Case Report

Recurring Local Tumor Progression After Cryoablation of Renal Cell Carcinoma

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Abstract

We describe three cases of renal cell carcinoma (RCC) with recurring local tumor progression, i.e., local failure following repeat cryoablation for a locally progressed tumor. A second local progression developed in all cases after cryoablation for the first local progression, despite there being a sufficiently large ice-ball margin. In two cases, the second local progression was treated with microwave ablation and controlled in the follow-up. In one case, a third cryoablation was performed, but a third local progression developed after 12 months. These cases suggest that some RCCs may be refractory to cryoablation. In cases of recurring local progression, switching from cryoablation to another ablation modality may be an alternative.

Key words: renal cell carcinoma, cryoablation, local progression

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Introduction

Cryoablation is a safe and effective treatment for renal cell carcinoma (RCC) [1]. In a meta-analysis, the local tumor progression rate after cryoablation was as low as approximately 4% [2]. In cases of local tumor progression, repeat cryoablation is feasible, offering a high secondary local tumor control rate [1, 3]. Recurring local progression, i.e., local failure following repeat cryoablation for a locally progressed tumor, is rare, as long as the repeat ablation is performed with an adequate ice-ball margin. Nevertheless, we recently experienced three cases of RCC with recurring local progression after repeat cryoablation despite a sufficiently large ice-ball margin (≥ 6 mm) [4, 5]. Here, we describe the details of those cases.

Case Report

Cryoablation was performed percutaneously under local anesthesia in all 3 cases. Two to four 17-gauge cryoprobes (IceSeed or IceRod; Galil Medical, Youknum, Israel) were placed under computed tomography (CT) fluoroscopy guidance. Ablation was performed using an argon-based cryoablation system (Cryo-Hit; Galil Medical) with two 15-min freeze cycles separated by at least 2 min of passive thawing. CT was performed at the end of each freezing cycle to assess the ice-ball margin. When the ice-ball margin was insufficient (≤ 6 mm), the cryoprobes were repositioned, and one or two freeze-thaw cycles were added to achieve an adequate ablation margin.

*Case 1 (*Figure 1*)*

An 86-year-old male presented with a biopsy-proven clear cell RCC (Fuhrman Grade 2; 27 mm in diameter; endophytic) in the right kidney. Cryoablation was performed after selective transcatheter renal arterial embolization (TAE) using a mixture of ethanol and iodized oil to enhance the local tumor control. Nine months later, CT showed a 15-mm enhancing focus in the treated area, which was histologically diagnosed as local progression using a needle biopsy. The local progression was treated with selective TAE followed

