Firm Mobile Nodule on the Scalp

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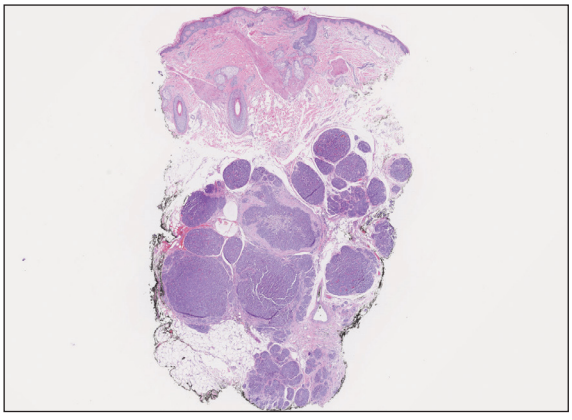

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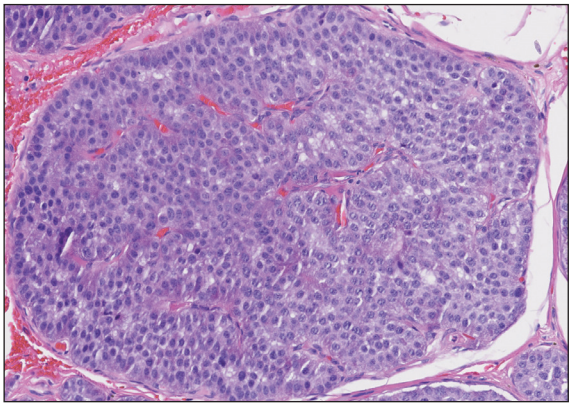

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A 47-year-old woman was admitted to the hospital with abdominal pain and flushing. She had a history of a midgut carcinoid that originated in the ileum with metastasis to the colon, liver, and pancreas. Dermatologic examination revealed a firm, nontender, mobile, 7-mm scalp nodule with a pink-purple overlying epidermis. The lesion was associated with a slight decrease in hair density. A 4-mm punch biopsy was performed.

THE BEST **DIAGNOSIS IS:**

a. basal cell carcinoma
b. Merkel cell carcinoma
c. metastatic carcinoid tumor
d. metastatic small cell lung carcinoma
e. superficial Ewing sarcoma family of tumors

PLEASE TURN TO PAGE 223 FOR THE DIAGNOSIS

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THE **DIAGNOSIS:** Metastatic Carcinoid Tumor

Carcinoid tumors are derived from neuroendocrine cell compartments and generally arise in the gastrointestinal tract, with a quarter of carcinoids arising in the small bowel.[1] Carcinoid tumors have an incidence of approximately 2 to 5 per 100,000 patients.[2] Metastasis of carcinoids is approximately 31.2% to 46.7%.[1] Metastasis to the skin is uncommon; we present a rare case of a carcinoid tumor of the terminal ileum with metastasis to the scalp.

Unlike our patient, most patients with carcinoid tumors have an indolent clinical course. The most common cutaneous symptom is flushing, which occurs in 75% of patients.[3] Secreted vasoactive peptides such as serotonin may cause other symptoms such as tachycardia, diarrhea, and bronchospasm; together, these symptoms comprise carcinoid syndrome. Carcinoid syndrome requires metastasis of the tumor to the liver or a site outside of the gastrointestinal tract because the liver will metabolize the secreted serotonin. However, even in patients with liver metastasis, carcinoid syndrome only occurs in approximately 10% of patients.[4] Common skin findings of carcinoid syndrome include pellagralike dermatitis, flushing, and sclerodermalike changes.[5] Our patient experienced several episodes of presyncope with symptoms of dyspnea, lightheadedness, and flushing but did not have bronchospasm or recurrent diarrhea. Intramuscular octreotide improved some symptoms.

