

BRIEF ARTICLES

Renal Cell Carcinoma (RCC) Stain Negative Metastatic Clear Cell Renal Cell Carcinoma Masquerading as a Pyogenic Granuloma on the Scalp

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ABSTRACT

Metastasis occurs in 25-50% of patients diagnosed with primary renal cell carcinoma (RCC), however only 6% of RCC metastases manifest on the skin. We present a unique case of a slowly growing clear cell RCC metastasis of the scalp in a middle-aged male that was RCC stain negative. Clinically, the lesion appeared to be a benign pyogenic granuloma, however, the diagnosis of metastatic clear cell renal cell carcinoma was made based on histology. Because cutaneous metastases may masquerade as other more benign tumors, the physician must be clinically suspicious of vascular appearing lesions on the scalp.

INTRODUCTION

Renal cell carcinoma (RCC) accounts for approximately 3% of all malignancies and more than 90% of all primary renal malignancies.^{1,2} The classic triad of symptoms associated with primary RCC are flank pain, presence of an abdominal wall mass, and hematuria.² Metastases can spread to any organ and usually occurs within 5 years of diagnosis in patients with a history of primary RCC. However, metastasis occurs before initial diagnosis in 30% of cases. The vascular-rich nature of RCC results in metastases to distant sites via hematogenous spread.³ Symptoms of metastatic RCC are often attributed to the

metastases themselves resulting in variable clinical presentation depending on the site. While up to half of patients diagnosed with RCC will have metastasis, cutaneous metastases of RCC occurs in 6% of cases.^{2,4} Often times these cutaneous lesions have a vascular appearance and may mimic a host of other more benign lesions, such as pyogenic granulomas.⁵ Ultimately, to make the correct diagnosis, a combination of cutaneous lesion histology and immunohistochemistry are employed. Common stains to confirm the diagnosis of RCC metastasis are RCC stain, epithelial membrane antigen (EMA), PAX-2, and PAX-8. Notably 25% of these metastases are RCC stain negative.³ We report a case of a slowly growing clear cell RCC metastasis of the scalp that was RCC stain negative.

July 2020 Volume 4 Issue 4

CASE PRESENTATION

A 45-year-old Caucasian man with a past medical history of primary renal cell carcinoma status-post right partial nephrectomy 4 years prior, diabetes mellitus type 2, cholecystectomy, and daily tobacco use presented to the dermatology clinic for a gradually enlarging mass on the scalp for 6 months. Patient reported associated pain and tenderness, but denied any weight loss, fever, lymphadenopathy, or other pertinent systemic symptoms. Physical exam revealed a solitary, hemorrhagic friable nodule on the right parietal scalp (Figure 1). A deep shave biopsy performed at the initial visit revealed an asymmetrical and poorly circumscribed neoplasm in the dermis compromised of clear cells with small monomorphous nuclei (Figure 2). The cells formed collections with very significant arborizing vascularity. Special stains for Melan-A, S-100, SOX10, CK903, PSA, RCC, and AE1/3 were negative. Figure 3 shows a negative RCC stain on pathology. Histologic examination and clinical history points to the diagnosis of metastatic clear cell renal cell carcinoma of the scalp. Patient was referred to oncology, but was lost to follow-up in the dermatology clinic.

DISCUSSION

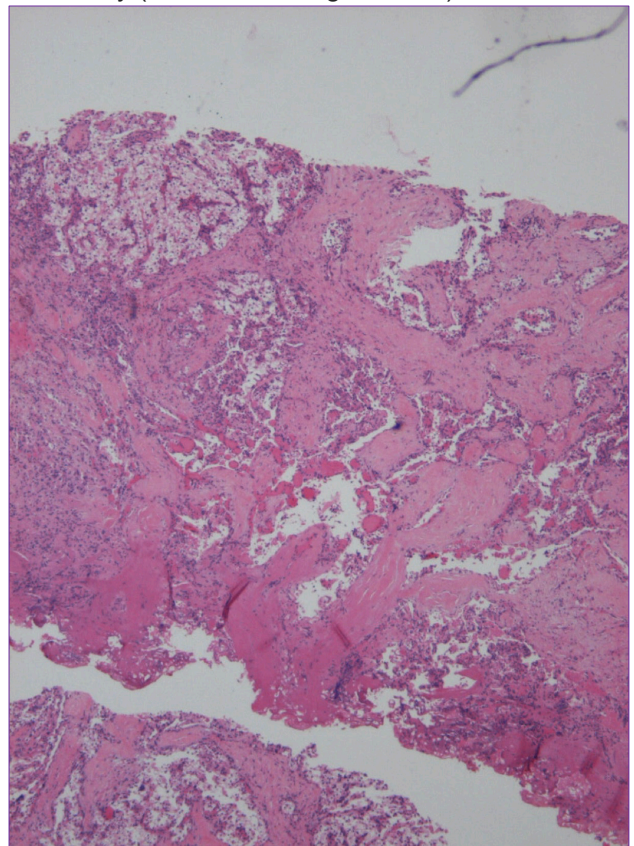
According to the American Cancer Society, it is estimated that there will be 74,000 newly diagnosed cases of kidney cancer in 2020.⁶ RCC occurs more commonly in males compared to females. The use of tobacco products is the single most important risk factor for developing RCC.⁷

Metastasis occurs in 25-50% of patients diagnosed with primary RCC, usually within 5 years of nephrectomy.⁸ Skin metastasis,

Figure 1. Solitary, hemorrhagic nodule on the right parietal scalp.



