

Case Report

A Combination Therapy of Partial Nephrectomy and Cryoablation Achieved Good Cancer Control and Renal Function in Bilateral Synchronous Renal Cell Carcinoma

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We report the case of a 58-year-old Japanese man with bilateral synchronous renal cell carcinoma (RCC). The diameters of the right and left tumors were 56 and 69 mm, respectively. Both tumors were endophytic. Cryoablation with prophylactic embolization was performed for the left tumor, and 1 month later, a right open partial nephrectomy was performed. No recurrence was observed during a 16-month follow-up, and the serum creatinine level has been stable. The prognosis of bilateral synchronous RCC is better than that of dialysis patients. The novel approach of combining cryoablation and partial nephrectomy can achieve good cancer control and renal function in bilateral RCC.

Key words: cryoablation, multiple renal masses, nephron-sparing surgery, renal cell carcinoma, synchronous multiple primary

The prevalence of nonhereditary bilateral renal cell carcinoma (RCC) is 4-5% in the world [1,2]. The proportion of patients with bilateral RCC who have synchronous tumors ranges from 47% to 71% [3,4]. Bilateral RCC does not belong to any clinical stage. The prognosis of synchronous bilateral RCC is comparable to that of unilateral RCC [3,4]. Among dialysis patients, the prognosis and quality of life are poor, Japanese Society of Dialysis Therapy <<http://docs.jsdt.or.jp/overview/>>, accessed March 30, 2016.

When a patient is being treated for bilateral RCC, the curability and the preservation of the patient's renal function should be taken into account. Partial nephrectomy (PN) has become the standard of care for stage T1 RCC, because of its decreased risk of resulting in chronic kidney disease and favorable cancer control

[5,6]. Thermal ablation has emerged as a valid alternative to nephron-sparing surgery. Cryoablation (CA) was approved by the Japanese national health insurance program in 2011 and has been increasingly used. We report the case of a patient with bilateral RCC treated by a combination of CA and PN in order to maximize the possibility of cancer control and preservation of renal function.

Case Report

A 58-year-old Japanese man was referred to our institution for the treatment of incidental bilateral renal tumors. His medical history was significant for diabetes mellitus (DM), hypertension (HTN), and hyperlipidemia (HL). He was taking nifedipine, olmesartan, rosuvastatin, doxazosin, spironolactone, and voglib-

ose. Laboratory test results were normal except for a hemoglobin A1c level of 7.2%. His serum creatinine level was 0.83 mg/dL. Computed tomography (CT) revealed bilaterally enhanced renal tumors (Fig. 1). The diameters of the right and left tumors were 56 and 69 mm, respectively. Both tumors were endophytic. The respective R.E.N.A.L. nephrometry scores and centrality indices, which are scoring systems to assess the difficulty of nephron-sparing surgery [7] were 11x and 1.01 for the right kidney and 10p and 0.96 for the left kidney. No metastatic disease was found.

The diagnosis was synchronous bilateral RCC. The treatment options and the order of treatments were thoroughly discussed with the patient, and included CA, PN, radical nephrectomy, and renal autotransplantation. We selected CA for the left tumor to maximize the possibility of preserving renal function, taking into account the possibility that the tumor in the right kidney might require a nephrectomy.

The patient underwent CA of the left kidney twice, with a 9-day interval between procedures. Prophylactic tumor embolization was performed to prevent bleeding 1 day before the first cryotherapy. Four weeks after the second CA, a right-side open PN was successfully performed without autotransplantation. The operative time was 6 h and 50 min; the cold ischemia time was 90 min, and the estimated blood loss was 550 mL. The tumor was resected with attention to meticulous hemostasis. Good hemostasis was obtained at the time of reperfusion, without the need for parenchymal suturing.

The pathological examination found clear cell carcinoma (45×40 mm, pT1b, G2>G1, INF-α, v0, ly0). The resection margin was negative for cancer. There has been no recurrence at 16 months after surgery. The patient's serum creatinine level has remained steady at 1.09 mg/dL, and the patient does not have proteinuria (Fig. 2).

Discussion

We have reported a case of bilateral synchronous RCC treated by a novel method that allowed successful bilateral renal preservation. This combination strategy has never been reported before, to our knowledge. Bilateral synchronous RCC can be considered to be independent primary tumors rather than a single primary tumor with contralateral renal metastasis. The reported 5-year cancer-specific survival of patients with bilateral synchronous RCC was high at 81.5% and 87.3% in the series from Becker *et al.* and Boorjian *et al.*, respectively, [3,4]. Amano *et al.* reported a 4% rate of local recurrence for bilateral synchronous RCC after PN, which was significantly lower than the recurrence rate of metachronous bilateral RCC (26%, $p=0.04$) [8].

