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journal homepage: www.casereports.comBreast metastases from a Renal Cell Carcinoma. A case report and review of the literature[☆]G. Falco^{a,*}, F. Buggi^b, P.A. Sanna^b, A. Dubini^c, S. Folli^b^a Second University of Naples, Department of Anaesthesiological, Surgical and Emergency Sciences, Naples, Italy^b Breast Unit, Morgagni-Pierantoni Hospital, Forlì, Italy^c Surgical Pathology Unit, Morgagni-Pierantoni Hospital, Forlì, Italy

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ABSTRACT

INTRODUCTION: Metastases to the breast from extra-mammary tumors are uncommon and few sporadic cases are reported in the international literature. An accurate differential diagnosis of secondary cancer is mandatory because both prognosis and treatment differ with respect to primary breast tumors.

PRESENTATION OF CASE: We present the case of a 70-year-old woman with an isolated metastasis to the breast occurring 9 years after undergoing a nephrectomy for Renal Cell Carcinoma (RCC).

Clinical examination revealed a palpable and mobile mass in the right breast with an enlarged ipsilateral axillary lymph node. Mammographic findings showed a dense, well circumscribed solid mass and the breast ultrasonography findings were those of a hypoechoic homogeneous solid nodule with no posterior attenuation but with prominent peripheral vascularity. A tru-cut biopsy was conclusive for a metastatic deposit by RCC. A whole-body CT scan showed no evidence of further recurrences. The patient underwent metastasectomy and exeresis of the papable lymphnode.

DISCUSSION: In patients with former surgery for RCC, a diagnosis based on a preoperative biopsy allows to indicate the proper surgical treatment: in facts, as compared to primary breast tumors treatment, the rationale to pursue wide surgical margins is pointless in cases of metastases and, similarly, the biopsy of the sentinel lymphnode is void of sense due to the lack of its physiopathological prerequisite.

CONCLUSION: We suggest to consider a micro-histological biopsy of any new breast lesion appearing in a patient with a history of treatment for RCC. Prompt diagnosis is necessary to choose the right treatment.

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1. Introduction

Renal Cell Carcinoma (RCC) is the third most common genitourinary tract tumor.¹ It accounts for approximately 3% of all adult neoplasms and in about 30% of patients it has a tendency to metastasize, usually to the lung (70%), lymph-nodes (55%), bone (42%), liver (41%), adrenal gland (15%) and brain (11%).^{1–4}

Breast metastases from extra-mammary tumors are much less common with respect to primary breast tumors (0.5–2% of breast cancer),^{5–8} and are usually due to melanoma, lymphoma and leukemia⁹; metastases to the breast from RCC are a rare occurrence and take place in 3% of all metastatic RCC.¹⁰ Overall, 25 such cases have been reported in the literature: eleven cases presented with metastasis as the initial sign of the disease and fourteen, among which 2 were bilateral, occurred as metachronous lesions after

a former nephrectomy.^{3,4,11–17} We report a case of RCC metastasis to the breast occurring 9 years after primary surgery for RCC. The difficulties in obtaining a correct diagnosis, which is crucial to avoid unnecessary mastectomy, and the management of axillary ipsilateral axillary lymph nodes are discussed.

2. Presentation of case

A 70-year-old woman was referred to our institution on April 2013 due to a quickly enlarging lump located in the upper inner quadrant of her right breast. In her medical history, she reported having undergone a right radical nephrectomy in 2004 for RCC. At the time of the operation the tumor was limited to the kidney compressing the renal capsule but with no sign of infiltration and there was no vascular invasion as well; surgical margins were free and the disease was therefore staged as T3N0M0 (G2). The patient received no further treatment and was followed up with annual whole-body computed tomography (CT) scan and MRI. In april 2011 she underwent a pylorus-preserving pancreatic head resection because of a solitary, hypervascular and homogeneous mass located in close proximity to the head of the pancreas, measuring 16 mm. Pathology showed a metastatic clear cell renal carcinoma, with free surgical margins. The patient was thereafter asymptomatic until December 2011, when she noted a quickly enlarging lump in the right breast.

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* Corresponding author at: Second University of Naples, Department of Anaesthesiological, Surgical and Emergency Sciences, Piazza Miraglia, 80138 Napoli, Italy. Tel.: +39 3391519790.

E-mail address: giuseppe.falco81@gmail.com (G. Falco).

