Firm Pink Nodule on the Scalp

Rachel McAndrew, MD; Pedram Ghasri, MD

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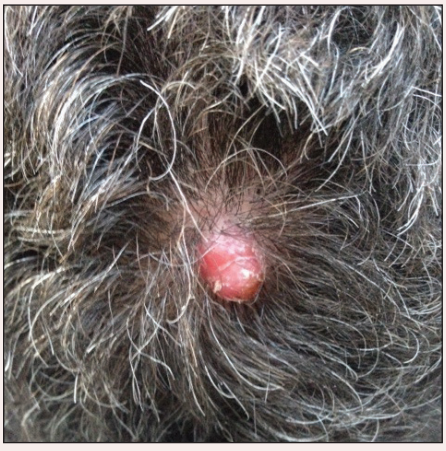

A 69-year-old man with stage IV renal cell carcinoma (RCC) but no history of skin cancer presented with a nodule on the right side of the posterior scalp of 2 months' duration. He noted that the lesion bled intermittently and crusted over. Three years prior, the patient had a left-sided nephrectomy, which showed a 7-cm tumor consistent with clear cell RCC (Fuhrman nuclear grade 2). Over the last 6 months, RCC metastases to the right kidney, lungs, and right cervical lymph nodes were found. His current chemotherapy treatment was axitinib; he was previously on pazopanib and everolimus. Physical examination revealed a 10×10-mm, pink-yellow, firm nodule with overlying telangiectases on the right side of the posterior scalp.

What's the diagnosis?

a. atypical fibroxanthoma
b. basal cell carcinoma
c. cutaneous angiosarcoma
d. metastatic renal cell carcinoma
e. pyogenic granuloma

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Dr. McAndrew is from the Department of Dermatology, Dell Medical School, University of Texas at Austin. Dr. Ghasri is from the Department of Dermatology, University of California, Irvine.

The authors report no conflict of interest.

Correspondence: Rachel McAndrew, MD, Department of Dermatology, Dell Medical School, University of Texas at Austin, 601 E 15th St, CEC C2.470, Austin, TX 78712 (mcandrew@utexas.edu).

The Diagnosis: Metastatic Renal Cell Carcinoma

A shave biopsy of the right occipital scalp lesion demonstrated large clear cells arranged in oval nests with mildly atypical central nuclei (Figure). The findings were consistent with the clear cell type of metastatic renal cell carcinoma (mRCC) with tumor involvement in the deep margin. PAX8 immunostain was positive in the tumor, further supporting the diagnosis of mRCC.

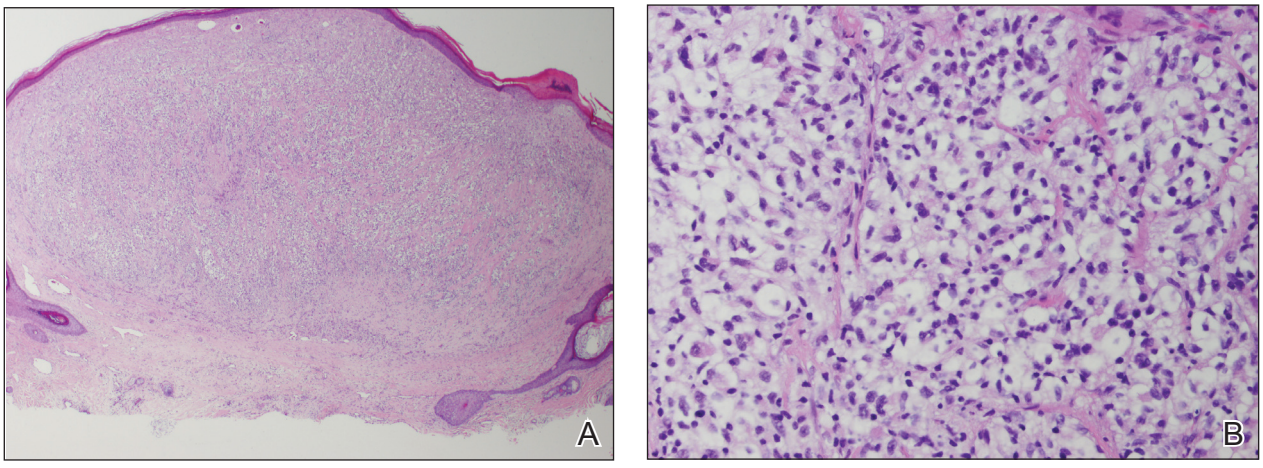
The most common patient demographic diagnosed with renal cell carcinoma (RCC) is men in the sixth and seventh decades of life.[1,2] The classic presentation of RCC includes the triad of flank pain, hematuria, and a palpable abdominal mass. Other symptoms may include fatigue, weight loss, and anemia; however, small localized tumors rarely are symptomatic, and less than 10% of patients with RCC present with this classic triad.[3] Many RCCs are diagnosed from incidental findings on abdominal imaging or from the presentation of metastatic disease.[1,2] The lungs, bones, and liver are the most common sites of metastases, while skin metastases are rare.[2] One study found only 3.3% (10/306) of RCC cases had cutaneous metastases and the scalp was the most common location. In half of these patients, the skin metastases were present at initial RCC diagnosis.[4]

