Violaceous nodules in a patient with endometrial adenocarcinoma

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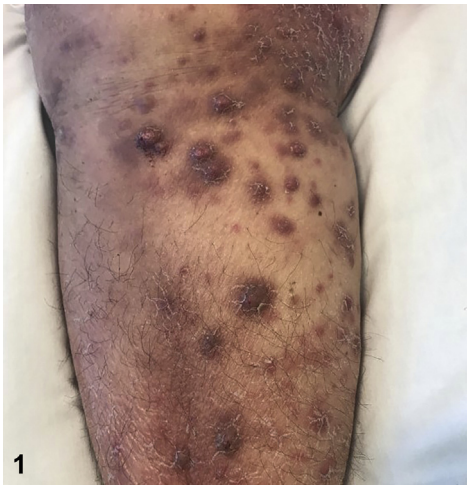

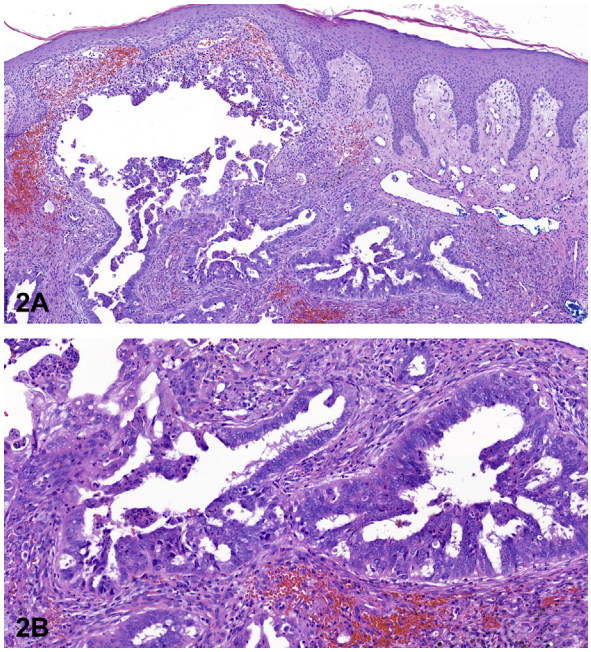

A 65-year-old woman with chemotherapy-resistant endometrioid endometrial adenocarcinoma presented with an 8-month history of firm violaceous nodules on her right leg. She complained of worsening right leg pain and chronic edema isolated to her right lower leg after local radiation therapy for known iliopsoas metastases. Physical examination revealed an edematous right lower extremity, with pitting edema of the lower portion of her right leg, and numerous scattered indurated violaceous nodules on her right thigh and the proximal lower portion of her right leg (Fig 1). Punch biopsies were performed (Fig 2, *A* and *B*). The neoplastic cells were cytokeratin (CK)7^{+} but GATA3^{-}, caudal-type homeobox transcription factor 2 $(CDX2)^{-}$, and $CK20^{-}$.

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Question 1: What is the most likely diagnosis?

A. Atypical mycobacterial infection

B. Metastatic endometrial carcinoma

C. Histoplasmosis

D. Kaposi sarcoma

E. Aspergillosis

Answers:

A. Atypical mycobacterial infection—Incorrect. Although atypical mycobacterial infections may have a similar clinical presentation, the differentiating histopathologic features include acid-fast bacilli and granulomatous inflammation.[1]

B. Metastatic endometrial carcinoma—Correct. Cutaneous endometrial metastases can present with a variety of morphologies, including nodules, plaques, and ulcers.[1,2] Histopathology reflects the features of a metastatic adenocarcinoma but may not conclusively identify the site of origin. While endometrial carcinoma is among the more common malignancies in women, it rarely metastasizes to the skin and represents less than 1% of cutaneous metastases.[2,3] However, the identification of these metastases is important for their prognostic implication, which is poor and frequently leads patients to undergo palliative care.[2]

C. Histoplasmosis—Incorrect. Disseminated histoplasmosis may present with violaceous nodules clinically but can be histopathologically differentiated by the presence of tuberculoid granulomas and macrophages parasitized with ovoid yeast.[1]

D. Kaposi sarcoma—Incorrect. Kaposi sarcoma is histopathologically characterized by dermal spindle cell proliferation, plump endothelial cells lining irregular vascular spaces, and a lymphoplasmacytic infiltrate.[1] In addition, nuclear HHV-8 expression can be demonstrated by immunohistochemistry.

