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Diffuse Cutaneous Metastases From Endocervical Adenocarcinoma: A Rare Pattern of Recurrence

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Abstract

Cutaneous metastases from cervical cancer are uncommon and can resemble benign inflammatory or treatment-related dermatoses. We report a 54-year-old woman with International Federation of Gynecology and Obstetrics (FIGO) stage IIIC2 endocervical adenocarcinoma who received carboplatin-paclitaxel chemotherapy followed by cisplatin-based chemoradiotherapy and uterovaginal brachytherapy. Six months after completing locoregional treatment, she developed rapidly progressive erythematous-violaceous plaques and micropapules that began in the inguinal regions and proximal thighs, extended to the abdomen and breasts, and were accompanied by marked vulvar swelling. A skin biopsy showed dermal involvement by a poorly differentiated carcinoma. The tumor was positive for CK7 and p16, showed weak, heterogeneous estrogen receptor (ER) expression, and was negative for CK20 and vimentin. Comparison with the primary cervical tumor supported cutaneous metastasis from the known endocervical adenocarcinoma. Thoracoabdominopelvic computed tomography showed no distant metastatic lesions. This case emphasizes that persistent, progressive, or atypical skin lesions after treatment for cervical cancer require early biopsy. Extensive cutaneous dissemination may occur even in the absence of radiologically detectable distant extracutaneous metastases.

Categories: Obstetrics/Gynecology, Radiation Oncology, Dermatology
Keywords: cervical cancer, cutaneous metastasis, endocervical adenocarcinoma, immunohistochemistry, skin biopsy

Introduction

Cervical cancer remains a major global health burden, with approximately 604,000 new cases and 280,000 deaths estimated worldwide in 2024 [1]. Squamous cell carcinoma is the predominant histological type, whereas endocervical adenocarcinoma represents a smaller but clinically important proportion of cervical malignancies. Most endocervical adenocarcinomas are associated with high-risk human papillomavirus (HPV), although HPV-independent subtypes are recognized [2]. Diffuse, block-type p16 immunoreactivity may support an HPV-associated phenotype, but p16 is a surrogate marker and does not establish HPV infection in the absence of HPV-specific testing. Distant metastatic spread most commonly involves the lungs, bone, and liver, whereas cutaneous dissemination is distinctly uncommon [3].

Cutaneous metastases from cervical cancer have been reported in approximately 0.1-2% of patients and may present as nodules, papules, plaques, maculopapular eruptions, or inflammatory-appearing lesions [4-7]. This variability in reported incidence may reflect differences in study design, disease stage, study period, and case-ascertainment methods. Because these manifestations can mimic benign dermatological conditions, diagnosis may be delayed unless a biopsy is performed. Although squamous cell carcinoma accounts for most published cases, cutaneous metastases from cervical adenocarcinoma are well documented but remain unusual [8-12]. We report a rapidly progressive, diffuse cutaneous metastatic recurrence of endocervical adenocarcinoma with extensive involvement from the thighs to the breasts and marked vulvar swelling approximately six months after completion of locoregional treatment. This case highlights the importance of early biopsy of persistent or atypical skin lesions in patients previously treated for cervical cancer.

Case Presentation

A 54-year-old primiparous woman with insulin-treated diabetes mellitus and hypertension managed with an angiotensin II receptor blocker and a diuretic presented with vaginal bleeding and malodorous vaginal discharge that had persisted for five months. Her World Health Organization (WHO) performance status was 1 at presentation. Gynecological examination revealed an ulcerated, exophytic cervical tumor involving the vaginal walls down to the lower third of the vagina, with bilateral involvement of the distal parametria.

A cervical biopsy was performed. Histopathological examination, supplemented by immunohistochemical

analysis, revealed an invasive endocervical-type adenocarcinoma. Tumor cells showed strong and diffuse CK7 expression and weak, heterogeneous estrogen receptor expression, whereas CK20, p40, CK5/6, and vimentin were negative.

Radiological staging showed no extension to the pelvic wall but revealed multiple pelvic lymphadenopathies involving the bilateral external iliac and common iliac nodal regions. The largest node measured 23 mm in short-axis diameter in the left external iliac region. Several left para-aortic lymph nodes measuring up to 10 mm in short-axis diameter were also identified (Figures *1A*, *1B*).

