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## Case Report

# Recurrent renal cell carcinoma to the breast and thigh soft tissues. A case report and review of the literature<sup>☆</sup>

Angélica Lucía Alemán-Cabrera, MD, Alejandra Joanna Pozos-Garza, MS, Marco Antonio Ponce-Camacho, MD, PhD, Adrian Antonio Negreros-Osuna, MD\*, Yazmín Aseret Ramírez-Galván, MD, PhD\*

Department of Radiology and Imaging, Facultad de Medicina, Hospital Universitario “Dr. José Eleuterio González”, Universidad Autónoma de Nuevo León, Av. Francisco I. Madero y Gonzalitos S/N, Col. Mitras Centro, C.P. 64460, Monterrey, Nuevo León, México

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### ABSTRACT

The breast seldom harbors secondary malignant lesions and is rarer for the kidney to be the origin of the metastatic lesion. Keen Imaging analysis, as well as a high index of suspicion, are critical to differentiate a primary tumor from a metastatic lesion.

We describe an unusual case of a recurrent RCC presenting as metastatic lesions to the breast and soft tissue of the right thigh in a 51-year-old patient referred to our breast-imaging unit 10 months after therapeutic surgery.

An adequate and close follow-up accompanied by a thorough physical exam and appropriate imaging methods is essential to identify these types of cases.

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## Introduction

Renal cell carcinoma (RCC) is the second most common malignancy of the urogenital tract after bladder cancer. It represents approximately 3% of adult tumors, and it is considered the most lethal neoplasm of the urological system [1]. Metastatic lesions to the breast account for 0.2%–1.3% of all malignant breast lesions [2].

The classic triad of flank pain, severe hematuria, and palpable flank mass occur in only 6%–10% of RCC cases, while most of them are diagnosed incidentally (>50%) [3]. At diagnosis, 65% of patients have localized disease, 17% have spread regionally, and 16% have metastatic disease at presentation [4].

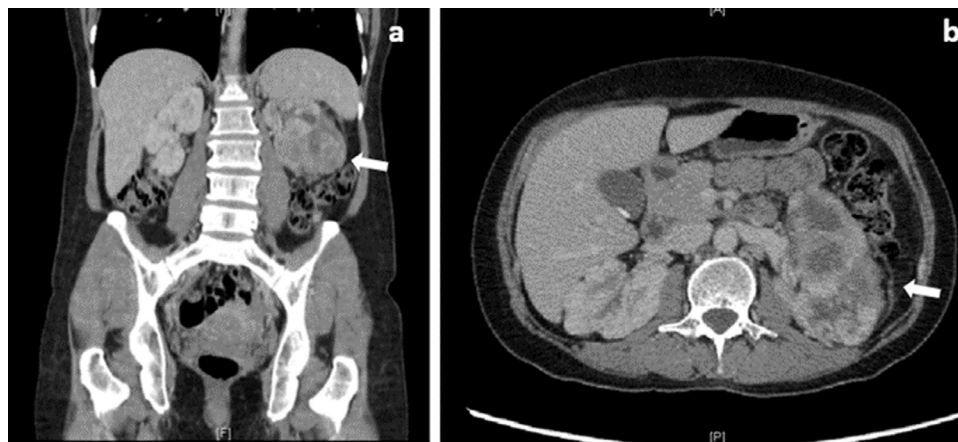
According to the histopathological features, RCC can be divided into: clear cell (75%–85%), papillary (10%–15%), granular

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\* Corresponding authors.

