Case Report

A case of complete response to avelumab plus axitinib combination therapy for metastatic clear cell renal cell carcinoma in a kidney undergoing dialysis

Ei Shiomi,[1] Yuta Goto,[2] Mizuki Hisano,[2] Rento Ito,[1] Makoto Moriwaka,[1] Daiki Ikarashi,[1] Shigekatsu Maekawa,[1] Renpei Kato,[1] Mitsugu Kanehira,[1] Takashi Ujiie[2] and Wataru Obara[1]

[1]Department of Urology, Iwate Medical University, Yahaba, and [2]Department of Urology, Iwate Prefectural Ofunato Hospital, Ofunato, Iwate, Japan

Abbreviations & Acronyms
Ave = avelumab
Axi = axitinib
Cabo = cabozantinib
CT = computed tomography
ICI = immune checkpoint inhibitor
irAEs = immune-related adverse events
Len = lenvatinib
Nivo = nivolumab
Pem = pembrolizumab

Correspondence: Ei Shiomi, M.D., Ph.D., 2-1-1 Idaidori, Yahaba-cho, Shiwagun, Iwate 028-3609, Japan. Email: icehockey-33-ei-@outlook.com

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Introduction: Combination therapies of immune checkpoint and tyrosine kinase inhibitors for end-stage kidney disease and patients on hemodialysis need careful consideration as few case reports provide suitable management decisions.

Case presentation: A 70-year-old man who had undergone hemodialysis for 6 years due to nephrosclerosis. Avelumab plus axitinib combination therapy was performed for repeated lung metastasis, and a complete response was achieved without major side effects.

Conclusion: A complete response was achieved after Ave plus Axi combination therapy for clear cell renal cell carcinoma in a patient undergoing dialysis. This suggests that Ave plus Axi combination therapy may be safe and effective for dialysis patients.

Key words: avelumab, axitinib, carcinoma, immune checkpoint inhibitors, renal cell, renal dialysis.

Keynote message

Our patient was treated with Ave plus Axi combination therapy for metastatic renal cell carcinoma on dialysis, and by taking drug withdrawal, reducing the dose, and controlling dialysis conditions, the patient was able to continue treatment without severe side effects and achieve CR. The use of the Ave plus Axi combination therapy is promising for patients with renal cell carcinoma on dialysis.

Introduction

Various drug therapies have recently been approved for treating metastatic renal cell carcinoma. Combination therapies of ICIs and tyrosine kinase inhibitors are widely accepted as an appropriate initial systemic therapy for metastatic renal cell carcinoma.

Although there is no renal clearance of these agents, the data on the use of ICIs in end-stage kidney disease patients on hemodialysis is scarce. In Japan, combination therapy for renal cell carcinoma in those undergoing kidney dialysis has been recorded in seven cases. Three of these cases used Ave plus Axi combination therapy.[1] but complete response was not obtained in any of the reported cases.

Here, we report a case of complete response to Ave plus Axi combination therapy for metastatic renal cell carcinoma in a patient undergoing kidney dialysis.

Case report

The patient was a 70-year-old man who had undergone hemodialysis for 6 years due to nephrosclerosis. Five years previously, he underwent laparoscopic total nephrectomy for right renal cell carcinoma. The pathological diagnosis was clear cell renal cell carcinoma, pT1b, pNx, pMx, G2, and Fuhrman grade 3 (Fig. 1). 2 years later, he had left lung metastasis and partial pneumonectomy, and the pathological diagnosis was clear cell renal cell carcinoma (Fig. 2). After that, he had no recurrence or metastasis until he presented with multiple right lung metastases (Fig. 3).

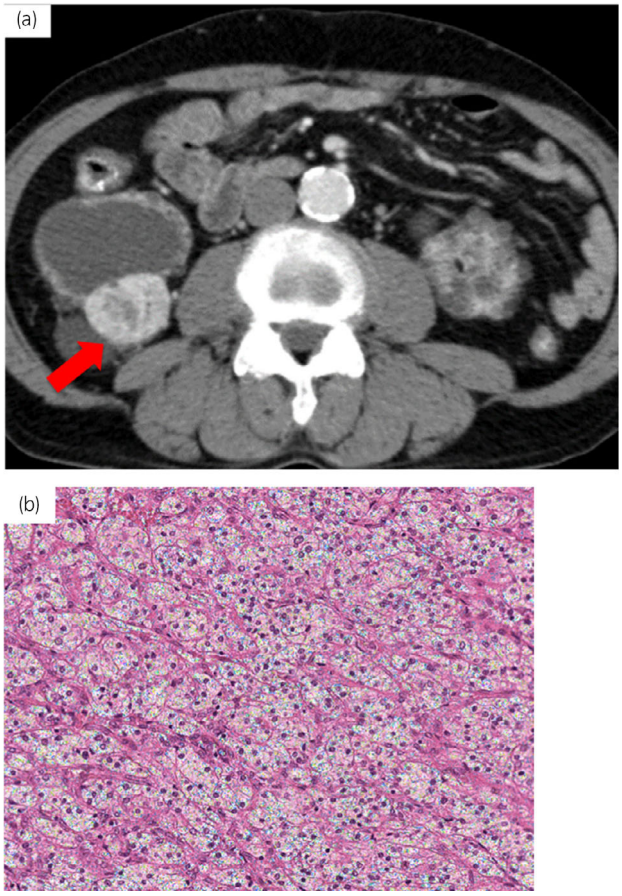

Fig. 1 (a) Right kidney tumor on contrast CT. (b) Clear cell renal cell carcinoma by hematoxylin–eosin stain.

