Case Report

Recurrence of renal cell carcinoma after simultaneous radical nephrectomy and cadaver renal transplant

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Abbreviations & Acronyms
CNI = calcineurin inhibitor
mTORi = mammalian target of rapamycin inhibitor

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Introduction: Generally, renal transplantation is contraindicated in cancer patients, and a certain follow-up period is required. We report a case of late recurrence of renal cell carcinoma in a patient who underwent simultaneous radical nephrectomy and cadaver renal transplantation due to renal cell carcinoma observed during renal transplantation after 12 years.

Case presentation: Incidental renal cell carcinoma was found in a 48-year-old man during kidney transplantation who subsequently underwent simultaneous cadaver kidney transplantation and radical nephrectomy. Twelve years after transplantation, he developed an anterior mediastinal tumor, a lung tumor which was resected and a right adrenal gland mass which was resected along with the right kidney. Currently, he is being treated with tyrosine kinase inhibitors owing to the metastasis in the left adrenal gland.

Conclusion: In patients with metastatic carcinoma undergoing renal transplant, the indications for surgical procedures and choice of immunosuppressants should be carefully considered.

Key words: immunosuppressive agents, kidney transplantation, radical nephrectomy, recurrence, renal cell carcinoma.

Keynote message

A kidney recipient with renal cell carcinoma underwent simultaneous nephrectomy and renal transplant. The late recurrence of renal cell carcinoma warrants reconsideration of the indications for renal transplant in patients with carcinoma.

Introduction

The Kidney Disease Improving Global Outcomes guidelines and the American Society of Transplantation recommend that a waiting period for kidney transplant is not necessary for incidentalomas of ≤3 cm and recommends a 2-year postoperative waiting period for small renal cell carcinoma, or 5 years after treatment for renal carcinoma with a large tumor size or invasive renal cell carcinoma.[1,2]

Here, we report the case of simultaneous radical nephrectomy and renal transplantation in a patient with renal cell carcinoma during cadaver renal transplantation.

Case presentation

A man in his 60s was commenced on hemodialysis at 32 years of age due to chronic renal failure caused by chronic glomerulonephritis. He underwent a renal transplant at the age of 48 years with a donor kidney from a man who died from cardiac failure in his 50s. At the time of transplantation, a tumor was found in the left kidney, and a left radical nephrectomy was performed simultaneously. The tumor was 52 mm in diameter and had not metastasized. Histopathological examination revealed clear cell carcinoma, G2, pT1b, expansive type, INFα. Immunosuppressive drugs including mycophenolate mofetil, tacrolimus, and

methylprednisolone were administered. Four years after the surgery, the patient was referred to our institution because it was accessible from his new location. His renal function was consistently good, and his serum creatinine level was stable at approximately 1.7 mg/dL. Twelve years after renal transplantation, an anterior mediastinal mass was observed by computerized tomography (Fig. 1a). Thoracoscopic resection of the anterior mediastinal mass was performed, and it was diagnosed as metastasis from renal cell carcinoma (Fig. 2a-c). A year later, a metastatic tumor was found in the left upper lung field (Fig. 1b), and resection of the left lung S1 + 2 segment was performed. Histopathological examination revealed that the lung tumor was a metastasis from renal cell carcinoma (Fig. 2d-f). At the same time, a 30-mm mass was found in the right adrenal gland (Fig. 1c); the right adrenal gland was resected together with the right kidney a year later and diagnosed as metastatic renal cell carcinoma (Fig. 3a-f). Eventually, the left adrenal gland also became enlarged, and the patient was administered sunitinib at 25 mg/day. Twenty-four months into the treatment, the gland increased in size to 30 mm. Currently, the patient is taking axitinib at 6 mg/day as a second-line treatment.

Discussion

One of the challenges in this case was whether it was appropriate to perform nephrectomy and renal transplant simultaneously in a recipient who was known to have renal cell carcinoma.

