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CEPHALIC TO PODALIC: EARLY AND ULTRA-LATE SOFT-TISSUE METASTATIC SPECTRUM OF RENAL CELL CARCINOMA

Oncology

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ABSTRACT

Renal cell carcinoma (RCC) is one of the most aggressive renal malignancies, known for its unpredictable pattern of spread and potential for both early and very late metastases. Although RCC commonly metastasizes to organs such as the lungs, liver, bone, and brain, soft-tissue involvement is exceedingly rare. Due to the unusual behavior of the tumor and the possibility of late recurrence, patients may present with metastatic lesions many years after nephrectomy, creating diagnostic and therapeutic challenges for clinicians. Soft-tissue metastases, especially to regions such as the scalp or gluteal musculature, often mimic benign lesions and therefore require careful evaluation. Early identification of these rare metastatic sites allows timely initiation of appropriate local and systemic treatments. In this report, two uncommon presentations of RCC metastasis—one appearing upfront and the other more than two decades after nephrectomy—are described to highlight the importance of clinical vigilance and the need for long-term follow-up in RCC survivors.

KEYWORDS

Renal cell carcinoma, soft tissue neoplasm, late recurrence, neoplastic cell dormancy

INTRODUCTION:

Renal cell carcinoma (RCC) accounts for 2–3% of adult malignancies and remains the most lethal urological cancer, with clear-cell RCC (ccRCC) being the predominant subtype [1,2]. Despite increased incidental detection with modern imaging, RCC continues to exhibit highly unpredictable behavior due to its strong tendency for hematogenous spread and biologically diverse metastatic pathways. Although 20–40% of patients develop recurrence or distant metastasis within the first five years after nephrectomy, RCC is also known for its capacity for prolonged dormancy, with recurrences documented even decades after initial treatment [3].

The lungs, liver, bone, and brain are the most common metastatic sites [4]. In contrast, metastases to soft tissue, skeletal muscle, or skin are distinctly uncommon, representing less than 3% of all metastatic deposits [4]. Scalp and gluteal muscle involvement are exceptionally rare and often mimic benign lesions, making clinical recognition challenging. Their rarity is generally attributed to the unique vascular, mechanical, and metabolic characteristics of these tissues, which are thought to be unfavorable for metastatic implantation.

RCC's ability to manifest both early aggressive dissemination and late reactivation after long periods of dormancy is linked to complex molecular mechanisms, including VHL gene inactivation, hypoxia-inducible factor (HIF) pathway dysregulation, enhanced angiogenic signaling, and immune microenvironment alterations that support metastatic survival and delayed outgrowth [5].

In this report, we present two highly unusual soft-tissue metastatic manifestations of RCC that illustrate this dual biological nature: a cephalic (scalp) metastasis presenting upfront as the first sign of an occult primary tumor, and a podalic (gluteal muscle) metastasis appearing more than two decades after nephrectomy. These contrasting cases underscore the unpredictable metastatic potential of RCC and highlight the need for careful evaluation of atypical soft-tissue lesions and long-term vigilance in survivorship care.

Case Report

Case 1: Cephalic Presentation

A 52-year-old woman with no significant medical history presented with a tender, progressively enlarging ulcerative nodule over the left parietal scalp. The lesion had developed over several weeks, becoming increasingly painful and intermittently bleeding. Examination revealed a firm, erythematous, ulcerated subcutaneous mass approximately 3 cm in size, without regional lymphadenopathy. Baseline laboratory tests were normal. Whole-body PET-CT demonstrated a 3 × 3.5 cm hypermetabolic scalp nodule (SUV 12.4), along with a hypermetabolic renal mass, confirming the scalp lesion as a metastatic manifestation of previously undiagnosed clear-cell RCC. Biopsy of the scalp lesion verified metastatic clear-cell RCC.

For symptomatic relief and local control, the patient received palliative Electron Beam Radiation Therapy, resulting in partial regression and significant pain reduction. She was subsequently started on Lenvatinib as systemic targeted therapy. Follow-up showed stable regression of the scalp lesion and good clinical response. This case represents an exceptionally rare instance of upfront metastasis from RCC, emphasizing the need to consider metastatic disease in atypical scalp lesions and the value of combined local and systemic therapy.

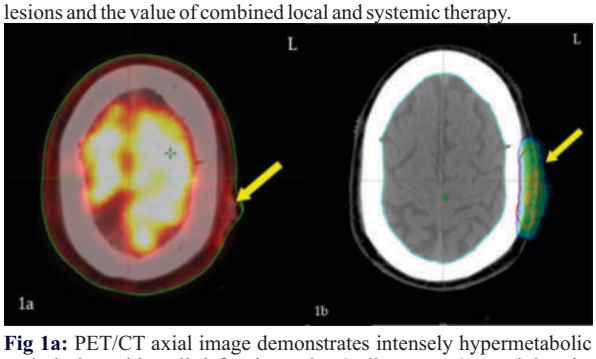

Fig 1a: PET/CT axial image demonstrates intensely hypermetabolic scalp lesion with well-defined margins (yellow arrow), overlying the left parietal region.

Fig 1b: CT-based radiotherapy planning images in axial plane illustrate the target volume (outlined) corresponding to the scalp lesion (yellow arrows). Dose color wash overlays delineate the planned radiation dose distribution encompassing the extracranial scalp metastasis.

