Original Study

Features of Ipsilateral Renal Recurrences After Partial Nephrectomy: A Proposal of a Pathogenetic Classification

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Abstract

This report concerns renal cell carcinoma: we investigate features of ipsilateral relapse after nephron-sparing surgery. This topic is poorly investigated in the literature, in particular if relapse could be related to a persistence of the primary tumor or to a newborn one. We analyzed 18 cases of relapse after partial nephrectomy subsequently submitted to salvage nephrectomy. After revision of the anatomical specimens we found 3 types of relapse related to different etiology, histology, and mostly to different prognosis.

Background: Poor data are reported on the pathogenesis of ipsilateral relapse (IR) after partial nephrectomy (PN). The objective of this study was to investigate features of IR after PN with the intention to propose a pathogenetic classification. **Materials and Methods:** Retrospective consultation of an institutional database that stores the data of 683 patients submitted to PN since 1993. The clinical, radiological, and follow-up data of the cases submitted to salvage nephrectomy due to an IR were analyzed. The slides of the sections from the tumor-parenchyma interface of PN and the bed of resection from the specimen of nephrectomy were reviewed. **Results:** Eighteen patients were submitted to salvage nephrectomy for an IR. In 12 cases the IR harbored into the site of PN and a mixture of cancer cells and granulomatous reaction was found at the resection bed (IR type A). In the remaining 6, in microscopy of the resection bed was found only fibrosis: 3 of these cases had a clear-cell renal cell carcinoma (RCC) with diffuse microvascular embolization and the relapse in the same portion of the kidney of the primary tumor (IR type B); the other 3 had a non–clear-cell RCC and the primary and relapsing tumors were located in distinct portions of the kidney (IR type C). Six patients (4 IR type A, 2 type B) had a further progression and 5 of them died due to RCC. **Conclusion:** More frequently an IR is due to the incomplete resection of the primary tumor (IR type A), in a minority of the cases to the local spread of the tumor by microvascular embolization (IR type B), or true multifocality (IR type C). The prognosis of IR not due to multifocality (type A and B) is poor, despite salvage nephrectomy.

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Introduction

Since a decade, partial nephrectomy (PN) has been preferred to radical nephrectomy for all cT1 renal cell carcinoma (RCC)[1] because of equivalent oncologic outcome but better renal function preservation and a lower incidence of chronic kidney disease.[2]

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Because of this trend, larger and more aggressive tumors are now treated in a conservative manner so that a higher incidence of oncological failures is expected.[3,4] However, the results of several large retrospective studies showed that the progression rate after partial versus radical nephrectomy is similar and depends on the features of the tumor, rather than the surgical procedure.[5,6] This evidence is easily acceptable in case of distant metastases, because micrometastasis already existing at the time of surgery are not amenable to be cured by any local treatment. Conversely, in case of a relapse in the kidney submitted to PN (IR, ipsilateral recurrence) some concerns on the primary procedure can be raised because, clearly, radical nephrectomy is not burdened by this risk.