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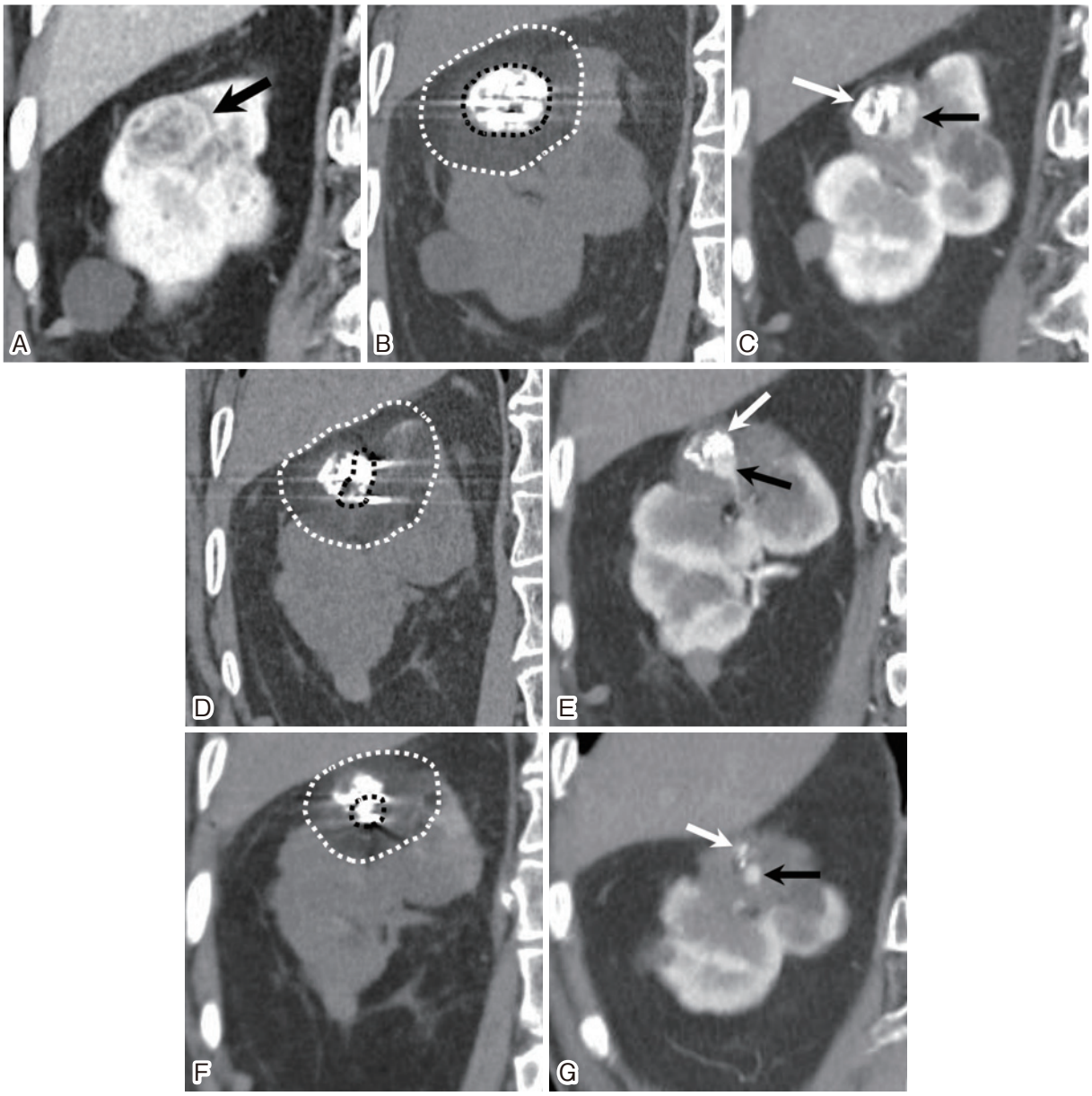

Figure 1. A: Pre-treatment computed tomography (CT) demonstrates a renal cell carcinoma measuring 27 mm in size in the right kidney (black arrow). B: Procedural CT during the first cryoablation using three IceRods following transcatheter renal arterial embolization shows the target tumor with iodized oil accumulation (black dotted line) involved in an ice-ball (white dotted line) with a margin exceeding 6 mm. C: CT performed nine months after the first cryoablation shows local progression, with a tumor, sized 15 mm (black arrow) adjacent to the remaining iodized oil accumulation (white arrow). D: Procedural CT of the second cryoablation using three IceRods shows the locally progressed tumor (black dotted line) involved in a large ice-ball (white dotted line) with a sufficient margin (>10 mm). E: CT performed 10 months after the second cryoablation shows recurring local progression, with a tumor, 10 mm in size (black arrow) at the center of the ablation zone. F: Procedural CT of the third cryoablation performed for local progression (black dotted line) using three IceSeeds with a large ice-ball (white dotted line) margin (>10 mm). G: CT performed 15 months after the third cryoablation shows a third local progression (black arrow). The white arrows in E and G indicate the remaining iodized oil accumulation.

by cryoablation with a large ice-ball margin (> 10 mm). Although the tumor enhancement completely disappeared after treatment, a CT conducted 10 months after the second cryoablation showed a nodular enhancing focus measuring 10 mm at the center of the re-treated area, indicating recurring local progression. A third cryoablation was performed with an ice-ball margin > 10 mm, resulting in the disappearance of the tumor enhancement. However, a nodular enhancing focus was found again at the center of the re-ablated area on CT after 15 months, indicating a third local progres-

