Tumour Seeding After a Thoracic Biopsy for Renal Cell Carcinoma: A Case Report and a Review of the Literature

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ABSTRACT: The role of percutaneous tumour biopsies had gain importance in the management of renal cell carcinoma to provide diagnostic specimen for the patients with metastatic disease that could benefit a systemic treatment. Among the possible complications of this procedure, however, there is the risk of tumoral cells seeding along the biopsy's tract; this complication, albeit being reported as anecdotal, could have devastating effects. Here we report a case of a young male who developed subcutaneous chest metastasis of renal cell carcinoma after a biopsy of a lung nodule. We subsequently reviewed other cases reported in literature

KEYWORDS: Neoplasm seeding, renal cell carcinoma, percutaneous biopsy complications

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Introduction

Renal cell carcinoma (RCC) is the most common malignant neoplasm of the kidney and accounts for approximately 5% of all cancers in men and 3% of all cancers in women.[1] Approximately 15% of the patients are metastatic at diagnosis and almost 20% to 25% of the patients who underwent radical surgery would develop at some point distant metastases.

In the last years, the paradigm of treatment for RCC has dramatically changed: in the metastatic setting, the introduction of new therapeutic options (anti-vascular endothelial growth factor (VEGF) tyrosine kinase inhibitors and, in more recent years, immune checkpoint inhibitors) improved the prognosis and decreased the importance of cytoreductive nephrectomy.[1,2] To provide diagnostic tissue for all those patients who are not candidate for primary surgery, the importance and the use of percutaneous biopsies had significantly increased.[3,4]

Moreover, it is widely known that metastatic spread could occur in lungs even years after the diagnosis and treatment of the primary renal cancer. In this case, a biopsy of the new lesion should be necessary to confirm the diagnosis and identify possible differential diagnosis, including second neoplasm. Elderly patients, smokers or former smokers, and professionals exposed patients can develop inflammatory mass or lung cancer, and discordance between imaging and histological assessment are reported.[5]

Besides, a new biopsy can help in identify molecular or genomic alterations which may guide the most appropriate treatment strategy.

Percutaneous (computed tomography [CT]-guided or ultrasound (US)-guided) biopsies are accurate and safe procedures, with few major complications when performed in experienced centres.[3,4] Nevertheless, for all kind of biopsies, there is an anecdotal risk of complications, included the tumour cell seeding along the biopsy tract.[4,6] Few cases of tumour seeding after percutaneous biopsies of RCCs have been reported and described. Here we reported the case of a young patient that developed metastases in the thoracic wall after the biopsy of a pulmonary nodule.

Case Presentation

The patient is a young man, 45 years old at the time of the diagnoses, who underwent nephrectomy and lymphadenectomy in November 2014 for a clear-cell carcinoma of the right kidney (pT3N0, Fuhrman grade 3). In July 2015, after development of pulmonary metastases (intermediate-risk class according to IMDC), he started treatment with sunitinib, with stability of the disease at the subsequently radiological assessments. In May 2016, a CT scan showed an increase in the dimensions of a single pulmonary lesion that was treated with radiation therapy, with long-term disease stabilization. In February 2019, he started cabozantinib because of disease progression. After 5 cycles, he started a third-line treatment with nivolumab, and unfortunately, the first CT scan assessment reported disease progression (Figure 1A). The patient was then referred to our Oncological Comprehensive Centre for consideration of a fourth-line, experimental treatment with immune checkpoint inhibitors. We decided for a biopsy of the lung nodule in the view of the availability of a clinical trial with mandatory pretreatment biopsy employing a new checkpoint inhibitor anti-CD73.