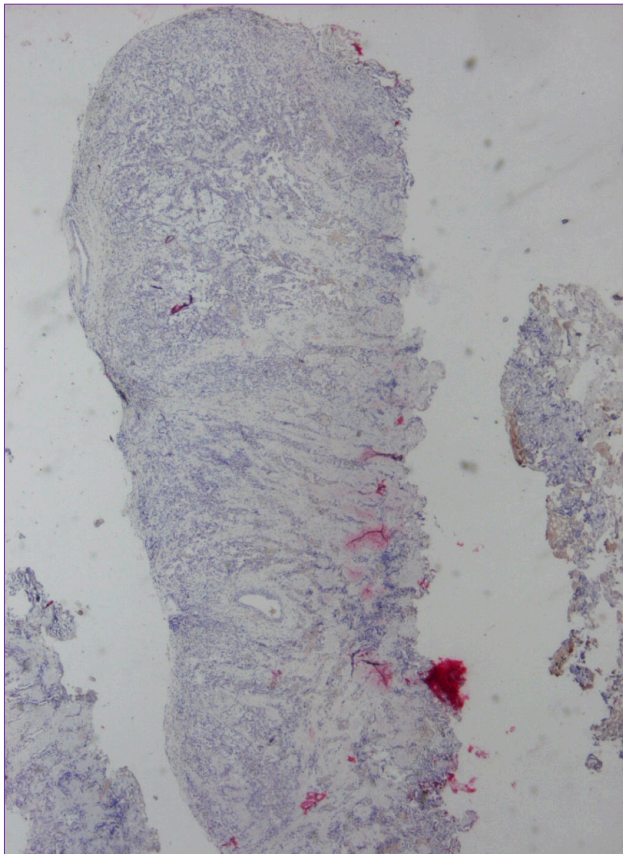
Figure 2. Micrograph of metastatic clear cell RCC. Collection of clear cells with significant arborizing vascularity (H&E at 10x magnification).



although very rare, occurs in 6% of metastatic RCC cases and acts as an important differential in patients with a history of the disease.² The most common

site of metastasis for cutaneous RCC is the scalp, followed by the trunk.³ Cutaneous manifestations of metastasis may include a vascular red, purple, or flesh-colored exophytic lesion that may be pulsatile in nature.^{2,9} Clinically, these lesions can mimic a host of other benign and malignant skin diseases and tumors, such as Kaposi's sarcoma, angiosarcoma, hemangioma, and pyogenic granuloma. McClees et al described a unique case of metastatic RCC presenting as isolated nail dystrophy.¹⁰ Histologic confirmation of these diseases is crucial for accurate and prompt diagnosis.⁹

Figure 3. RCC stain negative tumor (2x magnification).



Various cutaneous tumors can mimic metastatic clear cell renal cell carcinoma histologically including epithelioid angiomylipoma, metastatic clear cell adenocarcinoma, balloon cell melanoma,

angiosarcoma, clear cell squamous cell carcinoma, and malignant hidradenoma.

These entities must be considered in the histological differential diagnosis. Histopathologic features of clear cell RCC include large cells with clear cytoplasm and round nuclei. About 85% of RCC are of the clear cell subtype.¹¹ The nuclear-cytoplasmic ratio is often low, and lymphatic and vascular infiltration is common.⁵ A wide variety of immunohistochemical stains and markers are used in the differentiation of RCC and other clear cell neoplasms. The most common initially used positive markers for RCC are PAX2 and PAX8, along with either RCC marker or CD10.³ RCC marker has a specificity of nearly 100% and sensitivity of 65% in the diagnosis of cutaneous RCC metastasis². Only about 25% of RCC metastases are RCC marker negative. Additional markers that can be used in distinguishing RCC metastasis to specific organ systems include cytokeratin, vimentin, CAIX, and kidney-specific cadherin.^{3,12}

If histopathology and immunohistochemistry confirm RCC, the next step is identifying the primary lesion and ruling out other sites of metastasis. This should begin with a bone scan as well as a computed tomography (CT) of common sites of metastasis like the lungs, brain, adrenal glands, and liver.¹ The use of endoscopy may be beneficial in the diagnosis of GI metastasis. Unfortunately, in cases of cutaneous metastasis, survival usually ranges from 6-12 months.² Treatment is limited and once metastasis has occurred, treatment consists of full or partial nephrectomy, and, when possible, resection of any metastasized lesions, chemotherapy, and/or immunologic therapy.⁹ High-dose interleukin-2 (IL-2) is currently approved and available as a first line treatment for metastatic RCC. Vascular

endothelial growth factor-antibody (VEGF-AB), VEGF receptor tyrosine kinase inhibitor, and mammalian target of rapamycin (mTOR) inhibitors are more specific emerging therapies. These therapies have replaced nonspecific immunotherapy and have improved progression-free survival. However, even with treatment, metastatic RCC is still associated with a poor prognosis.¹³

Our case demonstrated RCC stain negative cutaneous clear cell renal cell carcinoma metastasis to the scalp in a patient with a history of primary renal cell carcinoma. The clinical and pathological presentation of our case is unique. Although the lesion clinically appeared like a pyogenic granuloma, the diagnosis of metastatic clear cell renal cell carcinoma was made based on histology. Because cutaneous metastases may masquerade as other more benign entities, the physician must be clinically suspicious of vascular appearing lesions on the scalp.

Conflict of Interest Disclosures: None

Funding: None

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