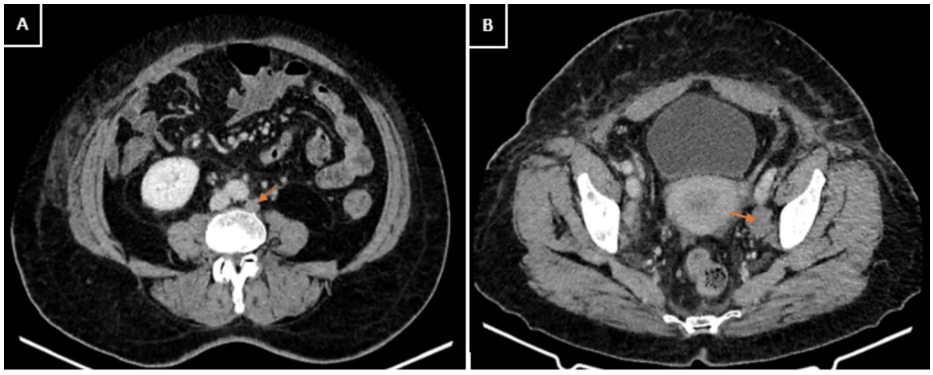


FIGURE 1: Computed tomography findings at initial staging.

(A) Axial contrast-enhanced CT image showing a left para-aortic lymph node measuring up to 10 mm in short-axis diameter (arrow). Despite its relatively small size, the lymph node was considered radiologically suspicious based on its morphology and density, as assessed by the radiologist. (B) Axial contrast-enhanced CT image showing the largest pelvic lymph node located in the left external iliac region, measuring 23 mm in short-axis diameter (arrow). Multiple pelvic and para-aortic lymph nodes were identified on staging CT, supporting the radiological classification as FIGO stage IIIC2.

FIGO: International Federation of Gynecology and Obstetrics

Based on the 2018 International Federation of Gynecology and Obstetrics (FIGO) staging system, the disease was classified as stage IIIC2 due to radiologically identified para-aortic lymph node involvement, without pathological confirmation. The patient initially received induction chemotherapy consisting of six weekly cycles of carboplatin (area under the curve {AUC} 2) and paclitaxel (80 mg/m^2), consistent with the induction strategy evaluated in the INTERLACE trial for locally advanced cervical cancer. This was followed by definitive concurrent chemoradiotherapy consisting of external beam radiotherapy using volumetric modulated arc therapy, delivering 46 Gy in 23 fractions to the cervix, uterus, vagina, parametria, and elective pelvic and para-aortic nodal regions, with weekly cisplatin at 40 mg/m^2.

External beam radiotherapy was followed by uterovaginal brachytherapy delivering 21 Gy in three fractions of 7 Gy. Additional external beam radiotherapy was then delivered to the high-risk volumes, consisting of a parametrial boost of 10 Gy in five fractions and a nodal boost of 20 Gy in 10 fractions, with weekly cisplatin at 40 mg/m^2. The overall radiotherapy treatment time, from the first fraction of external beam radiotherapy to the completion of the final radiotherapy fraction, was 65 days. A complete locoregional response was demonstrated by clinical examination and pelvic magnetic resonance imaging (MRI) three months after treatment completion, with no detectable residual cervical tumor or lymphadenopathy. The patient subsequently entered clinical and radiological surveillance.

Approximately six months after treatment completion, the patient developed erythematous-violaceous cutaneous lesions involving the inguinal regions and proximal thighs. The lesions extended superiorly to the mid-abdomen and were associated with marked vulvar swelling. The patient reported pain, predominantly in the pelvic region, and pruritus. The patient underwent several dermatological consultations, during which clinicians considered different provisional diagnoses and prescribed various symptomatic treatments. However, the exact diagnoses, medications, and treatment durations could not be reliably documented from the patient's history. No clinical improvement was observed despite these treatments.