In most cases of autosomal dominant polycystic kidney disease, nephrectomy is performed simultaneously with renal transplant to secure the transplant bed,[3,4] and there has been a previous report of incidentalomas.[5] Sultan et al. performed radical nephrectomy and renal transplant in 16 patients with renal tumors at the time of transplantation, 10 of whom had renal cell carcinoma.[6] They reported that simultaneous living-donor transplantation and laparoscopic radical nephrectomy may be an option for patients with T1 tumors ≤4.0 cm.[6] Pham et al. also reported that a waiting period is not necessary for incidental tumors of renal cancer.[7] Based on the literature reports and guidelines, carrying out renal transplantation in the presence of renal cell carcinoma is questionable.

Renal cell carcinoma has been reported to recur later in life than other carcinomas, sometimes more than 20 years after surgery; therefore, long-term follow-up is necessary.[8] In this case, the patient underwent simultaneous radical nephrectomy and renal transplant, and a recurrence of renal cell carcinoma was observed 12 years later. Conversely, considering that no recurrence was observed until 12 years after the surgery, this may provide a clue regarding the timing of transplantation in patients with carcinoma. In addition, the use of immunosuppressive drugs is an essential part of transplant surgery. A protocol for immunosuppressive therapy needs to be considered. As a mechanism of carcinogenesis by immunosuppressive drugs, it has been reported that oncoviruses may proliferate due to long-term immunosuppression, tumor cells may proliferate due to decreased immunological surveillance, and direct carcinogenic effects are possible.[9] There are also reports that cyclosporine stimulates transforming growth factor beta to promote carcinogenesis.[10] The use of mammalian target of rapamycin inhibitors (mTORi) has been reported to suppress post-transplantation carcinogenesis.[11] Lem et al. reported that switching from calcineurin inhibitor (CNI) to mTORi reduced the risk of developing all cancers up to 5 years after transplantation.[12] Sheraton et al. proposed an algorithm in which cancer risk is assessed before transplantation and risk factors are monitored after transplantation; CNI is reduced as much as possible and mTORi is introduced