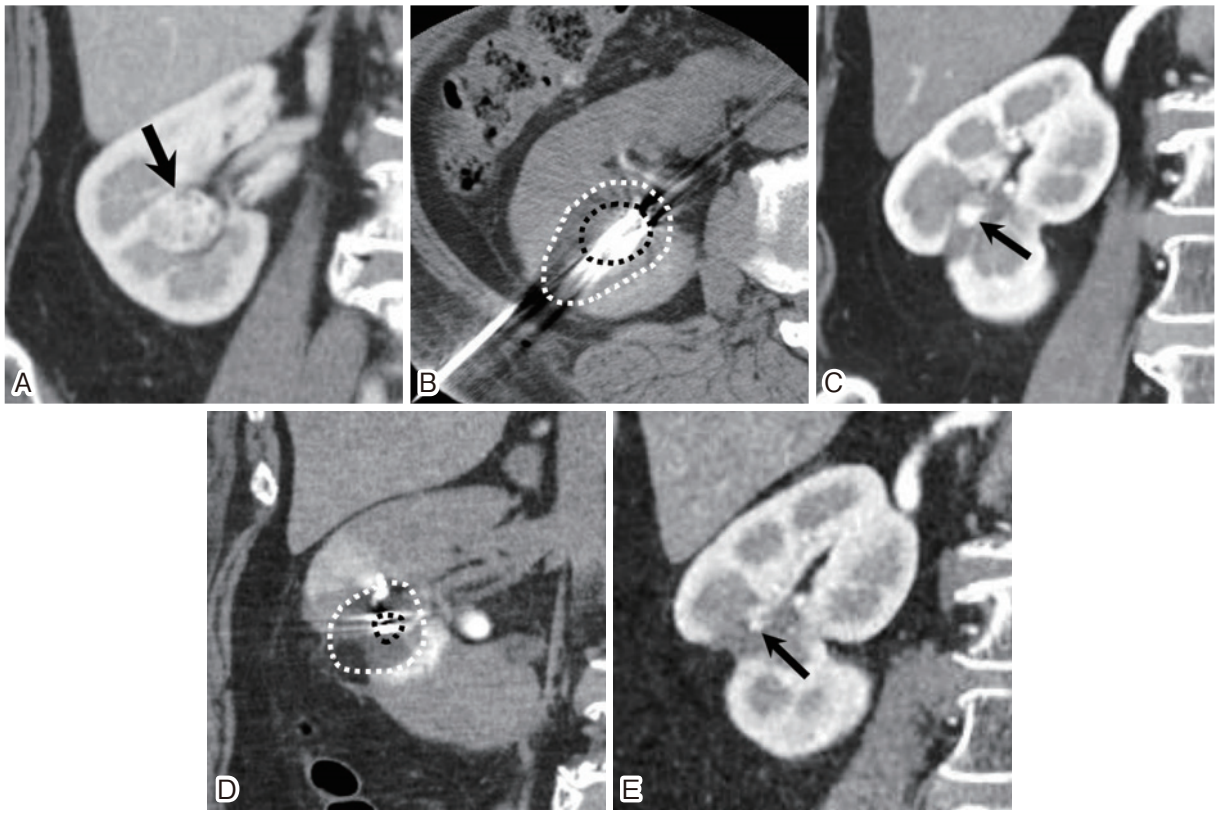

Figure 2. A: Pre-treatment coronal computed tomography (CT) image demonstrates a renal cell carcinoma measuring 24 mm in size in the right kidney (black arrow). B: A procedural axial CT image during the first cryoablation using four IceSeeds shows the target tumor (black dotted line) involved in an ice-ball (white dotted line). C: A coronal CT image acquired thirty-nine months after the first cryoablation shows local progression, with a tumor, sized 7 mm (black arrow). D: CT during the second cryoablation using two IceSeeds shows the locally progressed tumor (black dotted line) involved in an ice-ball (white dotted line) with a sufficient margin (>6 mm). E: CT 18 months after the second cryoablation shows local progression, with a tumor, 4 mm in size at the center of the ablation zone (black arrow).

sion. Considering that the tumor was refractory to cryoablation, radiofrequency ablation (RFA) was performed using a 17-Gauge internally cooled electrode (Cool-tip; Medtronic, Minnesota, USA) and a generator (CC-1; Medtronic) for the third local progression. No residual tumor was found on CT after 1 month.

