



Case Report

Renal cell carcinoma with atypical metastases sites revealed by diabetes mellitus: A case report



Nejmeddine Jelleli^{a,*}, Ahmed Loghmari^a, Oussama Belkacem^{b,c}, Ghassen Tlili^a, Bilel Jellali^d, Sabine Chouaya^e, Khaireddine Bouassida^a, Wissem Hmida^a, Mehdi Jaidane^a, Sihem Hmissa^{b,c}

^a Department of Urology, Sahloul Hospital, Sousse, Tunisia

^b Pathology Department, Sahloul University Hospital, Sousse, Tunisia

^c Research Laboratory LR21ES03, Medical School of Sousse, University of Sousse, Tunisia

^d Biochemistry and Clinical Biology Laboratory, Ibn-Eljazzar Hospital, Kairouan, Tunisia

^e Department of Emergency, Sahloul Hospital, Sousse, Tunisia

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ABSTRACT

Introduction and importance: Lung, bone, lymph nodes and liver are the most common metastatic sites. This observation presents a metastatic renal cell carcinoma (RCC) with atypical secondary sites and a rare mode of revelation corresponding to diabetes mellitus.

Case presentation: We report the case of a 64-year-old woman recently diagnosed with diabetes mellitus. A thoracic parietal nodule was palpated. An uro-CT scan had shown a renal tumor with unusual metastatic sites: pleura, pancreas, and contralateral kidney. The patient underwent a biopsy of the pleural nodule. The pathology report concluded to the diagnosis of clear cell RCC. She had a targeted therapy. Three months after admission, the patient had altered general condition and total hematuria.

Clinical discussion: RCC commonly metastasizes haematogenously via renal veins. Atypically, secondary lesions may involve pleura. Such a metastatic site may be of particular interest for percutaneous biopsy, as in our case. The rare metastatic invasion of the pancreas is most likely the cause of the inaugural diabetes in our patient. The contralateral kidney was involved in 1.4% of secondary lesions. For patients with poor prognosis, according to International Metastatic RCC Database Consortium classification, anti-angiogenic treatment is recommended. The median overall survival of patients with poor prognosis is 8 months.

Conclusions: Pancreas and contralateral kidney are rare secondary sites of RCC. The clinical expression of pancreas metastatic invasion can rarely fit with diabetes. Metastatic dissemination to these organs is most often associated with an unfavorable prognosis.

1. Introduction

Metastatic renal cancer constitutes 13.3% of all diagnosed kidney cancers [1].

The most frequent involved organ by metastatic RCC (mRCC) is lung, followed by bone, lymph nodes and liver [2]. It is a heterogeneous pathology including neoplasms with different prognostic characteristics.

We report here the clinical case of mRCC characterized by a rare discovery circumstance corresponding to diabetes as well as unusual metastatic sites.

This case report has been reported in line with the SCARE Criteria [3].

2. Case presentation

A 64-year-old woman, with no medical history, was referred to our institute for additional management of a left renal tumor. The reason for consultation was a recent polyurodyspic syndrome. Diagnosis was diabetes mellitus. The recent deterioration in general condition and the insulin-requiring nature of diabetes, justified the performance of abdominopelvic ultrasound. This was in favor of left renal tumor.

Upon admission, the patient had a Karnofsky Performance Index estimated at 50% (Table 1). She had no hematuria and no lumbar pain. On the physical examination, we palpated a small and a deep nodule located at the level of an anterior intercostal space. A thoraco-abdomino

* Corresponding author. Cité El Agba, Monastir, 5000, Tunisia.

E-mail address: jellelinejmeddine@gmail.com (N. Jelleli).

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Table 1
Overview of the Karnofsky performance status.

Performance	Karnofsky score (%)
No evidence of disease	100
Normal activity, minor signs of disease	90
Normal activity, signs of disease with effort	80
Self-care, unable to carry out normal activity	70
Assistance needed, able to care for most of own needs	60
Considerable assistance required	50
Disabled, special care and assistance required	40
Severely disabled	30
Supportive treatment needed	20
Moribund	10

–pelvic computerized tomography (CT) scan concluded to a large left renal tissue mass with a necrotic center and some intra-lesional calcifications (Fig. 1). There were multiple lung metastases associated with a parietal pleura nodule (Fig. 2). We have also identified multiple lesions in the pancreas and a small second localization in the right kidney (Fig. 3).

The patient underwent ultrasound -guided percutaneous biopsy of parietal pleura tumor.

On microscopic examination, the tumor consisted of solid nests divided by delicate fibrovascular septa. The neoplastic cells have abundant clear cytoplasm with distinct cell borders (Fig. 4a). Nuclei have an irregular nuclear membrane and coarsely granular chromatin (Fig. 4b). There was no calcification observed in the lesion.

Based on medical history and morphological features, the diagnosis of mRCC was made.

According to International Metastatic RCC Database Consortium (IMDC) classification (Table 2), our patient had a poor prognosis (Karnofsky Index <80%, time between diagnosis and systemic therapy < one year and thrombocytosis).

She had a targeted therapy based on antiangiogenic: Sunitinib at the dosage of 50 mg daily for four weeks.