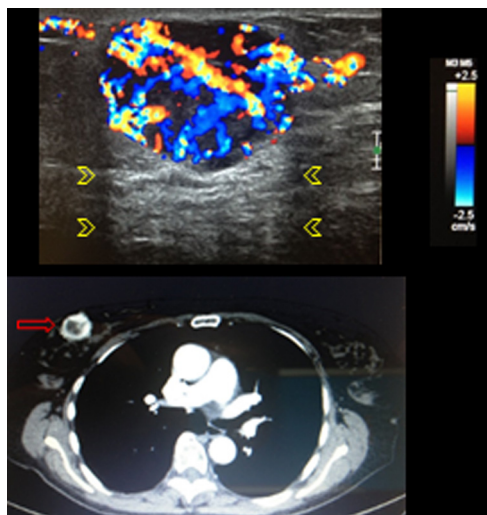


Fig. 1. Preoperative imaging. Top: ultrasound showing a hypoechoic homogeneous solid nodule with posterior acoustic enhancement (yellow gallons) and color Doppler showing peripheral and penetrating vascular network. Bottom: contrast-enhanced axial computed tomography image of the chest show an enhancing, homogeneous right breast mass (red arrow). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

On admission, clinical examination revealed a palpable and mobile mass in the upper inner quadrant of the right breast with an enlarged ipsilateral axillary lymph node; no skin or nipple retraction were noticed. A mammogram showed a dense well circumscribed solid mass, not spiculate, measuring 3 cm in diameter, with no adjacent parenchymal distortion and no sign of microcalcification; there were no signs of infiltration of the skin. Sonography showed a hypoechoic homogeneous solid nodule with no posterior attenuation of the acoustic wave but with prominent peripheral vascularity and penetrating vessels detected at color and power Doppler. The adjacent parenchyma was just displaced without obvious distortion, again with no skin thickening or duct ectasia. Multiple subcentimetric axillary lymphnodes were present, with a single one measuring 2 cm in diameter, with a preserved architecture. A contrast-enhanced whole body CT showed an enhancing, homogeneous right breast mass (Fig. 1), and fine needle aspiration cytology (FNAC) was unable to show malignancy. A tru-cut biopsy was then performed and revealed a tumor composed of nests and cords of cells with clear cytoplasm separated by a prominent sinusoidal vascular network (Fig. 2), which showed, at

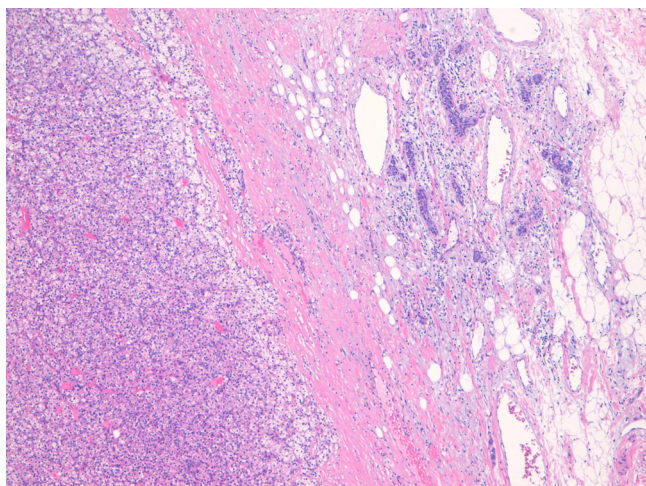


Fig. 2. Histology (H&E, 5x) clear cell carcinoma (left) metastatic to the breast (right).

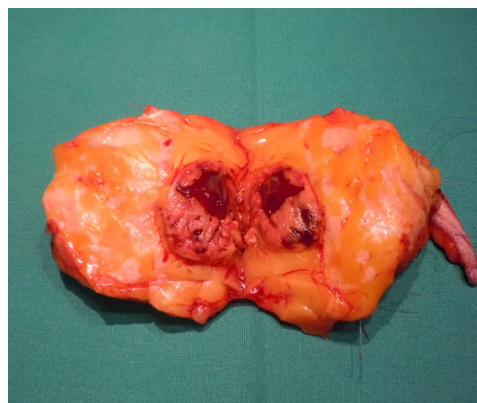


Fig. 3. Gross anatomy of metastasis to the breast from Renal Cell Carcinoma (RCC); see text for description.

immunohistochemistry, positive vimentin and CD10 staining while CK7 and CK20 were negative. Such pattern was consistent with Renal Cell Carcinoma of clear cell type (Fig. 3). After a multi-disciplinary discussion, the patient underwent metastasectomy and exeresis of the largest palpable axillary lymph node, that resulted unaffected at frozen section. The postoperative course was uneventful and no further adjuvant treatment was performed.