Over a period of approximately two months, the lesions progressively extended and eventually reached the breasts. Dermatological examination showed extensive, poorly demarcated erythematous-violaceous plaques with irregular borders and areas of infiltration extending from the thighs to the breasts. The cutaneous involvement was estimated to affect approximately 28% of the total body surface area. Lesions on the breasts and abdomen were partially covered with scales, and clusters of translucent micropapules were observed on the proximal thighs. Marked vulvar swelling persisted (Figures *2A*-*2D*).



FIGURE 2: Clinical presentation of the diffuse cutaneous lesions.

(A) Anterior overview showing the extensive distribution of lesions from the proximal thighs to the breasts. (B) Confluent erythematous-violaceous plaques involving the breasts and upper abdomen. (C) Infiltrated plaques over the abdomen and proximal thighs. (D) Closer view of the proximal thigh involvement.

Given the persistence and progressive extension of the atypical cutaneous lesions in the context of recently treated cervical cancer, a skin biopsy was performed on an infiltrated papular lesion of the abdomen approximately three months after the initial appearance of the lesions. Histopathological examination showed dermal involvement by a poorly differentiated carcinoma (Figures *3A*, *3B*). Immunohistochemical analysis showed strong and diffuse p16 expression, CK7 positivity, weak and heterogeneous estrogen receptor (ER) expression, and negativity for CK20 and vimentin (Figures *4A*-*4C*).

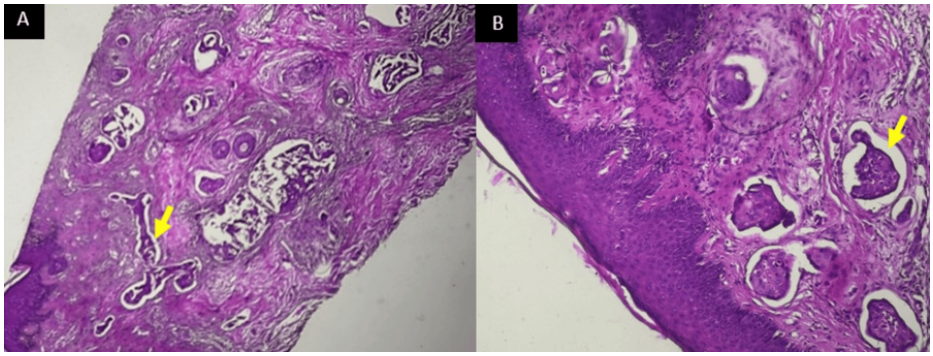


FIGURE 3: Histopathological findings in the skin biopsy.

Representative hematoxylin and eosin-stained sections (A and B) show malignant epithelial deposits involving the dermis, with irregular gland-like and nested architecture (arrows). Original magnification: ×20 for both panels.

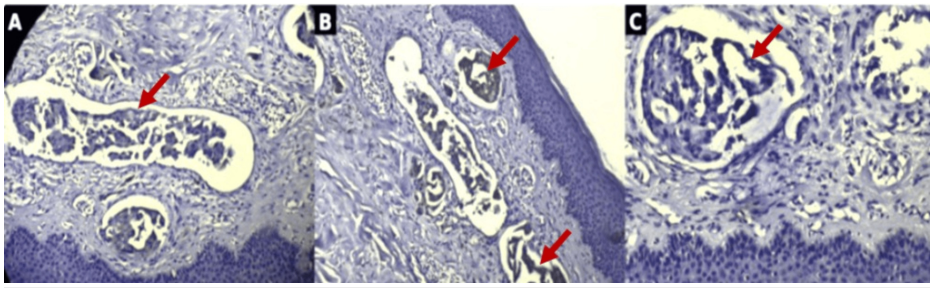


FIGURE 4: Immunohistochemical profile of the cutaneous metastasis.

(A) Positive CK7 expression in tumor cells (arrow). (B) Strong and diffuse nuclear and cytoplasmic p16 expression in tumor cells (arrows). (C) Weak, heterogeneous ER expression in tumor cells (arrow). Original magnification: ×40 for all panels. In conjunction with the morphology, negative CK20 and vimentin staining (not shown), and comparison with the histopathological and immunohistochemical findings documented in the original pathology report of the primary cervical tumor, this profile supports cutaneous metastasis from endocervical adenocarcinoma.

