Red-Blue Nodule on the Scalp

B. Joel Tjarks, MD; Tammie C. Ferringer, MD

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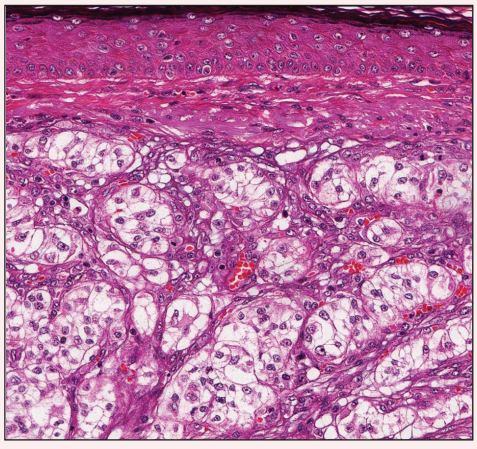

H&E, original magnification ×200.

A 59-year-old man presented with a 1.5×1.0-cm asymptomatic, smooth, red-blue nodule on the left parietal scalp. The nodule had been rapidly enlarging over the last 3 weeks. After resection, the cut surface was golden yellow and focally hemorrhagic.

The best diagnosis is:

a. balloon cell nevus
b. clear cell hidradenoma
c. metastatic clear cell renal cell carcinoma
d. sebaceous carcinoma
e. xanthoma

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Dr. Tjarks is from the Department of Pathology, Sanford School of Medicine, University of South Dakota, Sioux Falls. Dr. Ferringer is from the Departments of Dermatology and Laboratory Medicine, Geisinger Medical Center, Danville, Pennsylvania.
The authors report no conflict of interest.
Correspondence: B. Joel Tjarks, MD, Department of Pathology, Sanford School of Medicine, University of South Dakota, 1400 W 22nd St, Sioux Falls, SD 57105 (Joel.Tjarks@usd.edu).

Metastatic Clear Cell Renal Cell Carcinoma

The differential diagnosis of cutaneous neoplasms with clear cells is broad. Clear cell features can be seen in primary tumors arising from the epidermis and cutaneous adnexa as well as in mesenchymal and melanocytic neoplasms. Furthermore, metastatic disease should be considered in the histologic differential diagnosis, as many visceral malignancies have clear cell features. This patient was subsequently found to have a large renal mass with metastasis to the lungs, spleen, and bone. The histologic findings support the diagnosis of metastatic clear cell renal cell carcinoma (RCC) to the skin.

Approximately 30% of patients with clear cell RCC present with metastatic disease with approximately 8% of those involving the skin.[1,2] Cutaneous RCC metastases show a predilection for the head, especially the scalp. The clinical presentation is variable, but there often is a history of a rapidly growing brown, black, or purple nodule or plaque. A thorough review of the patient's history should be conducted if metastatic RCC is in the differential diagnosis, as it has been reported to occur up to 20 years after initial diagnosis.[3]

Histologically, clear cell RCC (quiz image) is composed of nests of tumor cells with clear cytoplasm and centrally located nuclei with prominent nucleoli. The clear cell features result from abundant cytoplasmic glycogen and lipid but may not be present in every case. One of the most important histologic features is the presence of delicate branching blood vessels (Figure 1). Numerous extravasated red blood cells also may be present. Positive immunohistochemical staining for PAX8, CD10, and RCC antigens support the diagnosis.[4]

Balloon cell nevi (Figure 2) most commonly occur on the head and neck in adolescents and young adults but clinically are indistinguishable from other banal nevi. The nevus cells are large with foamy to finely vacuolated cytoplasm and lack atypia. The clear cell change is the result of melanosome degeneration and may be extensive. The presence of melanin pigment, nests of typical nevus cells, and positive staining with MART-1 can help distinguish the tumor from xanthomas and RCC.[5]

Clear cell hidradenoma (Figure 3) is a well-circumscribed tumor of sweat gland origin that arises in the dermis. The architecture usually is solid, cystic, or a combination of both. The cytology is classically bland with poroid, squamoid, or clear cell morphology. Clear cells that are positive on periodic acid–Schiff staining predominate in up to one-third of cases. Carcinoembryonic antigen and epithelial membrane antigen can be used to highlight the eosinophilic cuticles of ducts within solid areas.[6]

Sebaceous carcinoma (Figure 4) most frequently arises in a periorbital distribution, although extraocular lesions are known to occur. Histologically, there is a proliferation of both mature sebocytes and basaloid cells in the dermis, occasionally involving the epidermis. The mature sebocytes demonstrate clear cell features with foamy to vacuolated cytoplasm and large nuclei with scalloped borders. The clear cells may vary greatly in number and often are sparse in poorly differentiated tumors in which pleomorphic basaloid cells may predominate. The basaloid cells may resemble those of squamous or