3. Discussion

The breast is a rare site of metastatic deposits, as emerges from the small number of cases reported in the literature. However, it is possible that the incidence of such finding will become more and more frequent because of the increasing number of patients who live longer bearing malignant disease.¹⁸ In facts, the 5-year and 10-year survival rates for the patients with RCC treated with nephrectomy are 95% and 91% for pT1; 80% and 70% for pT2; 66% and 53% for pT3a; 52% and 43% for pT3b; and 43 and 42% for pT3c, respectively.¹⁹ Metastases can take place either in a synchronous or metachronous fashion with respect to the primary tumor: out of 25 cases reported in the literature, 14 actually occurred after nephrectomy for RCC. A former history of RCC should therefore arouse suspicion of metastatic escape to the breast despite the fact that primary carcinoma of the breast is much more common.^{10,20}

Bowditch et al. reported a majority of metachronous presentation, that was claimed to carry a better prognosis than the synchronous metastases²¹; however, to the best of our knowledge, no strong evidence of a significant prognostic difference between metachronous and synchronous presentations can be argued from the data available in the literature.

Clinically, metastatic lesions in the breast present as painless and mobile discrete masses with rapid growth. The skin is usually not affected and axillary lymph node involvement is variable.^{9,22} One case reported the presence of a metastatic lymphnode.⁴

The findings of the traditional diagnostic workup most likely mimic a benign breast mass, due to the absence of desmoplastic reaction; in particular the deposits of malignant cells do not show spiculation or microcalcification on the mammogram and the sonography does not reveal posterior attenuation of the ultrasounds. The only finding that can be suggestive of malignancy is the prominent peripheral and penetrating vascular network, well evident to color and power Doppler, that is common to all cases reported in the literature.

Awareness of a former treatment for RCC should lead to stress the preoperative diagnosis because the treatment of breast secondary lesions differs from that of primary breast tumors, either as far as the lumpectomy margins width and the management of

axillary lymph nodes are concerned. In facts, the malignant extension to the breast can be explained by the spread of neoplastic cells from the renal vein into the inferior vena cava and then through the pulmonary circulation, eventually reaching the arterial circulation, diffusing throughout the whole body and thereby reaching the breast: therefore, the high rate of multiple lesions²³ that constitutes the rationale of the efforts aimed at obtaining wide tumor-free margins is pointless in secondary disease. Besides, the mechanism of metastatic diffusion renders the the biopsy of a sentinel lymph node void of sense in such cases; since malignant cells reach the breast (via hematogenous spread), sampling the efferent lymphatics that constitute a way of diffusion from the breast is pointless. Moreover, the staging role of SLNB obviously only applies to primary tumors, while sampling breast loco-regional lymph nodes for tumors originating elsewhere in the body makes no sense.

In cases of metastatic RCC, cytology may show atypical cells which differ from those of a primary breast tumor²⁴ but which, on the other hand, are frequently reported as benign.⁷ A diagnosis based on histopathological investigation is therefore crucial in order to avoid an unnecessary mastectomy with sentinel lymph node biopsy (or primary axillary dissection). Moreover, we suggest to avoid FNAC for the additional reason that the vascular network that characterizes metastases from RCC may lead to a high false-negative rates.

4. Conclusions

In conclusion, we suggest to consider a micro-histological biopsy of any new breast lesion appearing in a patient with a history of treatment for RCC as mandatory. A whole body CT scan may be included in the staging work-up. In the case of an isolated lesion, metastasectomy is the treatment of choice; axillary lymph nodes should be removed only in cases of overt metastatic deposits. So far, unfortunately, no effective adjuvant therapeutic option is available for disseminated RCC²⁵ because of the great resistance to chemotherapy and radiotherapy of this kind of metastases.

Conflict of interest

None.

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None.

Ethical approval

A written and signed consent to publish the case report was obtained from the patient.

Author contributions

The writer of the manuscript was Falco Giuseppe. Buggi Federico contributed in data collection. Sanna Paola Angela was the radiologist; Dubini Alessandra was the pathologist; and Folli Secondo was the supervisor.

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