ER: estrogen receptor

In correlation with the morphology and immunophenotype of the primary cervical tumor, these findings supported cutaneous metastasis from the known endocervical adenocarcinoma. Although the pathology report classified the tumor as human papillomavirus (HPV)-associated based on morphological and immunohistochemical findings, including p16 positivity, this classification remains presumptive because no HPV-specific testing was performed. A thoracoabdominopelvic computed tomography (CT) scan performed during the metastatic workup revealed no detectable distant extracutaneous metastases. The patient was subsequently referred to the medical oncology department for systemic treatment.

Discussion

Our case is particularly notable for the rapidly progressive and extensive cutaneous dissemination of endocervical adenocarcinoma, occurring approximately six months after treatment completion. This unusual presentation illustrates a rare pattern of metastatic spread in cervical cancer. In one of the largest series examining this pattern of spread, Imachi et al. identified skin metastases in 15 of 1,190 patients with cervical carcinoma (1.3%), with reported frequencies increasing from 0.8% in stage I disease to 4.8% in stage IV disease [4]. Contemporary reviews continue to describe cutaneous metastases from cervical cancer as rare, generally occurring in fewer than 2% of patients [5,6,13].

Squamous cell carcinoma is the most frequently reported histological subtype among published cases of cutaneous metastases from cervical cancer [5-7]. Alrefaie et al. identified approximately 80 published cases up to 2017, of which only 14 were adenocarcinomas [7]. Nevertheless, the Imachi et al. series suggested that, relative to the underlying histological populations, the incidence of skin metastasis appeared higher in adenocarcinoma and undifferentiated carcinoma than in squamous cell carcinoma [4]. Although this study provides valuable epidemiological insights, these observations should be interpreted cautiously given its historical setting and the limited number of cutaneous metastasis cases. Cutaneous metastases from cervical adenocarcinoma are therefore well documented but remain uncommon [8-12].

The clinical morphology of cutaneous metastases is heterogeneous and may delay recognition. In the Imachi series, 86.7% of patients presented with nodular lesions, and approximately two-thirds had multiple lesions [4]. Other reports describe maculopapular eruptions, plaques, inflammatory-appearing lesions, vesicle-like lesions, and diffuse cutaneous involvement [5,6,9,14,15]. This variability is clinically relevant because metastatic disease may initially be mistaken for a benign inflammatory or treatment-related dermatosis. Liu et al. described violaceous papules and plaques with overlying scale involving the vulva and lower extremities that were initially considered an immune-related toxicity before biopsy established metastatic cervical carcinoma [15]. In our patient, symptomatic dermatological treatment similarly failed, and progressive extension prompted histological assessment. More broadly, this case underscores the importance of maintaining clinical vigilance when evaluating atypical or progressively worsening symptoms in patients with a history of malignancy, as such manifestations may occasionally indicate disease recurrence.

Our patient's presentation was notable for both morphology and extent. The lesions initially involved the thighs and lower abdomen and were accompanied by marked vulvar swelling. They subsequently progressed cranially to involve the breasts. This distribution may suggest an initial regional lymphatic spread rather than direct contiguous extension, followed by more widespread cutaneous metastatic involvement. However, the precise route of dissemination could not be established in our patient. Examination showed extensive, poorly demarcated erythematous-violaceous infiltrated plaques, scaling over the breasts, and clusters of translucent micropapules in the proximal thigh regions. This differs from the discrete nodular pattern most frequently reported [4,6]. Jindal et al. described cervical adenocarcinoma with cutaneous metastasis and vulvar lymphedema [9], whereas other adenocarcinoma reports have documented vulvar, thigh, plaque-like, papular, and other atypical cutaneous presentations [10-12].

Several routes of cutaneous dissemination have been proposed, including direct extension, lymphatic spread, and hematogenous dissemination [6,13]. The abdominal wall, vulva, chest wall, and extremities are recurrently reported sites [4-6]. In our patient, early involvement of the vulvar region, thighs, and lower abdomen followed by superior extension may suggest an important lymphatic component. However, the anatomical distribution alone cannot establish the route of dissemination. Histological confirmation of lymphovascular tumor emboli would provide stronger support for this hypothesis.