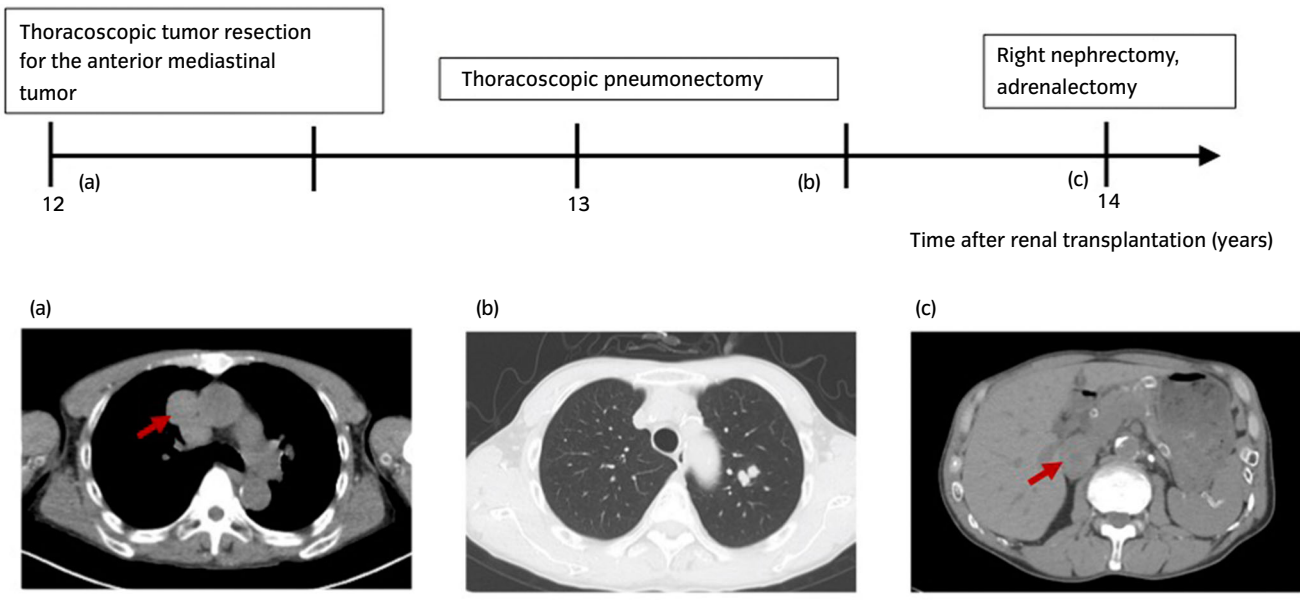

Fig. 1 (a) The red arrow indicates a 34 × 38 mm smooth mass shadow in the anterior mediastinum. (b) Two nodules of 10 mm and 8 mm adjacent to the S12 area of the left lung. (c) The red arrow indicates a 51-mm large mass shadow in the right adrenal gland. mm: millimeter.

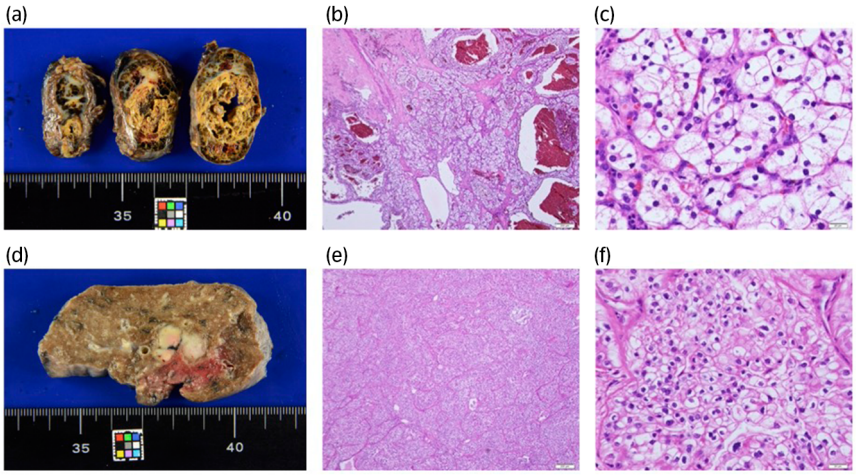

Fig. 2 (a) Gross findings of mediastinal tumor. The surface of the tumor was smooth, and the broken surface was yellow to grayish-white. (b) Scale bar = 200 μm, 4× objective lens. (c) Scale bar: 20 μm, 40× objective lens. Pale cystic carcinoma that grows in a chordate-to-sporophytic pattern with abundant intervening capillaries and fibrous growth. Lymphocytic infiltration occurs, but the tumor itself is expansive. Lymph node metastasis of renal cell carcinoma. (d) Gross manifestation of metastatic lung tumor. A grayish-white tumor with indistinct borders and a pale yellow tumor with relatively clear borders were present adjacent to the tumor. (e) Scale bar = 200 {m, 4× objective lens. (f) Scale bar: 20 μm, 40× objective lens. This image shows a pale vesicular carcinoma with polygonal cells with pale cytoplasm and capillaries growing in a full vesicular pattern. {m: micrometer.