E-mail addresses: [Adrian.negrerosos@uanl.edu.mx](mailto:Adrian.negrerosos@uanl.edu.mx) (A.A. Negreros-Osuna), [yazmin.ramirezgl@uanl.edu.mx](mailto:yazmin.ramirezgl@uanl.edu.mx) (Y.A. Ramírez-Galván).  
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**Fig. 1 – RCC in a 51-year-old woman. (a) Reformatted coronal and (b) axial view of an abdominal CECT showing a left primary renal mass in the lower pole of the left kidney (arrows). The mass had an irregular shape, showed heterogeneous enhancement, infiltrated the perirenal fat and did not invade the renal capsule, the artery or the vein. Metastatic disease was not observed.**

(7%), chromophobe (5%-10%), oncocytic (3%-7%) sarcomatoid (1.5%), and collecting duct tumors (<1%) [5,6]. A higher nuclear level or the presence of a sarcomatoid pattern is associated with a poor prognosis [7].

Despite complete surgical removal, 30% of RCC patients may develop metastases after surgery, especially the RCC Clear cell subtype [5]. The most common sites of metastasis are lung (45%), bone (30%), lymph nodes (22%), liver (20%), adrenal glands (9%), and brain (8%). Single metastases are more common (61%) than multiple metastases (38%) that are more common in young adults [8].

Breast is a rare site for metastasis from extramammary tumors. Nevertheless, when they develop, hematologic neoplasms and melanoma are more frequent [2]. Kidney acting as the source of breast metastases is around 3%, and until 2014 there were only 25 cases reported in the literature [9].

Breast metastases are generally superficial, solitary, and circumscribed lesions, with a preference for the outer upper quadrant [10], and it could be the first manifestation of an underlying malignant disease. Keen imaging analysis of a breast lesion, as well as a high index of suspicion, is critical to differentiate a primary tumor from a metastatic lesion to the breast [11].

We describe an unusual case of a recurrent RCC presenting as metastatic lesions to the breast and soft tissue of the right thigh in a 51-year-old patient referred to our breast-imaging unit 10 months after therapeutic surgery.

## Case report

A 51-year-old woman initially presented to the urology clinic with severe hematuria, weight loss, and weakness. They performed a CT abdomen with contrast, showing a left kidney mass without evidence for lymphadenopathy and metastasis, classified as clinical stage II (Fig. 1). The patient underwent radical nephrectomy as curative treatment.

Pathology revealed a Fuhrman Nuclear Grade 4 Renal clear cell carcinoma with negative resection margins and focal sarcomatoid differentiation. The tumor was negative for angiolymphatic and perineural infiltration without capsule invasion.

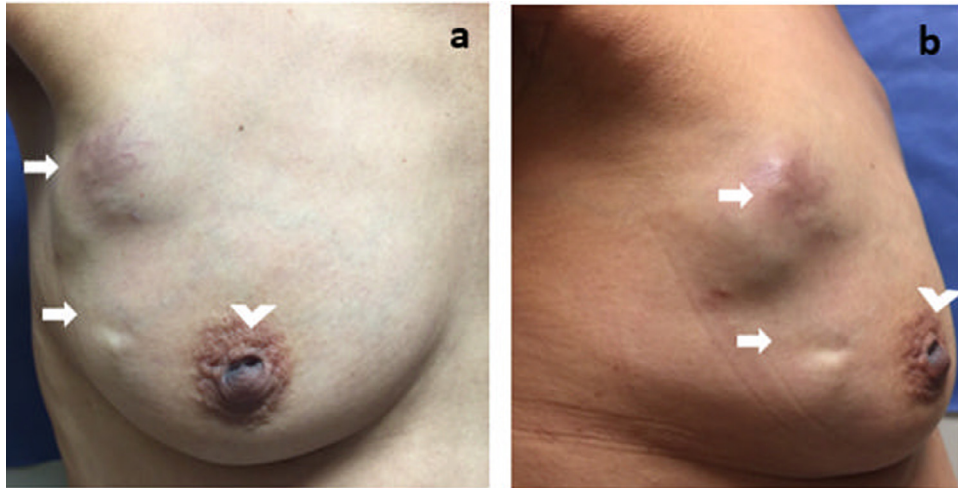
Ten months after the surgery, she detected a lump in her right breast. Physical examination at the UOQ revealed an erythematous, mobile, and painless nodule of 2 × 2 cm without skin retraction or palpable lymphadenopathy. They observed a second nodule at 9 o'clock with the same characteristics measuring 1 × 1 cm. Nipple retraction and color change were also visible (Fig. 2). Furthermore, they found a painless subcutaneous nodule fixed to the skin in the anteromedial aspect of the left thigh of 2 × 2 cm. With these findings, they referred the patient to our breast-imaging department.