At the last follow-up, 3 months after admission, the patient had total hematuria increasing the deterioration of her general condition (Karnofsky index at 40%).

3. Discussion

RCC is characterized by a high metastatic potential [4]. In our observation, the involvement of several organs (lungs, pleura, pancreas, and contralateral kidney) as well as the extensive nature of some of these secondary lesions (lungs and pancreas) illustrates this property of renal carcinoma. At the time of diagnosis, 30% of kidney cancers are metastatic [5]. In 95% of cases, it is a polymetastatic tumor disease [6].

The metastatic spread of carcinomatous renal cells may involve

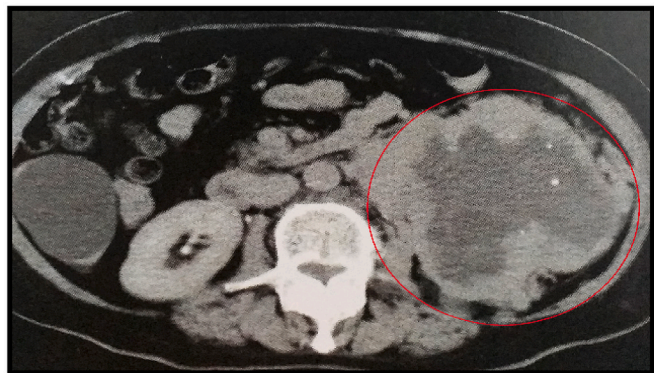


Fig. 1. Scannographic image showing a left renal tumor with central necrosis and microcalcifications.

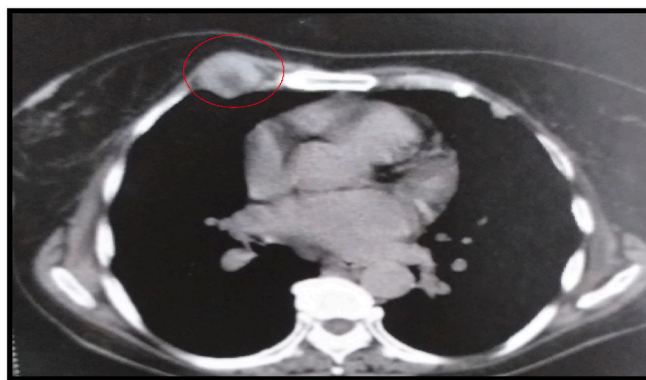


Fig. 2. Axial section of a thoracic CT scan showing a metastatic pleural nodule from kidney cancer.

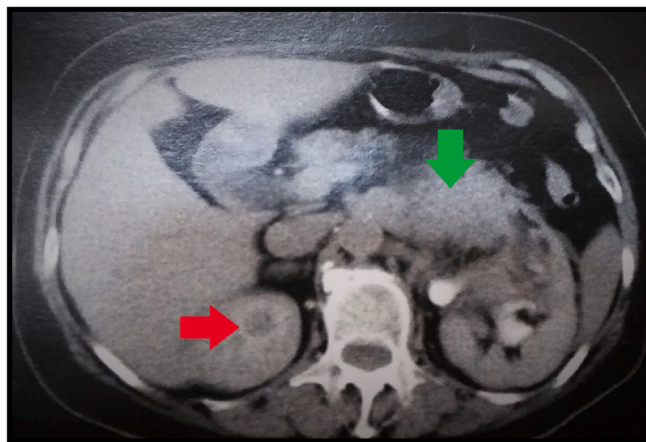


Fig. 3. Pancreatic invasion by left renal cancer (green arrow) and centimetric metastasis to the right kidney (red arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

lymphogenous, lymphohematogenous and hematogenous routes. This tumor commonly metastasizes haematogenously via renal veins [7].

Sometimes, the metastatic sites are unusual, generating puzzling clinical manifestations [8].

Multiple lung nodules is the most common form of thoracic metastasis. Atypically, secondary lesions may involve the parietal layer of the pleura, as we have demonstrated in our case. Metastatic invasion of the pleura may occur in 12% of cases [9]. It can be accessible to biopsy as in the case of our patient.

CcRCC is known to be the most common histological subtype of RCC [10].

Microscopically, architecture is acinar, nested, cords, tubular, and alveolar. Some of the lumens are larger, forming microscopic cysts of variable size. Neoplastic cells are cuboidal cells with typical optically cleared cytoplasm containing glycogen and lipid droplets.

CcRCCs are richly vascularized and have a delicate network of capillary vessels. Tumor may have calcifications with hemorrhage and/or necrotic areas [11]. In our case, the intra-tumor calcifications are limited to the primary tumor. Therefore, they were not detected on pathological examination. CcRCC in the pleura can pose differential diagnoses with metastases from ovarian clear cell carcinoma, endometroid carcinoma with clear cell carcinoma and chromophobe renal cell carcinoma. On immunohistochemical study, ccRCC is usually positive for cluster of differentiation 10 (CD10), cytokeratins (CK) AE1/AE3, EMA, vimentin and CAM5.2 but negative for CK7 and CK20 [12].