Of note, the 5-year survival rate of dialysis patients from the start of dialysis in 2009 is 60.5% in Japan. Therefore, the prognosis of dialysis patients is worse than the prognosis of patients with bilateral RCC. Renal preservation to prevent the need for dialysis and to prolong overall survival is a very important treatment

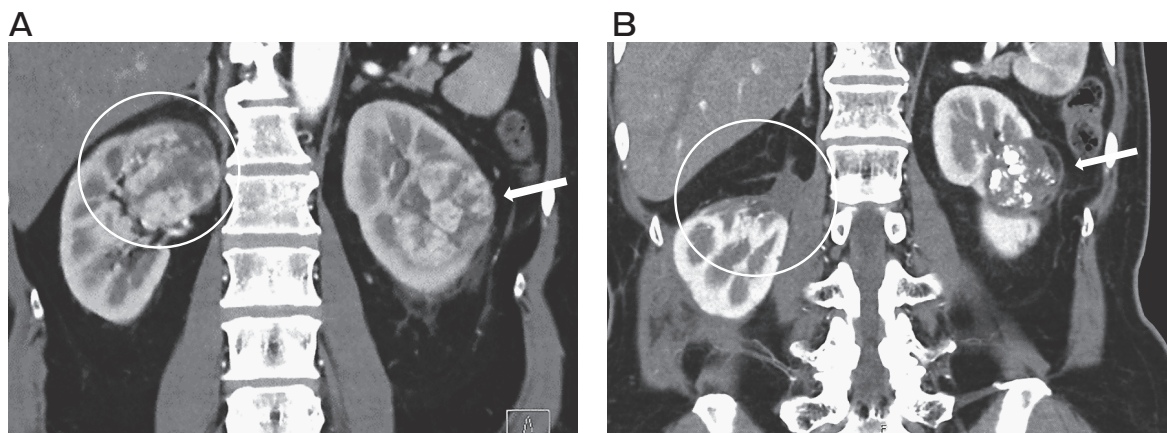


Fig. 1 A, Coronal CT with intravenous contrast medium shows bilateral enhancement of the renal tumors. The diameter. of the right and left tumors were 56 and 69 mm, respectively; B, Coronal CT with intravenous medium 16 months after the partial right nephrectomy shows no recurrence of tumor. Arrow: cryoablation treatment area. Circle: Partial nephrectomy.

consideration for patients with bilateral renal tumors. Our patient was of special concern, as he had several risk factors for chronic renal failure, including DM, HTN and HL.

When we planned the treatment, the first consideration was to decide which tumor we should treat first. It seemed easier to treat the left tumor compared to the right one because of the locations of the tumors. The tumor in the right kidney had a higher score compared to the left one, and it was too close to the renal vessels to be treated by any type of ablation therapy, including CA. There was a high possibility that the patient might lose his right kidney. We therefore treated the left renal tumor first to maximize the patient's renal function and avoid dialysis.

The second consideration was to decide which modality we should use to achieve good cancer control and the preservation of renal function. CA has recently emerged as a valid alternative to nephron-sparing surgery. The effectiveness of CA for treating T1a renal tumors is well established [5, 6]. In contrast, its effectiveness for T1b tumors remains undecided. However, the results have been promising. Atwell *et al.* reported an estimated 3-year local progression-free survival rate of 96.4% for 46 CA procedures for T1b tumors [9]; there were 7 (15.2%) major Clavien-Dindo grade II or higher complications. Most of the major complications were bleeding (4/7). Prophylactic embolization

was not performed in these patients [8].

At our institution, prophylactic embolization is performed to prevent bleeding for tumors > 3 cm, and our major bleeding rate is low at 1.3% (2/174). Moreover, our renal preservation rate after CA is 100%. In the present patient's case, we felt that CA for the left tumor had a better chance to preserve renal function compared to PN. However, since the long-term effectiveness of CA for T1b RCC is still unclear, we had to consider that the left renal tumor might lead to a radical nephrectomy in the future, even after CA. We thus had to preserve the patient's right renal function as much as possible. We prepared for renal autotransplantation at the time of surgery for the right renal tumor. Fortunately, the PN was successfully performed.