The tomosynthesis exam showed a circumscribed mass and nipple inversion (Fig. 3). Complementary ultrasound of the breast showed 2 hypoechoic masses with angular margins and no nipple underlying changes (Fig. 4). We classified both lesions as BI-RADS 4C [18] and obtained a core needle biopsy for both suspicious lesions. The pathology report came as metastatic lesions of clear renal cell carcinoma (Fig. 5).

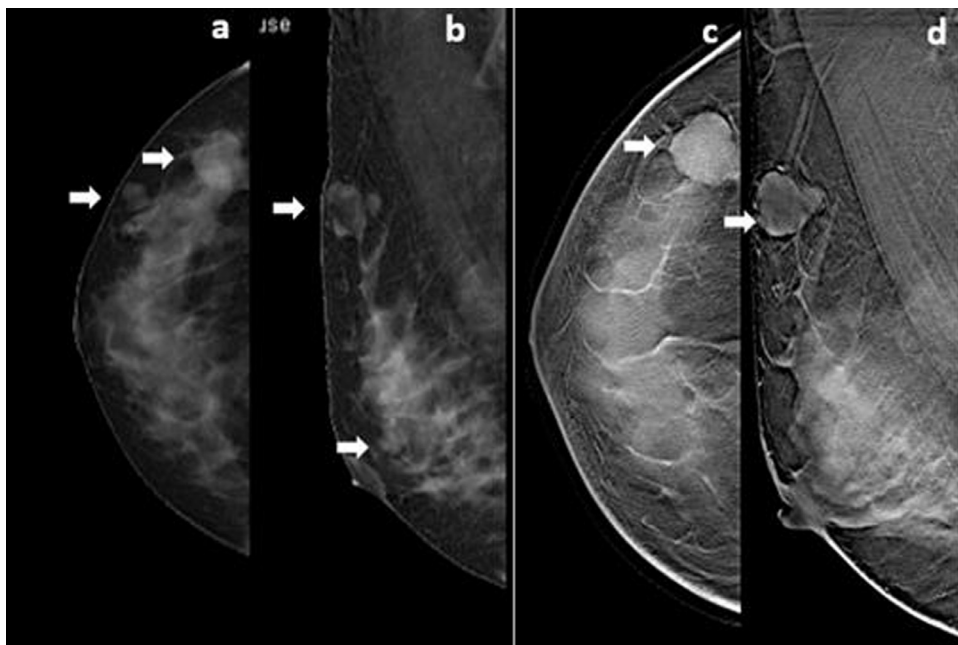
Two weeks later, the patient underwent breast-conserving surgery and right thigh lumpectomy that confirmed the diagnosis in the three lesions (Fig. 5).

## Discussion

We have described a case of a recurrent renal cell carcinoma presenting as metastatic disease to the soft tissues of the right breast and thigh without the evidence for an angiolymphatic or perineural invasion in the postsurgical specimen. A potential explanation for this might be a poorly differentiated tumor and sarcomatoid features found in the initial biopsy. Sarcomatoid RCC consists of a population of double cells, the typical clear RCC cells, and spindle cells, frequently



**Fig. 2 – Clinical examination. (a) Frontal and (b) lateral clinical pictures of the right breast of the patient at the physical examination. Two erythematous nodules (arrows) and changes in the nipple (arrowhead) can be depicted.**



**Fig. 3 – Recurrence of RCC to the right breast in a 51-year-old woman. (a, b) Mammogram in right craniocaudal (CC) and mediolateral oblique (MLO) views shows heterogeneously dense tissue, with a round, isodense nodule with obscured margin in the UOQ (arrows). A second mass with similar features was at 9 o'clock. (c, d) Tomosynthesis in right CC and MLO views, the nodule in the UOQ is better observed, in these images it showed circumscribed margin (arrows).**