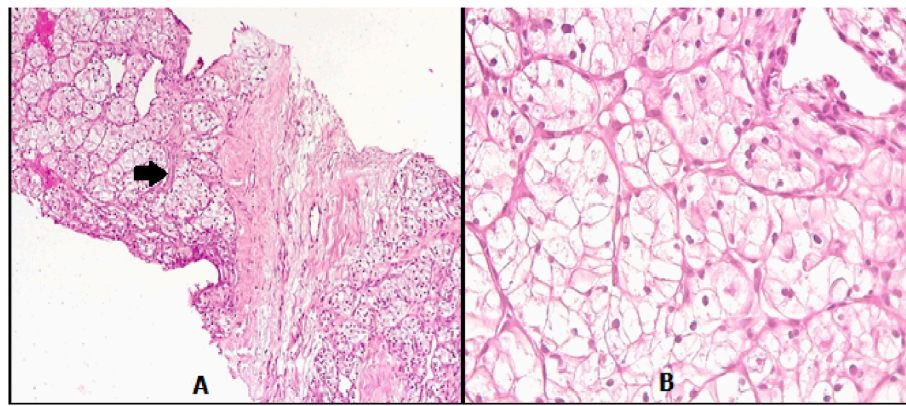


Fig. 4. Photomicrographs of CRCC metastasis in the parietal pleura (A), the nuclei are enlarged with mild atypia (B) (Hematoxylin & eosin, HE x400).

Table 2

International metastatic RCC database consortium (IMDC) risk model for metastatic renal cell carcinoma.

IMDC risk factors	
<ul style="list-style-type: none"> • Karnofsky Performance Status <80% • <1 year from time of diagnosis to systemic therapy • Hemoglobin < lower limit of normal • Corrected calcium > upper limit of normal • Neutrophils > upper limit of normal • Platelets > upper limit of normal 	
Risk profile	
Number of criteria	Group
0	Favorable
1–2	Intermediate
3–6	Poor

Pancreas constitutes a rare metastatic site of renal carcinoma. However, this organ is more frequently affected compared to the other viscera of the digestive tract [13].

The clinical expression of this metastatic tumor invasion is polymorphic. In the meta-analysis conducted by Sellner et al. including 236 cases of renal tumor metastasizing to the pancreas, 35% of these patients had no symptoms. The symptomatic forms are mainly abdominal pain (20%), gastrointestinal bleeding (20%), jaundice (9%) and pancreatitis (3%). Diabetes was found in 3% of patients [14]. No digestive signs were reported in our observation. The metastatic invasion of the pancreas is most likely the cause of the inaugural diabetes in our patient. Several arguments support this correlation:

- Absence of other elements of the metabolic syndrome.
- The insulin-requiring diabetes.
- Frequent decompensation of diabetes without any obvious factor.
- Recent deterioration in general condition.

Cancer cells can also engraft into the contralateral kidney as another rare metastatic location. Bianchi et al. studied the metastatic sites distribution of mRCC. The other kidney was involved in 1.4% of these secondary lesions [15].

To rationalize the choice of therapeutic option, the evaluation of individual risk for progression and death is necessary. The IMDC classification is now the most widely used in clinical practice [16]. For patients with poor prognosis, as is the case in our observation, anti-angiogenic treatment is recommended. The median overall survival of patients with mRCC in the poor prognosis group is 8 months [17].

Our study highlights the significant challenges in diagnosing patients with renal cancer. Diabetes mellitus can hide mRCC. Therefore, we encourage the realization of a radiological assessment in the case of suspected secondary diabetes.

The main limitation of our study is the short follow-up period.

4. Conclusions

Pancreas and contralateral kidney are rare metastatic sites for RCC. Parietal pleura represents an uncommon metastatic site. However, its invasion is not a rare event, particularly in the case of synchronous lung metastases. Metastatic invasion of pancreas may rarely result in diabetes. The polymetastatic aspect associated with atypical sites of RCC seems to be associated with poor prognosis. This encourages us to incorporate radiological features to existing prognostic models. Further investigations are necessary to verify the validity of our finding.

Provenance and peer review

Not commissioned, externally peer reviewed.

Ethical approval

Given the nature of the article, a case report, no ethical approval required.

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Author contributions

- * Study concept or design : GT, HA.
- * Data collection : EA, WF, RG.
- * Data interpretation : MJ, WM , SD.
- * Literature review : EA, WF, AA.
- * Drafting of the paper : HA, NJ, AA.
- * Editing of the paper : RG, WF, MJ.

Research registration (for case reports detailing a new surgical technique or new equipment/technology)

No registration is needed.

Guarantor

NJ.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the

written consent is available for review by the Editor-in-Chief of this journal on request.

Declaration of competing interest

The authors declare that they have no conflicts of interests.

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None.

This case report has been reported in line with the SCARE Criteria.

Abbreviation

ccRCC	Clear cell renal cell carcinoma
CD10	Cluster of differentiation 10
CK	cytokeratin
CT scan	Computerized tomography scan
IMDC	International Metastatic RCC Database Consortium
mRCC	Metastatic renal cell carcinoma

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2022.104480>.

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