*Case 2 (*Figure 2*)*

A 76-year-old female with post-left radical nephrectomy presented with a biopsy-proven clear cell RCC (Fuhrman Grade 1; 24 mm in diameter; entirely endophytic) in the right kidney. Thirty-nine months after the first cryoablation, an enhancing focus 7 mm in size was observed at the center of the ablated area on dynamic CT. It was radiologically diagnosed as local tumor progression without a biopsy. A second cryoablation was performed with an ice-ball margin exceeding 6 mm. The tumor enhancement disappeared on dynamic CT after 1 month. However, 18 months later, CT revealed a nodular enhancing focus measuring 4 mm at the center of the re-ablated area. It was radiologically diagnosed as recurring local tumor progression, and percutaneous microwave ablation (MWA) was performed using an MWA system (Emprint™; Medtronic). No local progression was observed in the last follow-up, 18 months after the MWA.

*Case 3 (*Figure 3*)*

A 76-year-old female presented with three right renal tumors (10, 14, and 13 mm in diameter; all exophytic). She had a history of left radical nephrectomy for RCC (clear cell carcinoma, Furhman Grade 2) seven years before and right adrenalectomy for adrenal metastasis four years prior. Two cryoablation sessions were performed for the three tumors. Thirty months after the first cryoablation, two nodular enhancing foci measuring 7 and 9 mm, respectively, were found at the center of the ablated areas. Those were radiologically diagnosed as local tumor progression, and a second cryoablation was performed with ice-ball margins exceeding 6 mm. However, 10 months later, CT showed small enhancing foci measuring 5 and 7 mm, respectively, at the center of the re-ablated areas, indicating recurring local progression. As in case 2, percutaneous MWA was performed, and no local progression was observed after 14 months.