The scalp accounts for approximately 15% of cutaneous metastases, the most common being from the lung, renal, and breast cancers.[6] Cutaneous metastases of carcinoid tumors are rare. A PubMed search of articles indexed for MEDLINE using the terms *metastatic* AND [*carcinoid* OR *neuroendocrine*] *tumors* AND [*skin* OR *cutaneous*] revealed 47 cases.[7-11] Similar to other skin metastases, cutaneous metastases of carcinoid tumors commonly present as firm erythematous nodules of varying sizes that may be asymptomatic, tender, or pruritic (Figure 1). Cases of carcinoid tumors with cutaneous metastasis as the initial and only presenting sign are exceedingly rare.[12]

Histology of carcinoid tumors reveals a dermal neoplasm composed of loosely cohesive, mildly atypical, polygonal cells with salt-and-pepper chromatin and eosinophilic cytoplasm, which are similar findings to the primary tumor. The cells may grow in the typical trabecular or organoid neuroendocrine pattern or exhibit a pseudoglandular growth pattern with prominent vessels (quiz image, top).[12] Positive chromogranin and synaptophysin immunostaining are the most common and reliable markers used for the diagnosis of carcinoid tumors.

An important histopathologic differential diagnosis is the aggressive Merkel cell carcinoma, which also demonstrates homogenous salt-and-pepper chromatin but exhibits a higher mitotic rate and positive cytokeratin 20 staining (Figure 2).[13] Basal cell carcinoma (BCC) also may display similar features, including a blue tumor at scanning magnification and nodular or infiltrative growth patterns. The cell morphology of BCC is characterized by islands of basaloid cells with minimal cytoplasm and frequent apoptosis, connecting to the epidermis with peripheral palisading, retraction artifact, and a myxoid stroma; BCC lacks the salt-and-pepper chromatin commonly seen in carcinoid tumors (Figure 3). Basal cell carcinoma is characterized by positive BerEP4 (epithelial cell adhesion molecule immunostain), cytokeratin 5/6, and cytokeratin 14 uptake. Cytokeratin 20, often used to diagnose Merkel cell carcinoma, is negative in BCC. Chromogranin and synaptophysin occasionally may be positive in BCC.[14]

The superficial Ewing sarcoma family of tumors also may be included in the differential diagnosis of small round cell tumors of the skin, but they are very rare. These tumors possess strong positive membranous staining of cytokeratin 99 and also can stain positively for synaptophysin and chromogranin.[15] Epithelial membrane antigen, which is negative in Ewing sarcomas, is positive in

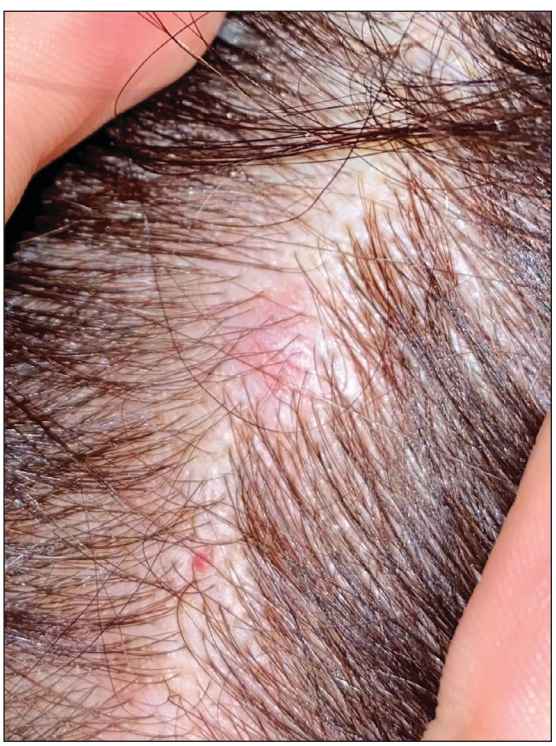

FIGURE 1. Metastatic carcinoid tumor. Firm, nontender, mobile, 7-mm dermal nodule with a pink-purple overlying epidermis on the frontal scalp.

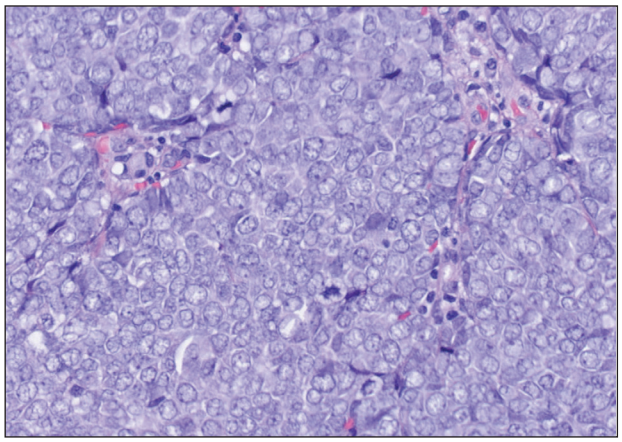

FIGURE 2. Merkel cell carcinoma. Small, round, blue tumor with oval nuclei, salt-and-pepper chromatin, high mitotic index, and indistinct nucleoli (H&E, original magnification ×400).

