

A Rare Case of Male Breast Metastasis from Previously Removed Renal Cell Carcinoma

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ABSTRACT

Renal cell carcinoma (RCC) is the most lethal pathology affecting the urinary system, especially in people over 65 years and with an incidence of about 2% per year. RCC can be classified according to histological findings, cytogenetic abnormalities, biological features and response to therapy. This article reports an extremely rare case of clear cell RCC in a 73 years old male patient with metastasis in the breast and in the bronchi, presented 15 years after surgical resection of primitive renal tumor.

Key words: Renal cell carcinoma; breast metastasis; bronchial metastasis; male breast

INTRODUCTION

Renal cell carcinoma (RCC) accounts for 90% of neoplastic diseases affecting upper urinary system. The 2004 World Health Organization Classification of adult renal tumors classified RCC into clear cell carcinoma, papillary and chromophobe tumor. Clear cell carcinoma is advanced for 96% of cases by deletions of the 3p chromosome leading to the inactivation of the VHL gene (Eble *et al.*, 2004; Motzer *et al.*, 2011 and Siegel *et al.*, 2015). Papillary renal carcinoma is characterized by the presence of malignant epithelial cells forming papillae and tubules and the cytogenetic abnormalities associated with the papillary subtype include trisomies of chromosomes 3, 7, 12, 16, 17 and 20, c-MET mutations and the loss of the Y chromosome (Gurel *et al.*, 2013; Sukosd *et al.*, 2003; Jones *et al.*, 2005). Chromophobe RCC has a homogeneous light brown appearance on the sample and histologically large polygonal cells with cross-linked cytoplasm can be observed (Eble *et al.*, 2004). Renal cell carcinoma can metastasize and the organs affected by this process are the lymphonodes and the lung, but there may be cases in which the metastasis affects the liver and the bone. During the diagnosis it can be very precise symptoms, such as a palpable mass in the abdomen or the presence of blood in the urine (the most obvious signal); these can be associated with weight loss, anemia and hypertension (Eble *et al.*, 2004; Gurel *et al.*, 2013; Amin *et al.*, 2002; Renal cell carcinoma, 2018).

CASE REPORT

This article reports an extremely rare case of clear cell renal carcinoma that metastasizes into a right breast and left bronchus in a 73-year-old patient. The primitive renal tumor was removed 15 years ago when the man underwent surgery for nephrectomy. In May 2018 the patient presented an unilateral and painful breast swelling. A fine needle aspiration cytological exam was performed on the right breast palpable mass, without diagnostic material. Histological examination on the removed surgical specimen was performed. At the macroscopic level an irregular fragment of 3x2x2 cm was sent to surgical pathology department. A cystic and hemorrhagic area of 1.5 cm was detected, corresponding to a cystic and capsulated neoplasia, consisting of papillary proliferation of large epithelial cells, with abundant and clear cytoplasm (Figs. 1, 2) and with an immunoprofile (Fig. 3,4) compatible with clear RCC (CK7-, CK20-, GATA3-, RCC antibody+, CD10 +, CK8 / 18 +, vimentin +). A diagnosis of metastasis from renal cell carcinoma was made. During laboratory and imaging exams performed for surgical intervention, a left bronchial nodularity was detected. The endoscopic bronchial biopsy was analyzed on histological level, confirming the presence of a tumor referring to metastasis of clear cell carcinoma with the same immunohistochemistry (IHC) panel positivity of the removed breast mass.

