A 68-year-old patient presented with an enlarging flesh-colored nodule on the thigh that was positive for cytokeratin 20 and negative for cytokeratin 7.

**THE BEST DIAGNOSIS IS:**

a. cutaneous endometriosis  
b. metastatic adenocarcinoma of the colon  
c. metastatic breast carcinoma  
d. primary cutaneous angiosarcoma  
e. primary cutaneous mucinous carcinoma

Please turn to page 282 for the diagnosis.
Cutaneous adenocarcinomas are uncommon, whether they present as a primary lesion or metastatic disease. In our patient, the histologic findings and immunohistochemical staining pattern were consistent with metastatic adenocarcinoma of the colon, an uncommon clinical presentation.

Colonic adenocarcinoma can cause cutaneous metastasis in 3% of cases. The most common sites of metastases include the abdomen, chest, and back. On histologic examination, hematoxylin and eosin (H&E)–stained sections of cutaneous metastatic adenocarcinoma illustrate a malignant gland-forming neoplasm in the dermis with luminal mucin and necrotic debris (quiz image). The glands are lined by tall columnar epithelial cells with hyperchromatic nuclei. Alternatively, poorly differentiated morphology can be seen with fewer glands and more infiltrating nests of tumor cells. Immunohistochemically, colonic adenocarcinoma typically is negative for cytokeratin (CK) 7 and positive for CK20 and caudal type homeobox transcription factor 2 (CDX-2).

Primary cutaneous mucinous carcinoma is characterized by islands of neoplastic cells floating in pools of mucin (Figure 1). It may be indistinguishable from metastatic mucinous carcinomas of the colon or breast. Immunohistochemistry can be helpful in differentiating metastatic breast vs colon carcinoma. Cytokeratin 7, GATA binding protein 3, gross cystic disease fluid protein 15, and estrogen receptor will be positive in carcinomas of the breast and will be negative in colonic adenocarcinomas. Furthermore, lesional cells in metastatic adenocarcinoma of the colon are positive for CDX-2 and CK20, while those in metastatic carcinoma of the breast are negative. Immunohistochemistry also can differentiate primary cutaneous carcinoma from metastatic adenocarcinoma. When used in combination, p63 and podoplanin (D2-40) offer a highly sensitive and specific indicator of a primary cutaneous neoplasm, as both demonstrate either focal or diffuse positivity in this setting. In contrast, these stains typically are negative in metastatic adenocarcinomas of the skin.

Endometriosis affects 1% to 2% of all reproductive-age females, of which extrapelvic manifestations account for only 0.5% to 1.0% of cases. Histologically, extrapelvic endometriosis is characterized by the triad of endometrial-type glands, endometrial stroma, and hemorrhage or hemosiderin deposition (Figure 2). The glands can enlarge and demonstrate architectural distortion with partial lack of polarity. These features initially can be concerning for adenocarcinoma, but on closer examination, nuclear morphology is regular and mitoses are absent. The diagnosis usually can be rendered with H&E alone; however, immunohistochemical stains for CD10 and estrogen receptor can highlight the endometrial stroma. Furthermore, endometrial glands will stain positive for paired box gene 8 (PAX8), a marker that is not expressed within the gastrointestinal tract and associated malignancies.

Primary cutaneous angiosarcoma may mimic adenocarcinoma, as the endothelial-lined vessels can be confused as malignant glands (Figure 3). Angiosarcoma often is seen in 1 of 3 clinical presentations: the head and neck of elderly patients, postirradiation treatment, and chronic lymphedema. Regardless of the location, the disease carries a poor prognosis, with a 5-year survival rate of 12% following initial diagnosis. Angiosarcoma is characterized by malignant endothelial cells dissecting through the dermis. Although the histology can be deceptively bland in some cases, the neoplasm most commonly demonstrates notable atypia with a multilayered endothelium and occasional intravascular atypical cells (“fish in the...
Within the histologic differential diagnoses, the most useful tool to diagnose metastatic adenocarcinoma of the colon often is a thorough clinical history. In the absence of a clinical history of adenocarcinoma, immunohistochemistry can be a useful adjunct to aid in the correct characterization and classification of a malignant gland-forming tumor.5,3,6

REFERENCES