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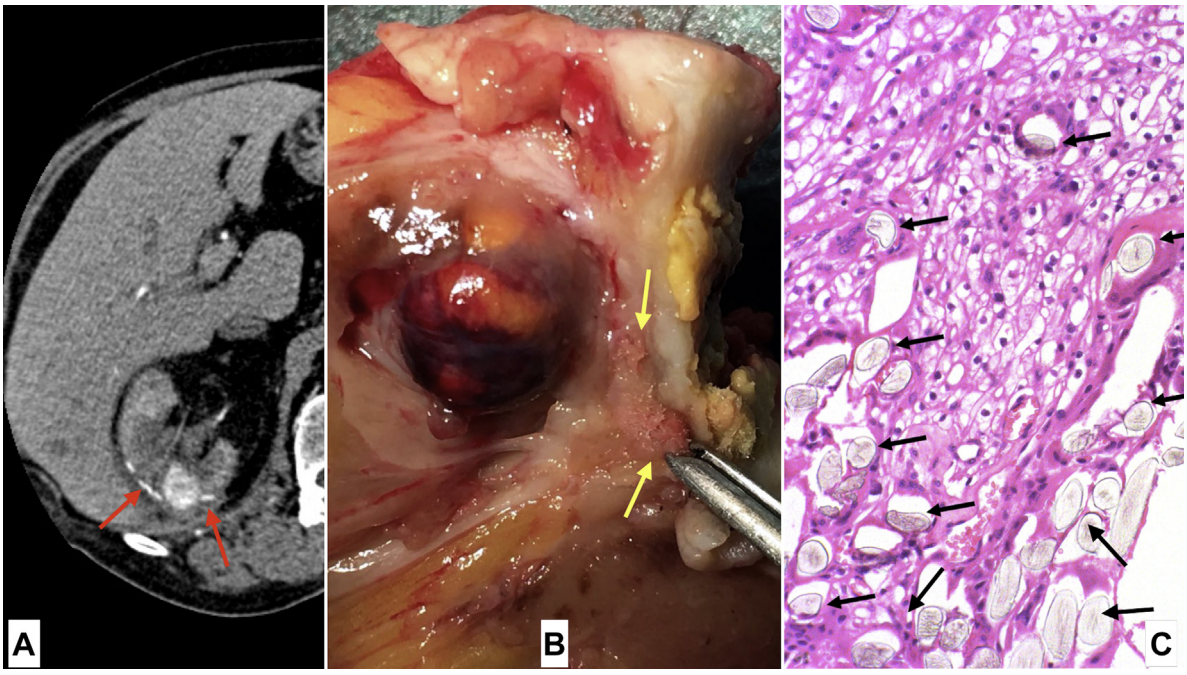
Figure 1 An Example of Ipsilateral Recurrence Type A (Case 18). (A) Computed Tomography Scan Shows an Enhancing Mass Close to the Hyperdense Spots Due to the Sutures of Partial Nephrectomy (PN; Red Arrows). (B) Macroscopic Image Shows the Relapsing Tumor Near to the Fibrous Reaction Secondary to PN (Yellow Arrows Indicate the Nonreadsorbable Teflon Plugs). (C) Microscopic Aspect of a Section of the Resection Bed, Showing Cancer Cells Mixed to the Granulomas Due to Sutures (Black Arrows)



An IR can develop following 3 pathways: some residual cancer left by an incomplete resection is able to evolve; the primary tumor microscopically spreads through the blood or lymphatic vessels and grafts into the healthy parenchyma; a newborn cancer with a different genetic asset develops in the remnant kidney, in the context of a true multifocality. These conditions have a different underlying biology and therefore should also have proper predictors, therapeutic implications, and prognosis. These issues remain actually not solved, because the literature on IR is quite poor, with results sometimes conflicting and, at to best of our knowledge, no attempts have been done to distinguish a relapse on the basis of its pathogenesis.[7-11]

The present study gives an insight of a series of IRs, specifically evaluating their pathological features at the time of primary and salvage surgery, with the aim of finding the aspects descriptive of a relapse due to an incomplete resection, local spreading of the primary tumor, or development of a newborn tumor.

Materials and Methods

An institutional prospectively maintained database that stores all the clinical, surgical, pathological, and follow-up data of more than 2500 consecutive patients submitted to renal surgery was consulted.

The indication to elective PN followed the contemporary Guidelines of the European Association of Urology[1] and, since 10 years, is given for any cT1 tumor deemed as technically resectable. Preoperative biopsy was generally not indicated, except for cases with a suspect of alternative diagnosis (lymphoma, metastasis, or benign nontumoral mass).

Surgery was performed using an open extraperitoneal, purely laparoscopic, or robot-assisted approach, depending on the period of the study, features of the tumor, and surgeon preference. In every case the resection strategy aimed at keeping a thin layer of healthy parenchyma around the nodule, according to the technique of enucleoresection; the renal artery was clamped depending on surgeon preference; the hemostasis was achieved with sutures fixed using Teflon plugs or nonadsorbable clips.

All the patients were controlled at an outpatient office dedicated to renal cancer follow-up, with a schedule that included a computed tomography (CT) scan at 4 months, CT and abdominal ultrasound alternated every 6 months for 2 years and then yearly, for an indefinite time, according to an already published protocol.[12] The diagnosis of an IR was done when CT scan showed an enhancing mass in the operated kidney that was not reported at the first CT control; because the clinical features of these patients were highly suggestive of a cancer relapse, generally no biopsy of the mass was requested. A total-body restaging was done and salvage surgery was offered to the patients fit for surgery and without concurrent distant metastasis.

In the present study we reviewed all of the cases submitted to salvage surgery for isolated IR after PN for sporadic RCC; the cases with a hereditary RCC, not submitted to salvage surgery or with metastasis at restaging were excluded. The topographic relationship