Histopathological confirmation is essential because the clinical appearance is nonspecific. The skin biopsy in our patient demonstrated dermal involvement by a poorly differentiated carcinoma. Immunohistochemistry showed CK7 and p16 positivity, weak ER expression, and negativity for CK20 and vimentin. The primary endocervical adenocarcinoma showed strong diffuse CK7 expression, weak heterogeneous ER expression, and negativity for CK20, p40, CK5/6, and vimentin. Taken together, the morphology, immunophenotypic concordance, and oncological history supported a cervical origin of the cutaneous disease. Immunohistochemical p16 positivity can provide supportive evidence in the appropriate clinicopathological setting but should not be regarded as independently diagnostic of cervical origin or HPV association [2,12].

The timing of recurrence is another important feature. The first cutaneous manifestations appeared approximately six months after completion of locoregional treatment, despite an initially favorable locoregional response. Imachi et al. reported an interval from cervical cancer diagnosis to cutaneous metastasis ranging from 0 to 69 months, with a mean of 16.9 months [4]. Agrawal et al. described lower abdominal maculopapular lesions two months after completion of chemoradiotherapy, followed by rapid progression to the inguinal, vulvar, and perineal regions [14]. Benoulaid et al. also reported cutaneous recurrence six months after chemoradiotherapy in one patient [16]. These observations show that cutaneous progression may occur early after definitive treatment and should remain in the differential diagnosis of new persistent skin lesions during surveillance.

Another distinctive feature is the contrast between extensive cutaneous involvement and the absence of radiologically detectable distant extracutaneous metastases. Computed tomography showed no distant metastatic lesions. In the Imachi series, skin metastasis was the first recognized metastatic manifestation in nine of 15 patients, although only four had neither local recurrence nor another distant metastatic site at diagnosis [4]. Agrawal et al. also reported rapidly progressive cutaneous disease without detectable metastases in other organs [14]. These observations suggest that extensive cutaneous dissemination may occur even in the absence of radiologically detectable distant visceral metastases. However, computed tomography may fail to detect small-volume metastatic disease, and the absence of documented PET/CT or other additional staging modalities limits a comprehensive assessment of the full extent of disease.

Cutaneous metastases from cervical cancer have traditionally been associated with an unfavorable prognosis. Agrawal et al., reviewing 47 reported cases, found a mean survival of approximately 8.5 months after diagnosis of cutaneous metastasis [14]. A recent review likewise reported a median survival of less than nine months [6]. Nevertheless, outcomes are heterogeneous. Mahapatra et al. described a marked clinical and metabolic response after systemic treatment in a patient with disseminated cutaneous metastases [17], whereas Sutedja et al. documented regression of cutaneous plaques and papules following paclitaxel-carboplatin chemotherapy in recurrent cervical adenocarcinoma [12]. Treatment should therefore be individualized according to disease extent, prior therapy, performance status, tumor biology, symptoms, and

available systemic options.

This case highlights the need to consider metastatic recurrence when a patient with a history of cervical cancer develops persistent, progressive, or atypical dermatological lesions. Plaque-like, inflammatory, or papulovesicular appearances may be particularly misleading. Early biopsy can establish the malignant nature of the lesions, permit comparison with the primary tumor, and trigger appropriate systemic staging. The combination of endocervical adenocarcinoma histology, rapid onset after definitive treatment, extensive erythematous-violaceous involvement from the thighs to the breasts, marked vulvar swelling, and histopathological confirmation represents an unusual pattern of recurrent cervical cancer.

Conclusions

Diffuse cutaneous metastases from endocervical adenocarcinoma are rare and may mimic benign inflammatory dermatoses. Persistent, progressive, or atypical skin lesions after cervical cancer treatment should prompt early specialist assessment and consideration of biopsy, even when computed tomography performed at the time of cutaneous recurrence reveals no detectable distant extracutaneous metastases. However, CT imaging cannot exclude occult microscopic or small-volume metastatic disease. Correlation of morphology, immunohistochemistry, and the primary tumor is essential for diagnosis. Early recognition enables diagnostic confirmation, appropriate staging, symptom-directed management, and timely oncology evaluation, although prognosis remains guarded and treatment must be individualized.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

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