E. Aspergillosis—Incorrect. On histological examination, aspergillosis demonstrates septate, dichotomously branching hyphal organisms.[1]

Question 2: Which of the following clinical presentations is most frequently described in cutaneous metastatic endometrial carcinoma?

A. Head and neck involvement

B. Alopecia

C. Bluish nodules

D. Papulovesicular metastases

E. Sessile, acrochordon-like cutaneous metastases

F. Cutaneous metastases at the initial site of surgery or radiation

Answers:

A. Head and neck involvement—Incorrect. While the head, neck, and trunk are the most common locations of cutaneous metastasis of most primary malignancies,[4] cutaneous metastatic endometrial carcinoma most commonly occurs locally.

B. Alopecia—Incorrect. Alopecia is associated with cutaneous metastases of breast and colorectal tumors.[4]

C. Bluish nodules—Incorrect. Bluish nodules may be seen in the cutaneous metastases of neuroblastoma, liver, and renal carcinoma.[4]

D. Papulovesicular metastases—Incorrect. Vesicular eruptions are an infrequent presentation of metastatic breast and colorectal adenocarcinoma.[4]

E. Sessile, acrochordon-like cutaneous metastases—Incorrect. Sessile, acrochordon-like papules may present in metastatic colorectal adenocarcinoma.[4]

F. Cutaneous metastases at the initial site of surgery or radiation—Correct. Cutaneous metastases of endometrial carcinoma most commonly occur at the site of initial surgical or radiological treatment.[1-3]

Question 3: Which immunohistochemical findings support the endometrial origin of metastasis?

A. CK 7^+, CK20$^-$, estrogen receptor/progesterone receptor (ER/PR)$^+$, carcinoembryonic antigen (CEA)$^+$

B. CK 7^+, CK20$^-$, ER/PR$^+$, CEA$^-$, Wilms tumor 1 (WT1)$^+$

C. CK 7^+, CK20$^-$, ER/PR$^+$, CEA$^-$, vimentin$^+$

D. CK 7^+, CK20$^-$, ER/PR$^-$, CEA$^+$, vimentin$^-$

E. CK 7^+, CK20$^-$, CEA$^+$, thyroid transcription factor-1 (TTF1)$^+$

Answers:

A. CK 7^+, CK20$^-$, ER/PR$^+$, CEA$^+$—Incorrect. This immunohistochemical profile is typical of breast adenocarcinoma. While both breast and endometrial carcinomas are CK 7^+, CK20$^-$, and ER/PR$^+$, breast carcinoma can be differentiated by

CEA, mammoglobin, and gross cystic disease fluid protein expression.[5]

B. CK 7^+, $CK20^-$, ER/PR^+, CEA^-, $WT1^+$—Incorrect. This immunohistochemical profile is seen in ovarian serous adenocarcinoma. While both ovarian and endometrial adenocarcinomas are $CK7^+$, $CK20^-$, ER/PR^+, and CEA^-, ovarian carcinoma can be differentiated by WT1 and mesothelin positivity.[5]

C. CK 7^+, $CK20^-$, ER/PR^+, CEA^-, vimentin$^+$—Correct. While there are no specific antibody stains for endometrial adenocarcinoma, immunohistochemistry can support an endometrial origin and exclude more common sources of metastatic adenocarcinoma. Endometrial adenocarcinoma is $CK7^+$ and ER/PR^+ but $CK20^-$.[5] CEA, GATA-3, and CDX2 are negative in endometrial adenocarcinoma. CEA is overexpressed in gastrointestinal, lung, and breast carcinomas, and GATA-3 is sensitive and specific for breast and urothelial carcinomas. CDX2 is frequently expressed by intestinal tumors.

D. CK 7^+, $CK20^-$, ER/PR^-, CEA^+, vimentin$^-$—Incorrect. This is observed in endocervical carcinoma.[5] While the immunohistochemical findings of endometrial carcinoma are similar, the absence of vimentin expression and reactivity with CEA can differentiate endocervical carcinoma.

E. CK 7^+, $CK20^-$, CEA^+, $TTF1^+$—Incorrect. This profile is characteristic of lung adenocarcinoma.[5] While both endometrial and lung adenocarcinomas are $CK7^+/CK20^-$, lung adenocarcinoma can be differentiated by CEA and TTF1 expression.

Abbreviations used:

CDX2: caudal-type homeobox transcription factor 2
CEA: carcinoembryonic antigen
CK: cytokeratin
ER: estrogen receptor
PR: progesterone receptor
TTF1: thyroid transcription factor-1
WT1: Wilms tumor 1

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