Research Letter

Nephrectomy After Complete Response to Immune Checkpoint Inhibitors for Metastatic Renal Cell Carcinoma: A New Surgical Challenge?

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The management of metastatic renal cell carcinoma (mRCC) is evolving rapidly. On the basis of results from the CARMENA trial, cytoreductive nephrectomy is debated and the question of delayed surgery is of new interest for selected patients [1]. The SURTIME trial showed that patients did not have more surgical complications after prior treatment with sunitinib [2]. In the current era of immune checkpoint inhibitors (ICIs), the role and timing of nephrectomy for kidney residual disease for patients with a radiological complete response (CR) at metastatic sites are still unknown. Moreover, it is unclear if prolonged ICI treatment adversely influences surgical conditions and how such treatment might impact postoperative complications.

We aimed to retrospectively evaluate the feasibility of delayed nephrectomy in patients who received prolonged ICI treatment for mRCC and with CR at metastatic sites. Patients who underwent nephrectomy for symptomatic disease or in a neoadjuvant ICI setting were excluded.

Eleven patients treated in eight French centers were included (Supplementary Table 1). All patients had clear-cell RCC on initial biopsy. ICI was administered as first-line therapy in 36.4% of cases (4/11) and as a second-line option after tyrosine kinase inhibition in 63.6% of cases (7/11). The treatments regimens were nivolumab + ipilimumab (n = 3), nivolumab + tivozanib (n = 2), or nivolumab alone (n = 6). The median duration of ICI treatment was 10 mo (range 3–38) and the mean number of cycles was 27 (range 6–75). Toxicities of any grade were observed in 63.6% of patients (n = 7), with 27.3% grade 3/4 toxicities requiring treatment discontinuation (n = 3).

The median operative time was 243 min (range 135–345) and mean blood loss was 909 cm³ (range 40–4000).

In 81.8% of the cases (9/11), surgeons experienced difficulties in finding dissection planes because of adhesions and inflammatory reactions at the kidney and the surrounding tissue. In two cases, the extent of surgery or the surgical approach changed during the procedure. The median length of stay was 7 d (range 2–15). The 30-d postoperative complication rate was 54.6% (6/11, including 2 major complications [grade III-V]) and 1 surgery-related death; Supplementary Table 2). Pathology revealed lymphocyte and/or macrophage infiltration in 54.6% of cases (6/11) and complete pathological response in two cases (18.2%; Fig. 1).

The median follow-up was 15 mo, with 73% of patients (8/11) free from progression and 54% (6/11) free from systemic treatment at 1 yr.

To the best of our knowledge, this is the first series of surgical reports and oncological outcomes for patients undergoing delayed nephrectomy following ICI. The difficulties experienced during the procedure were assessed according to subjective criteria reflecting the overall feeling of the surgeon. It is noteworthy that in our series, 81.8% of patients still have residual viable tumor with no radiographic feature that can predict the histological response. Significantly longer follow-up is needed to determine whether durable CR provides a cure in such selected patients [3–5].

Finally, if nephrectomy can help to achieve CR after ICI for mRCC, we highlight the fact that inflammatory infiltration after long exposure to ICI results in challenging surgery. Patients should be referred to expert centers to reduce potential perioperative morbidity.
Confl icts of interest: The authors have nothing to disclose.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.eururo.2019.12.018.

Fig. 1 – Microscopic examination of a post-immunotherapy nephrectomy specimen showing a pathological complete response and fibrotic alterations with inflammatory infiltration.

References


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December 23, 2019