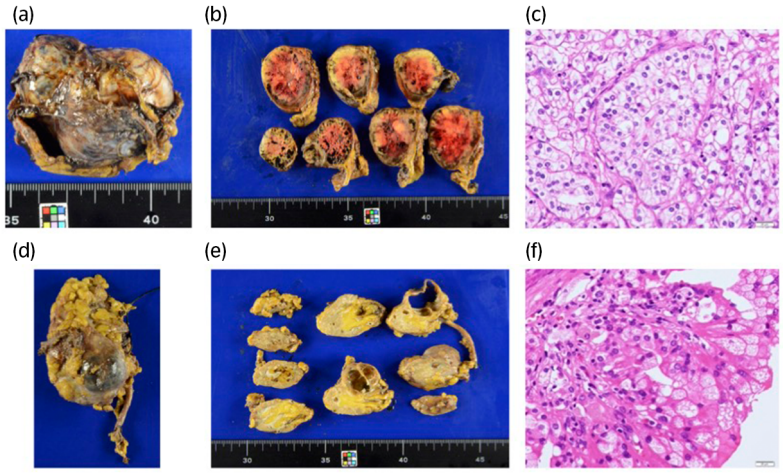

Fig. 3 (a) Gross appearance of right adrenal tumor. (b) 55 × 42 × 33 mm, yellowish, well-defined mass. (c) Heteromorphic cells with pale sporangial bodies proliferate in a fleshy to cystic manner. Histological image showing metastasis of pale cystic carcinoma. Scale bar = 20 μm, 40× objective lens. (d) Gross findings of the right kidney. (e) Atrophied kidney with multifocal cysts and multiple renal calculi. (f) Cystic growth of cells with pale sporangial bodies 3 mm in size. Metastasis of panniculus cystic carcinoma is indicated. Scale bar = 20 μm, 40× objective lens. mm: millimeter; {m: micrometer.

with a low immunosuppressive protocol for high cancer risk.[9] Reviewing the protocol for immunosuppressive therapy after transplantation may be useful in suppressing post-transplantation carcinogenesis.

Conclusion

When a patient with metastatic carcinoma receives a renal transplant, the indications for surgery and long-term follow-up are similar to that of postoperative renal cell carcinoma. In addition, protocols for immunosuppressive drugs should be considered according to the risk of cancer development.

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Author Contributions

Shinya Inoue: Writing – original draft. Akihiro Shioya: Visualization. Kenshiro Kunii: Writing – review and editing. Kodai Suga: Writing – review and editing. Nobuyo Morita: Writing – review and editing. Ippei Chikazawa: Writing – review and editing. Tatsuro Tanaka: Supervision. Katsuhito Miyazawa: Supervision; writing – review and editing.

Conflict of interest

The authors declare no conflict of interest.

Approval of the research protocol by an Institutional Review Board

N/A.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Registry and the Registration No. of the study/trial

N/A.

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Editorial Comment

Editorial comment to A case of recurrence of renal cell carcinoma after simultaneous radical nephrectomy and cadaver renal transplant

Malignancy is among the primary causes of mortality in renal transplant recipients. The risk of new malignancies in renal transplant recipients is 2–3 times higher than in the general population.[1] If a possible recipient has a cancer history, a waiting period before renal transplantation is often required after cancer treatment. Immunosuppression after renal transplantation might not affect the prognosis of low-risk renal cell carcinomas.[2] Posttransplant malignancies, which can occur de novo or as cancer recurrences, result from chronic exposure to immunosuppressive drugs and are often more aggressive than those that develop in the nontransplant setting. Malignancy after renal transplantation requires cautious and long-term follow-up.

Inoue et al. reported a case of renal cell carcinoma recurrence in a patient who received simultaneous treatment with radical nephrectomy for a left renal tumor and cadaver renal transplantation.[3] The tumor was a clear cell carcinoma (G2, pT1b). Twelve years after renal transplantation, an anterior mediastinal mass and lung and bilateral adrenal metastases were observed. Noteworthy points of this case are the association between immunosuppressive drugs and recurrence and the effect of simultaneous treatment with radical nephrectomy and renal transplantation on tumor control in patients with renal cancer.

Mammalian target of rapamycin (mTOR) inhibitors have immunosuppressive and antitumor effects. Treatment conversion to mTOR inhibitors is correlated with a low incidence of malignancies and is safe for renal function and graft survival in patients with a cancer history.[4] The use of immune checkpoint inhibitors is another treatment option for renal cancer. However, it might be associated with a high risk of acute rejection.[5] Renal transplantation might not be correlated with a high risk of recurrence compared with dialysis in patients with low-risk renal cancer.[2] Nevertheless, recurrence of malignancy after renal transplantation requires cautious and long-term follow-up. Expectantly, considering the various risks in renal transplant recipients, optimal treatment regimens with immunosuppressive drugs and standard doses will be determined in the future.