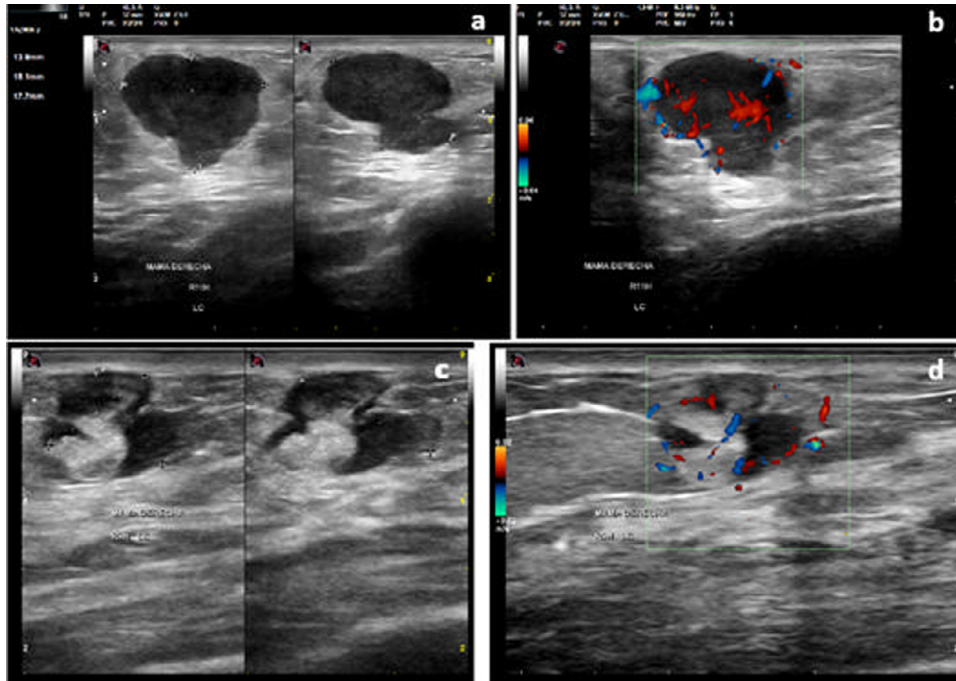
accompanied by necrotic regions [13]. This type of RCC has high proliferative activity, is locally aggressive, and has a higher risk for the development of metastasis and harbors a poorer prognosis (median survival of 6-12 months). Surgical resection alone does not change the clinical prognosis, and benefits for systemic treatments are limited [14].

The breast as a site for metastasis originates in three percent of RCC(1), and might be higher when other factors such as smoking, obesity, high protein intake, and SAH are present.