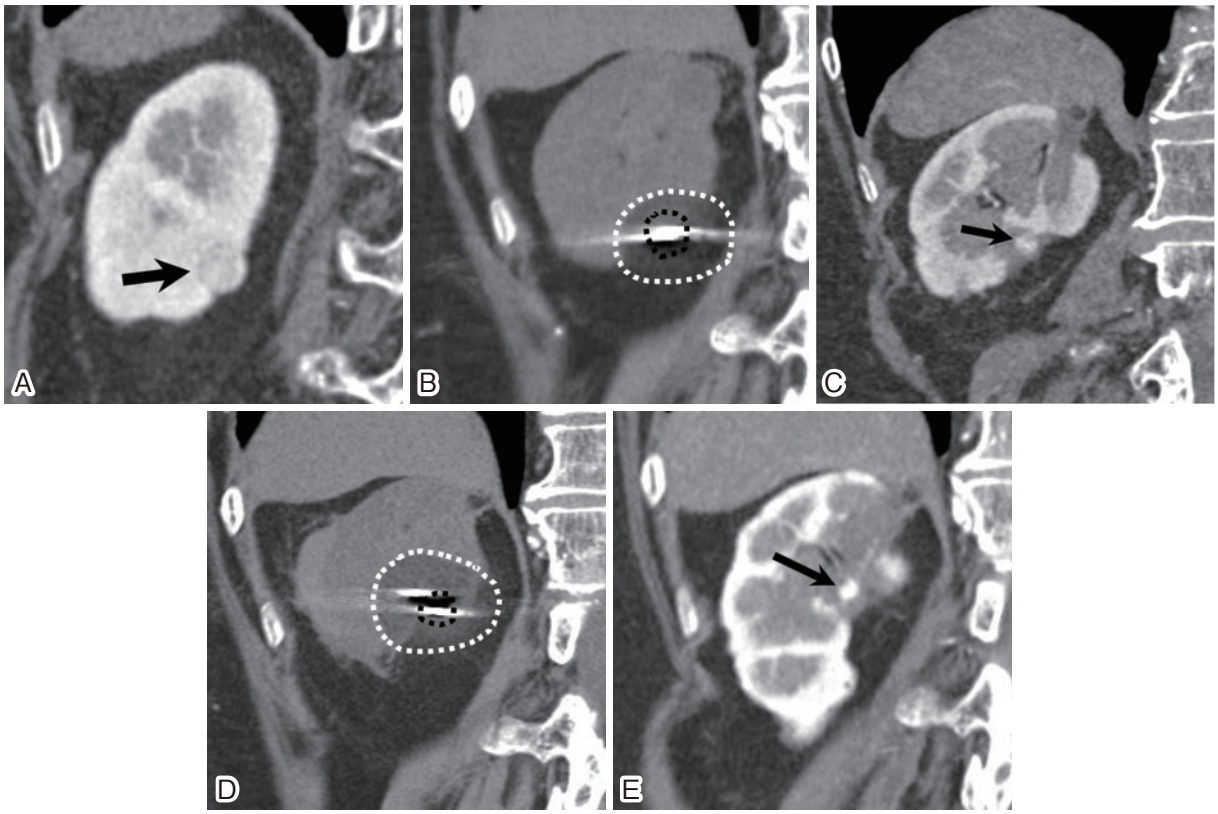

Figure 3. A: A pre-treatment coronal computed tomography (CT) image demonstrates a renal cell carcinoma measuring 14 mm in size (black arrow). B: Procedural CT during the first cryoablation using two IceSeeds shows the target tumor (black dotted line) involved in an ice-ball (white dotted line). C: CT performed 30 months after the first cryoablation shows local progression, with a tumor, 7 mm in size (black arrow). D: Procedural CT of the second cryoablation using two IceSeeds shows the locally progressed tumor (black dotted line) involved in an ice-ball (white dotted line) with a sufficient margin (>6 mm). E: CT performed 10 months after the second cryoablation shows local progression, with a tumor, 5 mm in size (black arrow) at the center of the ablation zone.

Discussion

Second local progression after repeat cryoablation for RCC is rare [3, 4]. A large tumor size (> 3 cm) and insufficient ice-ball margin (< 6 mm) are risk factors for local progression after percutaneous cryoablation [4, 6]. Yamanaka et al. reported a case of RCC located between the renal artery and vein, showing a second local progression after repeat cryoablation [4]. All the locally progressed tumors in the present report were small in size and treated with a sufficient ice-ball margin (≥ 6 mm) in the second and third percutaneous cryoablation sessions. However, second and third local progressions occurred.

The mechanisms of cell death due to cryoablation include direct cell injury caused by ice crystal formation, failure of microcirculation, and induction of apoptosis and necrosis [7]. Exposure to temperatures under -40℃ is generally recommended to ensure the death of renal cancer cells, as such low temperatures may injure the cells through intracellular crystal formation [8]. In the present report, all the locally progressed tumors were located at the center of the ice-ball during freezing, where the temperature was under -40℃ based on the isotherm shown in a swine model study using the same cryoprobe as that in the present report [5]. Additionally, the tumors were not adjacent to large blood vessels that potentially prevent a decrease in temperature through the heat pump effect. Thus, local progression in our cases was unlikely to result from failure to expose the tumors to temperatures under -40℃. Previous *in-vivo* experiments have indicated that exposure to a temperature of -40℃ may not be lethal for some types of malignant cells [7]. Furthermore, altered tumor characteristics because of incomplete ablation in the first cryoablation session may have contributed to the subsequent local progression. Further investigations are necessary regarding the existence of renal cancer cells anomalously resistant to cryoablation.

In the present report, RFA was performed for recurring local progression in one patient. Furthermore, MWA was performed for the three locally progressed tumors in two patients. All of them were successfully controlled in the follow-up. In previous studies, the local progression rates were not different between MWA and cryoablation for the first treatment of small renal tumors [2, 9]. However, in

cases refractory to cryoablation, switching from cryoablation to a different ablation modality, such as MWA or RFA, may help to avoid repeat local progression. A second local progression reported by Yamanaka et al. was also successfully controlled with RFA [4].

In conclusion, the present report described three cases of RCC refractory to repeat cryoablation with an adequate ablation margin. These cases suggest that some RCCs may be resistant to cryoablation. Switching from cryoablation to another ablation modality, such as MWA or RFA, may be an alternative for such tumors.

Conflict of interest: none

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