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Received: 30-08-2018

Accepted: 17-09-2018

Available Online: 01-10-2018

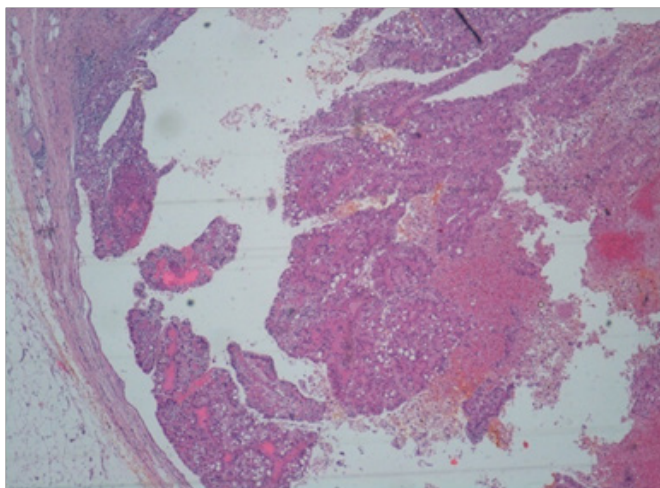


Fig. 1: EE. Slide of cystic breast metastatic tumor (4X)

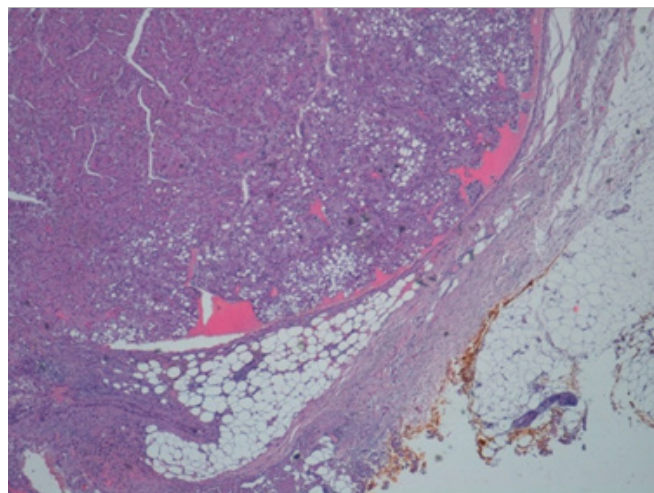


Fig. 2: EE. Slide evidencing neoplastic cells features (4X)

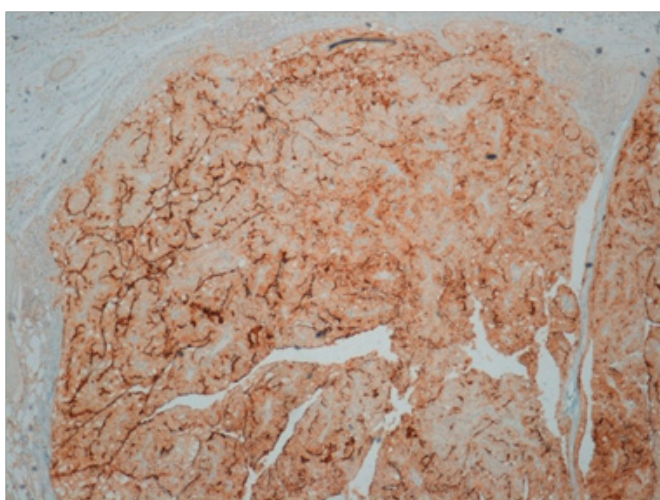


Fig. 3: CD10 IHC positivity of breast tumor (10X)

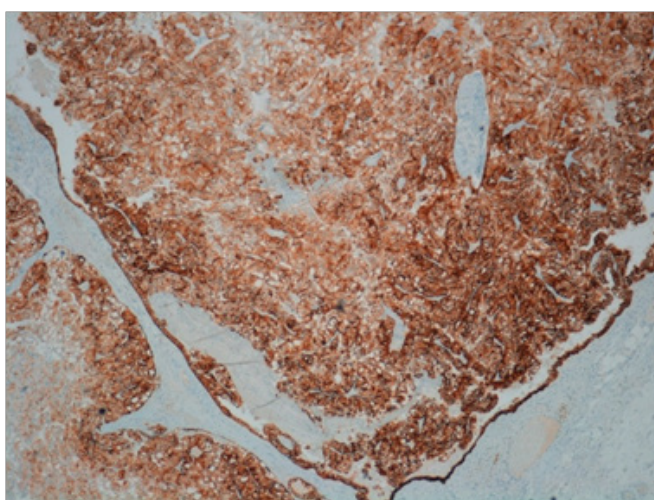


Fig. 4: RCC antibody IHC positivity of breast tumor (10X).