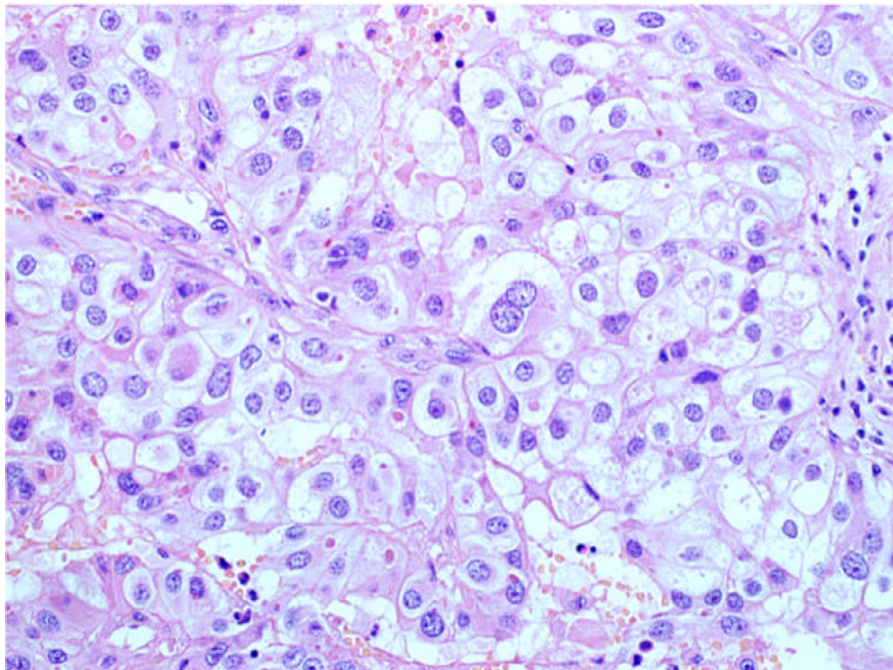
At the time the primary tumor is diagnosed, only 23% of these metastases are found [12]. Identification of metastatic soft tissue lesions takes place months or years after the initial diagnosis [15]. During the follow-up of patients with RCC, any new soft-tissue mass should raise a reasonable suspicion for metastatic disease, especially if the primary tumor shows aggressive histological features.

Metastatic breast lesions do not exhibit classic imaging features of the primary malignant tumors [16]. RCC metastatic





**Fig. 4** – Recurrence of RCC to the right breast in a 51-year-old woman. (a) Ultrasound shows an irregular, hypoechoic, superficial mass with angular margin, located at 11 O'clock line C of the right breast. (b) Color Doppler examination of the same mass shows an increased central and peripheral vascular flow. (c) Ultrasound shows a second superficial mass located at 9 o'clock line b of the right breast, the mass had an irregular shape, with angular margin and heterogeneous echogenicity. (d) Color Doppler examination of the same mass also shows peripheral and central vascular flow.



**Fig. 5** – Hematoxylin & Eosin 20X of a tumor section from one of the tumors in the right breast. At microscopic examination, the tumor depicted classical features of a renal cell carcinoma. Large cells with abundant clear cytoplasm, atypical large nuclei with inconspicuous nucleoli were seen.

lesions show increased vascularity, easily recognizable on color Doppler interrogation, the most reliable ultrasound tool in diagnosing these lesions [17].

In PET-CT, any lesion demonstrating increased metabolism compared to parenchymal background should be considered suspicious of malignancy. However, PET-CT alone can not distinguish metastatic lesions from primary carcinomas, and mammography with complementary breast ultrasound is needed to confirm the diagnosis [11].

In our case, the superficial location of the masses, the angular margins depicted on ultrasound, and marked vascularization on color Doppler examination was sufficient to justify the suspicion of metastases. Furthermore, proper physical examination was essential to find a different mass in the soft tissue of the right thigh, which resulted in metastatic disease with sarcomatoid features. Currently, there is no established treatment for these patients, and chemotherapy is not considered effective [14].

According to NCCN guidelines, the recommendation for treatment of recurrent or stage IV disease includes the combination of a TKI inhibitor with an anti-PD-1 inhibitor (axitinib/pembrolizumab) in patients with favorable-risk, and in those patients with poor/intermediate-risk they recommend a combination of a CTLA-4 inhibitor with an anti-PD-1 inhibitor (ipilimumab/nivolumab) [12]. Not all patients will have a satisfactory response, and further research in this field is crucial.

## Conclusion

In conclusion, recurrent RCC can manifest as metastatic lesions in unusual locations such as the breast and soft tissues. An adequate and close follow-up accompanied by a thorough physical exam and appropriate imaging methods is essential to identify these types of cases.

## Patient consent statement

The patient gave her consent to publish this case report. All information contained in this report is anonymous, and there are no personal identifiers in the entire manuscript and figures.

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## REFERENCES

[1] Yu C, Leckey BDJ, Wang E, Shen S, Yang L, Wang L, et al. Breast metastases from renal cell carcinoma in a male patient: a rare case and review of the literature. *Int J Clin Exp Med* 2018;11(6):6322–6.

