



## Oncology

# Late metastasis of renal cell carcinoma cloaked in a non-healing foot ulcer: A very rare presentation

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## ABSTRACT

A 67-year-old male who underwent right radical nephrectomy 15 years prior to current diagnosis for pT2bN0M0 ccRCC presented with an isolated purulent ulcer on left foot. Data was collected from records, radiological scans and histological reviews. The non-healing ulcer did not respond to antibiotic therapy and surgical debridement. Biopsy and histology confirmed a ccRCC metastasis. Late cutaneous ulcer is an aggressive and rare presentation of ccRCC metastasis. Awareness of a non-healing skin ulcer on a background history of ccRCC is important in order to avoid misdiagnosis and mistreatment.

## Introduction

Kidney cancer accounts for 3% of adult cancers. The age of the patients at the time of diagnosis is more than 50 years old in most cases. Nowadays, with the increased use of cross-sectional imaging, kidney cancer exhibits an excellent 5-year survival rates after surgery, however 35% of patients with a local disease experience local or distant recurrence after surgery.<sup>1</sup> We report hereby a rare late unique metastasis of clear cell renal carcinoma presenting as a non-healing foot ulcer and discuss its prognosis.

## Case presentation

A 67-year-old man on regular hemodialysis treatment for six years due to end stage renal failure secondary to type II diabetes mellitus presented with 3 weeks of worsening non-healing, necrotizing lesion over the dorsolateral aspect of the left forefoot associated to 5th toe pain, swelling and bluish discoloration. Past medical history included hypertension, dyslipidemia, chronic smoking (40 pack-years) and coronary artery disease. He had undergone radical nephrectomy 15 years back for a right sided clear cell renal cell carcinoma (pT2bN0M0).

Local examination revealed a 3 × 5 cm painful ulcer over the dorsolateral aspect of the left forefoot, with purulent discharge and rise in local temperature associated to blackish discoloration of the 4th and 5th toe [Fig. 1]. Dorsalis pedis, posterior tibial and popliteal artery pulsation was well appreciated. Arterial Doppler revealed diffuse parietal

calcifications with no obvious obstruction. Blood results showed leukocytosis and an elevated C-reactive protein level.

An intravenously antibiotic therapy was initiated, and a surgical debridement was performed with an amputation of the 3rd, 4th and 5th toes. A vacuum assisted device was used to accelerate wound healing. Four months later, at his follow-up appointment, a non-healed wound area with red to purple protruding lesion 15x15 × 10 mm was noted [Fig. 1]. Clinical diagnosis of a non-healing ulcer was made, and a biopsy specimen was sent for pathologic analysis.

Anatomopathological exam identified a tumoral proliferation in the dermis, with a visibly normal epidermis. AE1/AE3 immunohistochemistry exhibited positivity for tumor cells, indicating their epithelial nature. PAX8 immunohistochemistry showed nuclear positivity of tumor cells, consistent, given the history of renal carcinoma, with skin metastasis from ccRCC. [Fig. 1]. A staging PET-CT showed no other metastasis.

## Discussion

No previous case was published concerning a late distant metastasis of a renal cell carcinoma presenting as a non-healing foot ulcer. 15% of patients normally develop distant metastasis during the ensuing 10 years, most commonly in the lungs, followed by bone, pancreas, brain and adrenal glands. The estimated late distant metastasis-free survival rate at 10 and 15 years after nephrectomy is respectively 93% and 86%. Few cases of skin metastasis of renal cancer have been published,<sup>2,3</sup> and

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in a 12 years retrospective study of 306 patients that had been operated for renal carcinoma, only one patient exhibited late skin metastatic lesion and none as a non-healing ulcer.<sup>2</sup>

The location of cutaneous metastasis of urological tumors are mostly at the level of the head, neck and trunk, rarely located at the extremities and caudal part of the body. They are usually described as single lesions of a few millimeters in diameter, in the form of well-defined subcutaneous nodules or fast-growing pink or red infiltrating painless plaques, and have no tendency to ulcerate.<sup>4</sup> In the presented case, the lesion was located over the forefoot and was treated primarily as an infected diabetic foot ulcer and therefore a toe amputation was performed. It has not been possible to confirm or to rebut the tumoral nature of the gangrene since the lesion was not initially sent to pathology. The persistence of red to purple protruding lesion alarmed the team and a redo excision and biopsy of the lesion was performed.

Two pathways can explain the relationship between malignancies and wounds: a chronic wound can degenerate into cancer and malignancies can manifest as chronic wounds. An irregular cell growth pattern with infiltration by epithelial cells with numerous atypia and cellular mitosis, areas of necrosis and hemorrhage can be seen.

Immunohistochemistry techniques demonstrate positivity for epithelial markers, keratin, epithelial membrane antigen (EMA), carcino-embryonic antigen (CEA), and vimentin. Immunohistochemical studies clarify the nature of the lesions, especially when the primary renal tumor has not been diagnosed and when the cutaneous metastases do not resemble the primary tumor due to cell dedifferentiation and anaplasia.<sup>5</sup> In the presented case, Pax8 and pancytokeratin yielded the diagnosis.

Clinicopathologic characteristics associated with late distant metastasis include tumor size, primary tumor stage and histologic subtype. A single centimeter increase in initial tumor size at the time of nephrectomy is associated with a 7% increased risk of late distant metastasis, and patients with 2010 stage pT1b, pT2a, pT2b, or pT3-pT4 tumors are respectively 2.8, 4.5, 3.4 and 5.1 times more likely to develop significantly late distant metastases than are patients with stage pT1a. Moreover, the histopathological subtype is an important factor for the development of metachronous metastasis whereas clear cell renal cell carcinoma are 4 times more likely to develop late distant metastases than are patients with papillary or chromophobe renal cancer.<sup>1</sup> In the presented case, the patient had initially a renal cell carcinoma operated 18 years ago with a radical nephrectomy and was at the highest risk of



**Fig. 1.** (a) Infected gangrene dorsolateral forefoot (as on day 1) (b) Non healed wound (16 weeks after) (c) hematoxylin and eosin staining showing normal epidermis and tumoral proliferation in the dermis (x50 HPF) (d) Hematoxylin and Eosin (H & E) staining of the dermis showing tumoral proliferation (x100 HPF) (e) Immunohistochemical study showing positivity for AE1/AE3 (x50 HPF) (f) Immunohistochemical study showing positivity for PAX8 (x100 HPF).

developing late distant metastasis considering that he had a pT2b clear cell carcinoma cancer at the time of diagnosis.

In general, late distant metastasis exhibit a poor prognosis, being associated in up to 90% of cases with synchronous visceral metastases, and with a specific overall survival of less than 6 months.<sup>4</sup> For the palliative treatment of skin metastases, surgical excision of solitary skin lesions, radiation therapy alone or in combination with surgery, or intralesional injection of therapeutic agents such as interferon may be proposed.<sup>5</sup>

### Conclusion

Late solitary cutaneous ulcer metastasis from ccRCC is a rare urological and vascular finding. Awareness of non-healing skin ulcer on a background history of ccRCC is a key factor to avoid misdiagnosis and mistreatment. Histopathology and immunohistochemistry are invaluable diagnostic tools to reach a conclusive diagnosis. Limited available data suggest dismal and poor prognosis.

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