A combination of CA and PN can be used for bilateral synchronous RCC with preservation of renal function. This strategy is a novel method for treating patients with renal tumors that have characteristics suggesting that bilateral PN will be difficult.

References

1. Grimaldi G, Reuter V and Russo P: Bilateral non-familial renal cell carcinoma. *Ann Surg Oncol* (1998) 5: 548-552.
2. Patel M, Simmons R, Kattan M, Motzer R, Reuter V and Russo P: Long-term follow-up of bilateral sporadic renal tumors. *Urology* (2003) 61: 921-925.
3. Becker F, Siemer S, Tzavaras A, Suttman H and Stoeckle

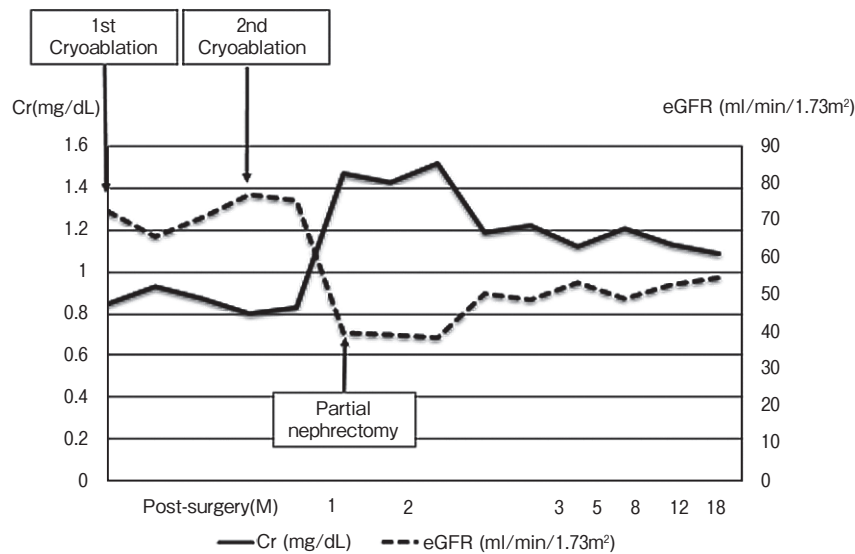


Fig. 2 The patient's serum creatinine levels and estimated glomerular filtration rate (eGFR) over the course of treatment and follow-up.

- M: Long-term survival in bilateral renal cell carcinoma: a retrospective single-institutional analysis of 101 patients after surgical treatment. *Urology* (2008) 72: 349–353.
4. Boorjian SA, Crispen PL, Lohse CM, Leibovich BC and Blute ML: The impact of temporal presentation on clinical and pathological outcomes for patients with sporadic bilateral renal masses. *Eur Urol* (2008) 54: 855–863.
 5. Campbell SC, Novick AC, Belldegrun A, Micheal LB, George KC, Chow IH, Martha MM, Jihad HK, Raymond JL, Surena FM, Paul Russo and Robert GU: Guideline for management of the clinical T1 renal mass. *J Urol* (2009) 182: 1271–1279.
 6. Ljungberg B, Bensalah K, Canfield S, Steven C, Saeed D, Fabian H, Milan H, Markus AK, Thomas L, Lorenzo M, Axel SM, Peter M, Thomas P, Michael S, Alessandro V and Axel B: EAU guidelines on renal cell carcinoma: 2014 update. *Eur Urol* (2015) 67: 913–924.
 7. Chang X, Liu T, Zhang F, Cheng Q, Changwei J, Xiaozhi Z, Guangxiang L and Hongqian G: The comparison of R.E.N.A.L., PADUA and centrality index score in predicting perioperative outcomes and complications after laparoscopic radio frequency ablation of renal tumors. *J Urol* (2015) 194: 897–902.
 8. Amano H, Kondo T, Hashimoto Y, Kobayashi H, Iizuka J, Shimada K, Nakazawa H, Ito F and Tanabe KI: Contralateral metachronous tumor occurrence is more frequently associated with distant metastases or postoperative intrarenal recurrence in renal cell carcinoma patients. *Int J Urol* (2010) 17: 615–622.
 9. Atwell TD, Vlaminc JJ, Boorjian SA, Kurup AN, Callstrom MR, Weisbrod AJ, Lohse CM, Hartman WR, Stockland AH, Leibovich BC, Schmit GD and Thompson RH: Percutaneous Cryoablation of Stage T1b Renal Cell Carcinoma: Technique Considerations, Safety, and Local Tumor Control. *J Vasc Interv Radiol* (2015) 26: 792–799.