1. Case report

A 35-year-old woman presented with a 10% weight loss within 3 mo, right hip pain, and a Karnofsky performance score of 70%. Physical examination revealed a palpable right abdominal mass. Patient also presented anemia (hemoglobin: 11 g/dl) and elevated lactic dehydrogenase (LDH). A computed tomography (CT) scan showed a 12-cm right renal mass with diffuse necrosis and extension outside the Gerota’s fascia. Furthermore, massive retroperitoneal lymphadenopathy was present (Fig. 1). Chest CT scan revealed multiple lung metastases. A bone scan was also performed and revealed an isolated right hip metastasis. Brain CT scan was negative for metastases. Due to the extent of the disease, a renal mass biopsy was obtained that revealed an eosinophilic unclassified non–clear cell renal cell carcinoma (RCC) (Fig. 2). The option of neoadjuvant temsirolimus treatment was offered to the patient. This was based on the recent trial by Logan et al. [1] suggesting that neoadjuvant temsirolimus may be offered to patients with advanced renal cancer and poor risk features with benefits in overall survival. Temsirolimus at 25 mg weekly was administered to the patient. Pain improved after the first week of treatment. LDH decreased, and anemia normalized after 2 wk. A CT scan was performed at 6 wk that showed a significant downstaging of the disease and complete disappearance of the metastases were noticed on computed tomography scan. Three months later, a laparoscopic radical nephrectomy and lymphadenectomy was performed. Final pathology confirmed a high-grade non–clear cell RCC, with necrotic changes on lymph node specimens, pT1bN0Mx.
non–clear cell RCC Fuhrman grade III, with fibrotic and necrotic changes on lymph nodes specimens, pT1bN0Mx (Fig. 5). At 4-mo follow-up, a CT scan of the chest and abdomen was negative for recurrence. The patient will continue with temsirolimus treatment and further follow-up with serial CT scans.

2. Discussion

Non–clear cell renal cell carcinoma represents 25% of all metastatic RCCs [2]. Few data specifically address the possible therapeutic options for these tumors. Immunotherapy and chemotherapy have not proven any benefits for patients with such disease [3]. Targeted therapies with tyrosine kinase and mammalian target of rapamycin inhibitors have been limited historically to the clear cell RCC histology [4]. Despite this, temsirolimus has been recently shown to be beneficial in terms of overall survival for those patients with advanced metastatic RCC and multiple adverse prognostic factors independently of primary tumor histology [5,6].

The historical role of cytoreductive nephrectomy in metastatic RCC [7,8] has also been argued since the advent of the new targeted therapies. A recent retrospective study evaluated the influence of prior nephrectomy versus no nephrectomy on overall and progression-free survival in metastatic patients treated with temsirolimus versus interferon. The study found that nephrectomy status did not affect temsirolimus efficacy with respect to either overall or progression-free survival. Therefore, the authors suggested that patients treated with temsirolimus may not need a cytoreductive nephrectomy [1].

Based on these findings, the European Association of Urology guidelines recommend temsirolimus as first-line
treatment in high-risk patients with advanced metastatic RCC, regardless of tumor histology or nephrectomy status, to attempt to increase overall survival [7].

Given the fact that our patient had very poor prognostic factors, we decided to offer a neoadjuvant treatment with temsirolimus. After 6 wk of treatment, a CT scan was performed and showed a complete radiologic disappearance of the metastases and a significant downstaging of the tumor from stage T4 to T1b. Three months later, a laparoscopic radical nephrectomy with lymphadenectomy was performed. The surgery was uneventful, and no increased difficulties were encountered to suggest that the treatment with temsirolimus had not affected the surgical planes. The final staging was pT1bN0Mx, non–clear cell RCC with an eosinophilic component.

We believe these findings are important because they indicate that temsirolimus may offer not only some benefits in terms of overall survival but also a cytoreductive option in non–clear cell RCC that may therefore render a radical surgery possible. Furthermore, the role of a renal mass biopsy in metastatic RCC may be crucial in planning the therapeutic options. In our case, it was key to the final decision regarding a neoadjuvant treatment [9,10].

These findings have to be taken with all the limitations of a case report. However, we believe and hope that such a case may stimulate further investigations.

Conflicts of interest: Joan Palou is a consultant for Sanofi-Pasteur, Lilly, and AMGEN. She receives company speaker honorariums from Sanofi-Pasteur and has participated in trials by Lilly and Zambon Group.

References


EU-ACME question

Please visit www.eu-acme.org/europeanurology to answer the following EU-ACME question online (the EU-ACME credits will be attributed automatically).

Question:

What are the options for the management of metastatic non–clear cell renal cell carcinoma?

A. Neoadjuvant treatment with temsirolimus, sunitinib, sorafenib.
B. Chemotherapy.
C. Immunotherapy.
D. Radical nephrectomy.

Fig. 4 – Intraoperative images showing the kidney, inferior vena cava, and lymphadenopathy.

Fig. 5 – Final pathology. Unclassified non–clear cell renal cell carcinoma with eosinophilic cells Fuhrman grade III.

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Fig. 5 – Final pathology. Unclassified non–clear cell renal cell carcinoma with eosinophilic cells Fuhrman grade III.