The most common presentation of a cutaneous metastasis of RCC entails the rapid development of a reddish blue nodule on the face or scalp.[4,5] The differential diagnosis may include basal cell carcinoma, hemangioma, cutaneous angiosarcoma, pyogenic granuloma, and atypical fibroxanthoma. Careful elicitation of a medical history indicating any of the classic or systemic signs associated with RCC or a personal history of RCC should raise the suspicion for mRCC and prompt a biopsy.

Clear cell RCC is the most common type of primary RCC and 81% of mRCCs were found to be of the clear cell type. Clear cell RCC classically exhibits clear ballooned cytoplasm with distinct cell borders.[6] Immunohistochemistry stains with PAX2 and PAX8 are helpful in diagnosing the renal origin of the metastatic tissue, with PAX8 being especially helpful (89% sensitivity).[7]

The von Hippel-Lindau gene, *VHL*, is involved in up to 60% of sporadic clear cell RCC cases, in addition to its involvement in VHL syndrome.[1] von Hippel-Lindau syndrome is associated with clear cell RCC, retinal angiomas, hemangioblastomas of the central nervous system, and pheochromocytomas.[1] The mutated *VHL* gene is associated with an increased expression of vascular endothelial growth factor (VEGF), which promotes angiogenesis, endothelial mutagenesis, and vascular permeability.[8] These physiologic responses are likely responsible for the proliferation and dissemination of neoplastic cells in clear cell RCC.[9] The understanding of this pathogenic mechanism has led to the development of targeted effective treatments in RCC.

Systemic treatments for mRCC are rapidly evolving and improving.[9] Vascular endothelial growth



Histology revealed a clear cell–type tumor with extension into the deep margin (A) and large clear cells arranged in oval nests with mildly atypical central nuclei (B)(both H&E, original magnifications ×20 and ×200).

factor tyrosine kinase inhibitors such as sorafenib, sunitinib, and pazopanib, as well as the VEGF monoclonal antibody bevacizumab, have all demonstrated notable efficacy in the treatment of RCC. Phase 3 clinical trials for the treatment of mRCC have demonstrated that the new, more biochemically potent VEGF tyrosine kinase inhibitor axitinib has superior efficacy to sorafenib, the prior standard of care.[9] Our patient noted that the cutaneous mRCC lesion seemed to be improving after starting treatment with axitinib 2 months prior to presentation. In addition to systemic chemotherapy, the surgical removal of lesions often is indicated for the treatment of cutaneous mRCC.[5,10] Our patient has continued axitinib and is doing well.

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