Case 2: Podalic Presentation

A 72-year-old man presented with a progressively enlarging, painful right buttock mass that limited sitting and mobility. His history included a radical nephrectomy for localized RCC 20 years earlier, with no prior evidence of recurrence. Examination revealed a firm, deep-seated tender gluteal mass without skin changes or neurological deficits. Laboratory tests were normal. Pelvic MRI showed a 12 × 12.6 × 6.8 cm infiltrative lesion within the right gluteus medius muscle, demonstrating restricted diffusion and heterogeneous enhancement, consistent with malignant soft-tissue metastasis. Biopsy confirmed metastatic clear-cell RCC.

Given significant pain and functional limitation, the patient received palliative Photon Beam Radiation Therapy, resulting in substantial symptomatic improvement. He was subsequently started on Pazopanib for systemic disease control. Follow-up imaging demonstrated stable disease, with improved pain and mobility. This

case highlights RCC's capacity for late recurrence, even decades after nephrectomy, emphasizing the need for long-term vigilance when evaluating new soft-tissue lesions in RCC survivors.

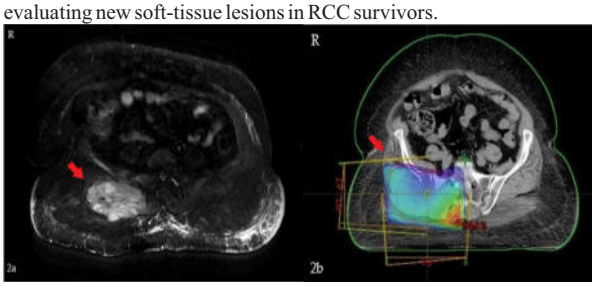

Fig 2a: Axial T2-weighted MRI image shows a well-defined, hyperintense metastatic lesion in the right gluteal region (red arrow), illustrating the extent and morphology of soft tissue involvement.

Fig 2b: Axial planning CT image used for radiotherapy delineation displays the target lesion (red arrow) with dose distribution color wash superimposed, highlighting coverage of the metastasis within the prescribed radiation field.

DISCUSSION:

Renal cell carcinoma (RCC) is notable for its highly unpredictable metastatic course, characterized by both early aggressive dissemination and exceptionally late recurrence[5]. The two cases presented illustrate this dual biological behavior: one demonstrating upfront cephalic soft-tissue metastasis as the initial manifestation of an undiagnosed primary tumor, and the other representing ultra-late podalic gluteal metastasis occurring 20 years after nephrectomy—an extraordinary example of metastatic dormancy and delayed reactivation. Soft-tissue metastases from RCC are exceedingly rare, representing less than 3% of all metastatic lesions; scalp and skeletal muscle involvement is particularly uncommon, likely due to local vascular, mechanical, and metabolic factors that impede tumor implantation[6].

Upfront metastasis in RCC often reflects inherently aggressive tumor biology, characterized by early hematogenous dissemination before the primary lesion becomes clinically apparent [6]. These presentations are typically driven by high proliferative activity, robust angiogenic signaling, and a tumor microenvironment primed for rapid metastatic spread[7]. Clinically, early soft-tissue metastasis—especially to rare sites such as the scalp—suggests a biologically active and highly vascular tumor capable of bypassing traditional metastatic routes. This is exemplified in the first case by the scalp lesion's marked hypermetabolism (SUV 12.4), which served as the sentinel indicator of disseminated disease.

In contrast, the gluteal metastasis in the second case highlights RCC's well-recognized capacity for prolonged dormancy. While recurrences beyond 10 years are known, metastatic reappearance after two decades is exceptionally rare. Potential mechanisms include cellular dormancy, in which disseminated tumor cells remain quiescent for extended periods; microenvironmental shifts involving changes in immune surveillance or angiogenic balance that allow reactivation; and molecular aberrations—particularly VHL inactivation and HIF pathway dysregulation—that enhance angiogenesis, invasion, and metastatic potential once triggered[8,9]. These contrasting timelines underscore the profound biological heterogeneity of RCC, in which some tumors disseminate early and aggressively while others remain clinically silent for decades.

From a diagnostic standpoint, soft-tissue metastases often mimic benign lesions—including lipomas, epidermal cysts, or vascular malformations—leading to potential delays in recognition. Advanced imaging modalities, particularly PET-CT and MRI, are invaluable for differentiating malignant lesions, assessing local extent, and detecting occult or recurrent disease. Management of such metastases requires a multimodal approach. In both cases, palliative radiotherapy provided effective symptom control, particularly for pain and ulceration. Systemic therapy with VEGF-targeted tyrosine kinase inhibitors-Lenvatinib in the upfront metastatic case and Pazopanib in the late recurrence-remains central to contemporary treatment paradigms and aligns with the underlying molecular biology of RCC[10].

Together, the cephalic and podalic metastases presented here expand the spectrum of RCC metastatic behavior and highlight the need for persistent clinical vigilance when evaluating unusual soft-tissue lesions, irrespective of the time elapsed since primary tumor treatment.

Clinical pearls

➔ RCC can metastasize to rare soft-tissue sites such as the scalp and skeletal muscle.

➔ Soft-tissue masses may represent the first sign of occult RCC.

➔ Ultra-late metastasis can occur decades after nephrectomy, requiring long-term surveillance.

➔ Multimodal management, including radiotherapy and targeted therapy, is key for symptom control and disease stabilization.

CONCLUSION:

Scalp and gluteal soft-tissue metastases from RCC are exceedingly rare and reflect highly atypical patterns of spread. The contrasting presentations-one upfront cephalic metastasis and one ultra-late podalic recurrence decades after nephrectomy-highlight the marked heterogeneity of RCC behavior. These cases emphasize the need for a high index of suspicion when assessing unusual soft-tissue lesions and demonstrate the importance of early recognition and timely multimodal management. Their unpredictability reinforces the necessity for ongoing clinical vigilance and long-term surveillance in RCC patients.

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