DISCUSSION

The causes of RCC may be different, such as smoking, hypertension and obesity. Usually the kidney cancer is not hereditary but if more members of a same family develop the disease, the risk of getting sick is greater. The disease is performed through abdominal ultrasound exam made for the presence of no specific symptoms, such as haematuria, kidney stones, anemia and fever (Renal cell carcinoma, 2018). The RCC is classified according to the TNM staging system revisited in 2018 (Cancer staging, 2015). The main treatment for the carcinoma of the kidney is the surgical removal of the primary tumor site, as it was done for our patient. He was not submitted to adjuvant chemotherapy for the absence on oncological utility and he was well for many years. However, 15 years after the surgical removal of primitive malignancy, the carcinoma has metastasized to the right breast first and then the left bronchus. Nowadays the patient is been studied to submit drugs blocking the growth of cancer cells and slowing down the formation of new blood vessels. Among these

drugs there are tyrosine kinase inhibitors (TKI), such as sorafenib. Other therapeutic chances are offered from immune checkpoint inhibitors (Tabei *et al.*, 2018). In fact immune checkpoint inhibitors against PD-1/PD-L1 have recently emerged as new treatments for metastatic renal cell carcinoma, even if it hasn't been approved as the first therapeutic approach because there isn't evidence that immune checkpoint inhibitors are useful in preventing other metastatic localization of renal tumor (Iacovelli *et al.*, 2018). Some other literature studies on correct treatment of metastatic renal cell carcinoma analyze combinations of many molecular targets, with different role in renal carcinogenesis. An example is represented by combination of a tyrosine kinase inhibitor and an m-tor inhibitor, such as lenvatinib and everolimus (Matsubara *et al.*, 2018). This represents a novel approach proposed from some international oncology team (Leonetti *et al.*, 2017). In fact, it has been reported that median progression-free survival was improved by 9 months with the combination therapy compared to a single-agent. Lenvatinib is a novel potent multitarget TKI that performs its action through

the inhibition of VEGFR-1, VEGFR-2, VEGFR-3, PDGFR- β , RET, c-KIT and fibroblast growth factor receptors (FGFR). Everolimus demonstrates antiproliferative effects, whereas lenvatinib shows antiangiogenic properties. Combination of these two new pharmacologic entity block metastatic potential of renal cell cancer.

CONCLUSION

The described case is an extremely rare one since renal cell carcinoma usually metastasizes in the lungs, liver and bones and that is why it has attracted our attention, as the disease has spread at a distance of 15 years from the surgical removal of primitive tumor in the male breast and in a bronchus of the patient. The primitive renal neoplasia showed no morphological characteristics that could lead to an aggressive biological behavior. Despite this, distant metastases have been presented which clinically mimicked other pathologies. Although metastatic renal neoplasm's can benefit from a good clinical response with the latest drugs, the differential diagnosis of these lesions remains difficult, especially after years from the primary tumor. In fact, metastasis often present morphological and immunophenotypical aspects different from the primary tumor and a reliable histopathological diagnosis can't be separated from an accurate clinical and anamnestic evaluation of the patient.

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How to cite article: Stefania Erra, Simone Lo Mastro, Silvio Modena (2018). A rare case fo male breast metastasis from previously removed renal cell carcinoma. *Int. J. Appl. Pharm. Sci. Res.* 3(4):64-66. doi: <https://doi.org/10.21477/ijapsr.3.4.3>

Source of Support; Nil Conflict of Interest: None declared