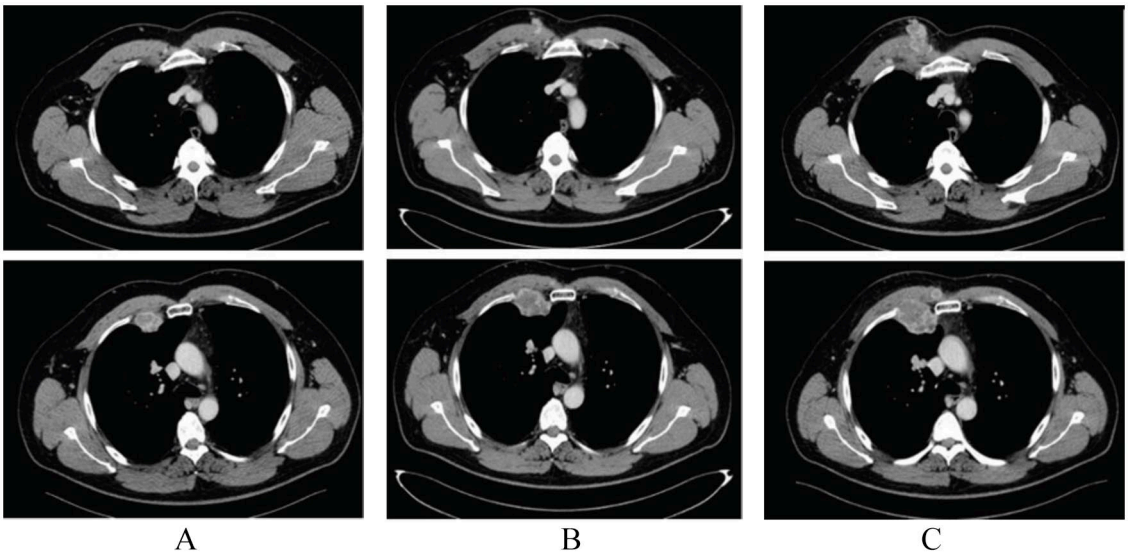

Figure 1. CT scans (A: at baseline; B: after 8 weeks and C: after 16 weeks from the beginning of the treatment) showing the appearance of 2 enlarging lesions in the chest wall close to the biopsied lesion.

Therefore, in November 2019, the patient underwent a CT-scan-guided, confirmatory, percutaneous core biopsy of a larger pulmonary mass in the right upper lobe. Histological examination confirmed the diagnosis of clear-cell RCC, with a high cellularity of 60% in the single specimen of 1.8 cm.

Thereafter, the patient was enrolled into a clinical trial and started an experimental treatment with anti-CD73 monoclonal antibody.

The first subsequent CT scan in February 2020 showed stable disease according to RECIST (Response Evaluation Criteria In Solid Tumours) 1.1, with the appearance, however, of a couple of small (maximum diameter 8 mm), contiguous nodules in the thoracic wall, close to the biopsied lesion (Figure 1B). Owing to their characteristic and their location, those nodules were initially thought to be procedure-related haemorrhages. Two months later, however, this gentleman observed the appearance of a subcutaneous, enlarging nodule in the second intercostal space. The subsequently CT scan showed enlargement of all the pulmonary and nodal lesions and huge increase of the dimensions of the nodules in the thoracic wall previously described, that spread from the subpleural space to the skin (Figure 1C). The patient discontinued the treatment and was referred to his local hospital to proceed with a new treatment.

Discussion

The role of needle core biopsy of renal masses is primarily to rule out nonrenal cell primary tumours or identify benign conditions which do not require treatments. Moreover, biopsy can also be used to confirm the diagnosis and the histological classification of a primary renal cancer in patients with disseminated disease or unresectable metastases.

Nowadays, the indications for this procedure are expanding. In fact, biopsy can also be considered before treating patients with advanced neoplasm because the indication for nephrectomy in RCC are changing and are still not full defined, even on the results of more recent clinical trials.[7]

A future goal is to go behind histological disease confirmation and to identify molecular or genomic alterations which may guide physician to choose the most appropriate treatment strategy and may reveal different clinical outcomes for RCC.

Potential complications of biopsies are tumour seeding along the needle tract, bleeding, infections and, for thoracic procedures, pneumothorax. The Society of Interventional Radiology[8] classified as major complication those which require treatment or lead to severe sequelae.

Tumour seeding is the phenomenon of implantation of tumour cells along the needle tract while performing fine needle aspiration biopsy or core needle biopsy. It is considered a very rare complication, and in the historical series, the overall risk is estimated about 0.01%.[9] More recently, in a survey based on more than 9000 biopsies in Japan, Tomiyana et al[10] reported a higher risk of 0.06% of tumour seeding after a biopsy of a lung lesion, regardless of the primary disease. In the modern literature, the largest reported series of seeding identifies a greater risk with a cumulative incidence of 1.2%.[6]

Nevertheless, the incidence of seeding seems to be consistent when considering procedures performed on abdomen: in a systematic review and meta-analysis on percutaneous biopsy of renal masses, Marconi et al[4] reported a single case of seeding with an incidence of 0.02%.

At the best of our knowledge, there are 22 cases of tumour seeding from RCC reported in the available literature, as summarized in Table 1.

However, the true incidence of seeding along the needle tract can be underestimated because not all the cases are diagnosed, and some patients may die before metastases become clinically evident. Most of all, tumour seeding after renal mass biopsy is underreported.

Table 1. Review of the cases of tumour seeding reported in literature.

