pleuritic chest pain and this new onset rash. She had not been on treatment for her metastatic adenosquamous carcinoma of the cervix for over 1 year. On examination, there were numerous hyperpigmented to violaceous papulonodules across the mons pubis and 3 ulcerated plaques of the left mons pubis. A 4-mm punch biopsy of a plaque was performed with histopathology demonstrating a dermal infiltrate of atypical, pleomorphic basaloid cells forming nests and cords within a fibromucinous stroma (Fig 2). Immunohistochemical staining was strong and uniformly positive for CK7, with rare focally positive cells for p63 and negative CK20. These findings were consistent with cutaneous metastasis from adenosquamous carcinoma of the cervix. She declined any additional treatments and passed away approximately 5 weeks later of respiratory failure secondary to sepsis and disease progression.

## DISCUSSION

Cervical cancer is the most common gynecologic cancer among women worldwide. The most common sites of metastasis include lymph nodes then liver, lung, and bone.<sup>2</sup> Cervical cancer rarely metastasizes to the skin, with a reported incidence of 0.1% to 2%. The most common locations of cutaneous metastases include abdominal wall, anterior chest wall and vulva. On examination, cervical cancer cutaneous metastases typically present as nodules, plaques and inflammatory telangiectasias. Ulcerations are uncommon; however, our patient presented with ulcerated plaques in addition to multiple nodules.<sup>1,4-6</sup>

Histopathologically, adenosquamous carcinoma metastases demonstrate a biphasic pattern of well-defined malignant

glandular and squamous features. Special stains may aid in diagnosis, including p63 for the squamous component and CK7+/CK20- for both cervical squamous cell carcinoma and adenocarcinoma components.<sup>7,8</sup> Among the subtypes of cervical cancer, metastasis to the skin from adenosquamous carcinoma of the cervix has been reported the least. In a review of 1185 cases of cervical cancer, Imachi et. al found that only 15 cases spread cutaneously, none of which were adenosquamous carcinoma<sup>5</sup> Similarly, Agrawal et. al found that adenosquamous carcinoma of the cervix was the least likely to metastasize to the skin; of the 47 metastases, 30 (63.8%) were squamous cell carcinoma, followed by 5 (10.6%) adenocarcinoma, 2 (4.2%) poorly differentiated or undifferentiated, 1 (2.1%) mixed adenosquamous carcinoma (2.1%), and in 9 cases (19.1%) histopathology was not reported<sup>6</sup>

To our knowledge, only 2 cases of adenosquamous carcinoma of the cervix spreading to the skin have been described in the literature. In 1966, Reingold added an addendum to his review of metastases from internal carcinoma to include a 43-year-old female who had metastases of adenosquamous carcinoma to the thighs and lower abdomen.<sup>3</sup> In 2010, Fumerton et al presented the first case report of adenosquamous carcinoma metastasizing to the lower abdomen, hips, and groin in a 32-year-old women who passed away within 3 months of the cutaneous lesions appearing.<sup>4</sup> Irrespective of histologic subtype, cutaneous metastases of cervical carcinoma predict a poor prognosis, as this usually occurs with local or regional recurrence.<sup>4,5,9,10</sup> The incidence of skin metastasis increases with an increasing initial tumor stage, with an incidence of 0.8% in stage I and 4.8% in stage IV.<sup>5</sup> Cutaneous metastases typically

present a year after the diagnosis of cervical cancer, although they may develop up to 10 years after the initial diagnosis.<sup>1</sup> Treatment options tried include radiation, chemotherapy, and surgery; however, the average length of survival after cutaneous metastases develop is 3 months.<sup>6</sup> Imachi et al found that only 20% of patients survived 1 year after the development of metastases to the skin.<sup>5</sup>

Our patient presented with nodules and ulcerative plaques on her mons pubis and groin with a biopsy supporting metastatic adenosquamous carcinoma of the cervix. Ulcerative plaques have not commonly been described as a morphologic subtype of cervical adenosquamous carcinoma metastases. In addition, her histologic subtype of adenosquamous is the least common variant to spread to the skin.<sup>5,6</sup> Stains such as CK7, CD20 and p63 may aid pathological diagnosis. She developed cutaneous metastases 11 years after her diagnosis, which is to our knowledge the longest reported interval from initial diagnosis to development of cutaneous metastases to date. Unfortunately, she passed away from her condition approximately 5 weeks after developing the cutaneous lesions, supporting the literature that cutaneous metastasis of cervical carcinoma portends a poor prognosis<sup>3,5,6,9,10</sup> Although rare, it is important to recognize cutaneous metastases of adenosquamous carcinoma of the cervix as it predicts a poor prognosis and treatment has not been shown to improve outcome

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