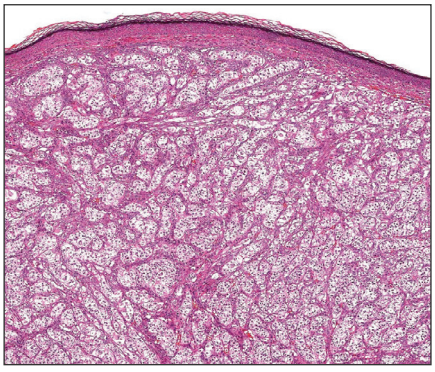

Figure 1. Metastatic clear cell renal cell carcinoma showing nests and cords of clear cells with centrally located nuclei within a delicate "chicken wire" vascular network (H&E, original magnification ×100).

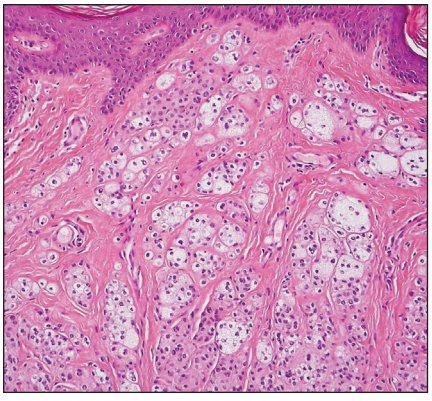

Figure 2. Balloon cell nevus showing nests of vacuolated dermal melanocytes with small round nuclei (H&E, original magnification ×200).

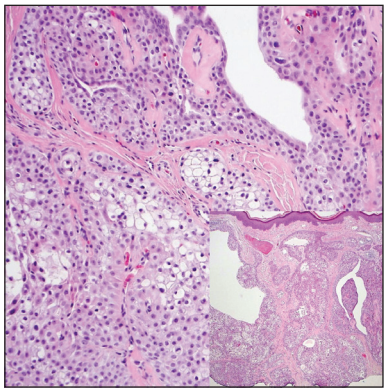

Figure 3. Hidradenoma with bland poroid and clear cells (H&E, original magnification ×200), along with cystic and solid architecture (inset [H&E, original magnification ×40]).

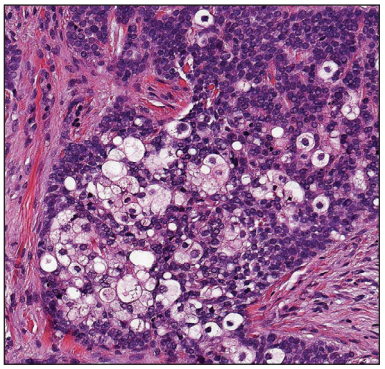

Figure 4. Sebaceous carcinoma showing an infiltrate of basaloid cells and vacuolated sebocytes with large scalloped nuclei in a desmoplastic stroma (H&E, original magnification ×200).

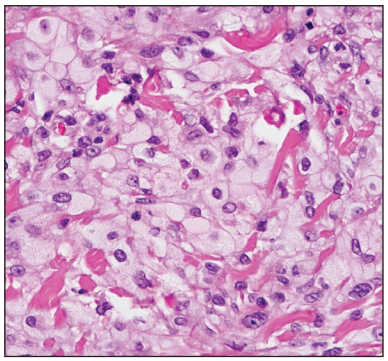

Figure 5. Xanthoma with sheets of foamy, lipid-laden macrophages (H&E, original magnification ×200).

basal cell carcinoma, leading to a diagnostic dilemma in some cases. Special staining with Sudan black B and oil red O highlights the cytoplasmic lipid but must be performed on frozen section specimens. Although not entirely specific, immunohistochemical expression of epithelial membrane antigen, androgen receptor, and membranous vesicular adipophilin staining in sebaceous carcinoma can assist in the diagnosis.[7]

Cutaneous xanthomas (Figure 5) may arise in patients of any age and represent deposition of lipid-laden macrophages. Classification often is dependent on the clinical presentation; however, some subtypes demonstrate unique morphologic features (eg, verruciform xanthomas). Xanthomas classically arise in association with elevated serum lipids, but they also may occur in normolipemic patients. Individuals with Erdheim-Chester disease have an increased propensity to develop xanthelasma. Similarly, plane xanthomas have been associated with monoclonal gammopathy. Histologically, xanthomas are characterized by sheets of foamy macrophages within the dermis and subcutis. Positive immunohistochemical staining for CD68 highlighting the histiocytic nature of the cells and the absence of a delicate vascular network aid in the differentiation from RCC.

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