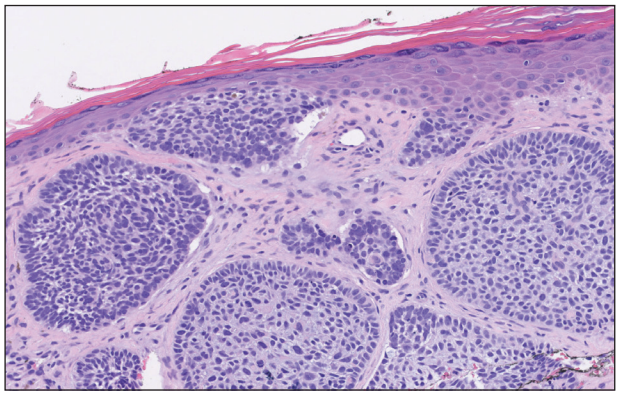

FIGURE 3. Basal cell carcinoma. Basaloid budding, connection with the epidermis, mucinous stroma, retraction artifact, and palisading blue cells in a picket fence–like distribution around the periphery (H&E, original magnification ×210).

carcinoid tumors.[16] Neuroendocrine tumors of all sites share similar basic morphologic patterns, and multiple primary tumors should be considered, including small cell lung carcinoma (Figure 4).[17,18] Red granulations and true glandular lumina typically are not seen in the lungs but are common in gastrointestinal carcinoids.[18] Regarding immunohistochemistry, TTF-1 is negative and CDX2 is positive in gastroenteropancreatic carcinoids, suggesting that these 2 markers can help distinguish carcinoids of unknown primary origin.[19]

Metastases in carcinoid tumors are common, with one study noting that the highest frequency of small intestinal metastases was from the ileal subset.[20] At the time of diagnosis, 58% to 64% of patients with small intestine carcinoid tumors already had nonlocalized disease, with frequent sites being the lymph nodes (89.8%), liver (44.1%), lungs (13.6%), and peritoneum (13.6%). Regional and distant metastases are associated with substantially worse prognoses, with survival rates

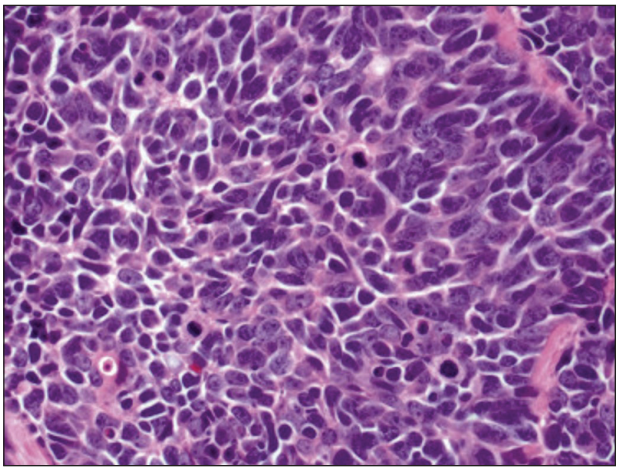

FIGURE 4. Small cell lung carcinoma. Round blue cells with minimal cytoplasm, nuclei with finely dispersed chromatin, indistinct nuclei, and a high mitotic rate. The stroma is thin and delicate, and apoptosis of individual cells commonly is seen (H&E, original magnification ×400).

of 71.7% and 38.5%, respectively.[1] Treatment of symptomatic unresectable disease focuses on symptomatic management with somatostatin analogs that also control tumor growth.[21]

We present a rare case of scalp metastasis of a carcinoid tumor of the terminal ileum. Distant metastasis is associated with poorer prognosis and should be considered in patients with a known history of a carcinoid tumor.

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