PATIENT DETAIL	TUMOUR TYPE	SEEDING LOCATION	NEEDLE DIAMETER	REF.
66 yo, W, renal mass	CCRCC	Perinephric fat	18 G	[6]
73 yo M, renal mass	PRCC	Perinephric fat	ND	[6]
44 yo M, renal mass	PRCC	Perinephric fat	18 G	[6]
71 yo F, renal mass	PRCC	Perinephric fat	18 G	[6]
49 yo M, renal mass	PRCC	Perinephric fat	18 G	[6]
60 yo M, renal mass	PRCC	Perinephric fat	18 G	[6]
74 yo M, renal mass	PRCC	Perinephric fat	18 G	[6]
54 yo M, adrenal and renal masses	PRCC	Perinephric fat	ND	[11]
60 yo F, renal mass	RCC (nos)	Abdominal wall	ND	[12]
50 yo M, renal mass	PRCC	Perinephric fat	17 G and 18 G	[13]
66 yo M, renal mass	CCRCC	Perinephric fat	16 G and 22 G	[14]
53 yo M, renal mass	PRCC	Perinephric fat	20 G	[15]
58 yo M, renal mass	PRCC	Perinephric fat	18 G	[16]
68 yo M, renal mass	PRCC	Perinephric fat	20 G and 22 G	[17]
83 yo M, renal mass	PRCC	Retroperitoneum	20 G and 22 G	[18]
61 yo M, bilateral renal masses	PRCC	Retroperitoneum	25 G and 20 G	[19]
38 yo M, lung nodule after nephrectomy	CCRCC	Chest wall	20 G	[20]
48 yo M, renal mass	PRCC	Renal capsule	20 G and 14 G	[21]
37 yo, renal mass	PRCC	Abdominal wall	20 G	[3]
40 yo M, renal mass	PRCC	Subcutaneous	23 G	[22]
59 yo M, renal mass	RCC (nos)	Chest wall	18 G	[23]

Abbreviations: CCRCC, clear-cell renal cell carcinoma; PRCC, papillary renal cell carcinoma; RCC (nos), renal cell carcinoma (no otherwise specified); G, Gauge; yo, years old; M, male; F, female.

Risk factors for tumour seeding are debated and the role of neoplasm size, histologic differentiation, number of needle passes, thickness of parenchyma along the needle tract, and needle types should be taken into consideration.[24] Most of the reported cases have described implantation while performing fine needle aspiration biopsy of abdominal organs. Generally, needle tract seeding appears earlier in high-grade or poorly differentiated neoplasm, and the detection of the seeding can range from 1 to several months.[25]

Some authors have also studied the use of different diameter needles, demonstrating that larger diameter and non-negative pressure needles have a higher risk to cause soft-tissue metastasis and to disseminate tumour cells along the path.[26]

Despite Yamada et al[27] showed that the number of passes does not affect the chances of seeding, many health workers believe the risk of tumour seeding is proportional to the number of passes in the lesion and the implantation has been detected even after single pass.[28]

Moreover, no data are available on the biological characterization of the seeding. It is known that metastases from RCC could be biologically and genetically different from the primary tumour,[29] and this heterogeneity could explain different responses to treatment.[30] However, in the setting of a seeding from primary renal mass, we could speculate that the biological asset is the same of the tumour, because of the procedure itself.

In our case, the patient underwent a CT-scan-guided biopsy of a lung mass performed in November 2019 with a large needle, 18 gauge. As per interventional radiologist's report, 2 needle passes were performed, and the procedure was free of acute complications. In fact, the patient had no bleeding or infections and, with a radiographic control, no pneumothorax was detected.

Few weeks after the procedure, the patient developed a palpable mass in the area of the biopsy, progressively enlarging. At a subsequent CT scan, he had frank disease progression, in the needle path and other multiple sites. This confirms that seeding in the path is possible in RCC, even when no other complications were developed.

Finally, the clinical significance of the metastases derived from tumour seeding has yet to be established. In fact, in patients with only primary tumour and no evidence of distant metastases, the appearance of a lesion from seeding could deeply modify the therapeutic pathway and the treatment strategy. In 6 out of 7 cases reported by Macklin et al,[6] the presence of perinephric fat seeding resulted in upstaging of the tumour (from stage pT1 to pT3a). Besides, an analysis from the US Nation Cancer Database has reported an incremented risk of upstaging to pT3a for primary renal cell cancers that had undergone biopsy, even if the impact on clinical outcome is not entirely clear.[31]

On the contrary, instead, for a patient with disseminated neoplasm, the presence of a new lesion in a needle path cannot be relevant in terms of available treatments and prognosis. As a matter of fact, in our patient, the seeding had a low impact and a poor clinical significance because the patient had disease progression in multiple sites.

Conclusions

Tumour biopsy has a high diagnostic yield and is associated with a low risk of major complications. Even though tumour seeding in the needle path is very uncommon and, in certain cases, its significance in the prognosis of the patient could be negligible, it is important that interventional radiologist perform the procedure with care and re-assess the cases of tumour seeding to improve technical ability. For sure, it is important that there is great awareness of potential risk of seeding among clinicians managing RCC. Anyway, if local experience is sufficient and the biopsy result has a potential impact in the treatment decision-making process, physicians should not consider to withhold the use of core biopsy to better characterize the neoplasm for the fear of tumour seeding.

Finally, multicentric and prospective studies on genetics and biological assets of seeding and their relevance on clinical outcome are warranted in the future.

Author Contributions

Base revision: MM, DM, RG, BD; revision of the literature: DM, BU, PF, CF; paper writing: DM, MM, PF, ZV; supervision: BU, MM; final approval: all the authors.

Patient's Consent

The patient provided written consent to the publication of his clinical data and images from CT scans.

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