[2] Mun SH, Ko EY, Han BK, Shin JH, Kim SJ, Cho EY. Breast metastases from extramammary malignancies: Typical and atypical ultrasound features. *Korean J Radiol* 2014;15(1):20–8.

[3] Ljungberg B, Hanbury DC, Kuczyk MA, Merseburger AS, Mulders PFA, Patard JJ, et al. Renal cell carcinoma guideline. *Eur Urol* 2007;51(6):1502–10.

[4] Howlader N, Noone AM, Krapcho M, Miller D, Brest A, Yu M, et al. SEER Cancer Stat Facts: Kidney and Renal Pelvis Cancer. [Internet]. april. 2020. Available from: <https://seer.cancer.gov/statfacts/html/kidrp.html>.

[5] Mikami S, Oya M, Mizuno R, Kosaka T, Katsube KI, Okada Y. Invasion and metastasis of renal cell carcinoma. *Med Mol Morphol* 2014;47(2):63–7.

[6] Störkel S, van den Berg E. Morphological classification of renal cancer. *World J Urol* 1995;13(3):153–8.

[7] Oda H, Machinami R. Sarcomatoid renal cell carcinoma. A study of its proliferative activity. *Cancer* 1993;71(7):2292–8.

[8] Bianchi M, Sun M, Jeldres C, Shariat SF, Trinh QD, Briganti A, et al. Distribution of metastatic sites in renal cell carcinoma: A population-based analysis. *Ann Oncol* 2012;23(4):973–80.

[9] Falco G, Buggi F, Sanna PA, Dubini A, Folli S. Breast metastases from a Renal Cell Carcinoma. A case report and review of the literature. *Int J Surg Case Rep* [Internet]. 2014;5(4):193–5 Available from. doi:10.1016/j.ijscr.2014.01.019.

[10] McCrea ES, Johnston C, Haney PJ. Metastases to the breast. *Am J Roentgenol* 1983;141(4):685–90.

[11] Bitencourt AGV, Gama RRM, Graziano L, Negrão EMS, Sabino SMPS, Watanabe AHU, et al. Breast metastases from extramammary malignancies: Multimodality imaging aspects. *Br J Radiol* 2017;90 20170197.

[12] National Comprehensive Cancer Network. Kidney Cancer (Version 1.2021). [https://www.nccn.org/professionals/physician\\_gls/pdf/kidney\\_blocks.pdf](https://www.nccn.org/professionals/physician_gls/pdf/kidney_blocks.pdf). Accessed October 13, 2020.

[13] Ding GTY, Hwang JSG, Puay HT. Sarcomatoid renal cell carcinoma metastatic to the breast: Report of a case with diagnosis on fine needle aspiration cytology. *Acta Cytol* 2007;51(3):451–5.

[14] Gómez García I, Burgos Revilla FJ, Sanz Mayayo E, et al. Carcinoma sarcomatoide de riñón. Aportación de un nuevo caso, y revisión de la bibliografía. *Actas Urol Esp*. 2003;27(8):649–53.

[15] Cangiano T, Liao J, Naitoh J, et al. Sarcomatoid renal cell carcinoma: biologic behavior, prognosis, and response to combined surgical resection and immunotherapy. *J Clin Oncol*. 1999;17(2):523–8.

[16] Botticelli A, De Francesco GP, Di Stefano D. Breast metastasis from clear cell renal cell carcinoma. *J Ultrasound* 2013;16(3):127–30.

[17] Toombs BD, Kalisher L. Metastatic disease to the breast: clinical, pathologic, and radiographic features. *Am J Roentgenol* 1977;129(4):673–6.

[18] D’Orsi CJ, Sickles EA, Mendelson EB, Morris EA, et al. ACR BI-RADS® ATLAS, Breast Imaging Reporting and Data System. Reston, VA. American College of Radiology 2013.