Since The International Metastatic Renal Cell Carcinoma Database Consortium risk was favorable, we chose Ave plus Axi combination therapy for the associated lower number of adverse events. The patient was started on Ave 10 mg/kg plus Axi 10 mg daily. In 2 months, grade 2 fatigue, grade 2 dyspnea, and grade 3 hypertension were noted. We stopped both drugs at the patient's request, and controlled the dry weight and time of hemodialysis, considering that the dialysis could be the cause. 4 months later, we restarted only Ave, but in 6 months, CT showed lung metastasis progression, and we restarted Axi 5 mg daily. 8 months later, CT showed that the lung metastasis had undergone partial response. Finally, 12 months later, CT showed that all the lung metastases had disappeared (Fig. 4). We stopped both drugs again as the patient requested, and 1 year later, no metastasis or recurrence has been noted.

Discussion

ICIs contribute to the prognosis of advanced malignancy and, in fact, have been shown to improve prognosis in a variety of tumors.[2]

However, patients with end-stage kidney disease and those receiving hemodialysis have been largely excluded from cancer therapy trials, including ICIs, because estimating the risk of harmful and irAEs is challenging.[2] Similarly, combination therapies such as Ave plus Axi have been excluded from key clinical trials.[2] Thus, combination therapies for those with end-stage kidney disease and patients on hemodialysis need careful consideration, and very few case reports provide suitable management decisions.

In a report by Band *et al.*, 7 patients were administered combination therapies for renal cell carcinoma, and none experienced severe irAEs. 3 patients received Ave plus Axi combination therapy, and these irAEs were only grade 1 and 2, and all cases experienced partial response.[1]

ICI combination therapies for metastatic renal cell carcinoma in Japan included Ave plus Axi, Pem plus Axi, Nivo plus Cabo, Pem plus Len, and Nivo plus Ipi. Appropriately using these drugs are important in treating metastatic renal cell carcinoma, but debates still exist regarding suitable modalities. Regarding trials for each therapy, the rate of irAEs > grade 3 was 30% (Ave plus Axi), 60.2% (Pem plus Axi), 65% (Nivo plus Cabo), 71.6% (Pem plus Len), and 46% (Nivo plus Ipi)[3–8]; Ave plus Axi showed the fewest irAEs.

This is why the Ave plus Axi is recommended for elderly patients and patients with multiple comorbidities. In our case, there were no severe irAEs, and these events may have been associated with molecular targeted agent or hemodialysis. Thus, it was possible to use the combination therapy after introducing appropriate drug breaks, dose reductions, controlling dry weight, and the time of dialysis.

In this case, it took 12 months to reach CR; however, the patient had repeated instances of drug withdrawal due to the

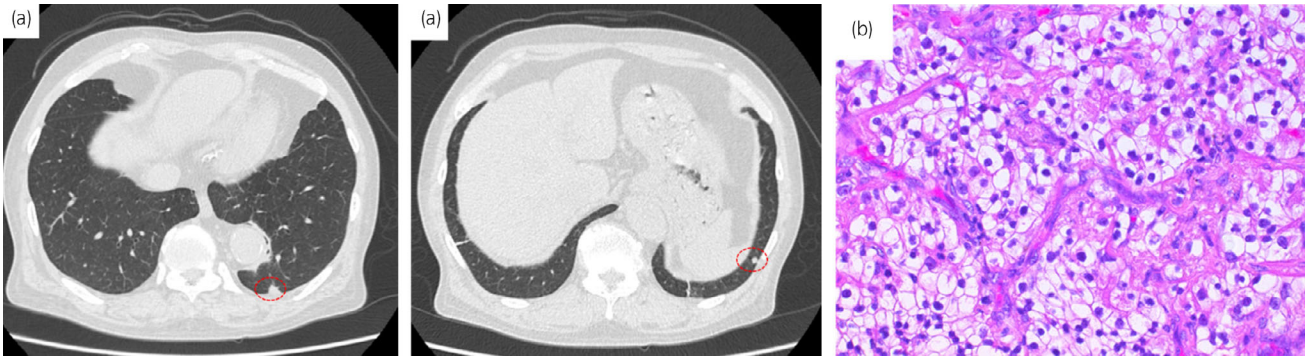

Fig. 2 (a) Metastatic left lung tumor. (b) Clear cell renal cell carcinoma by hematoxylin–eosin stain.

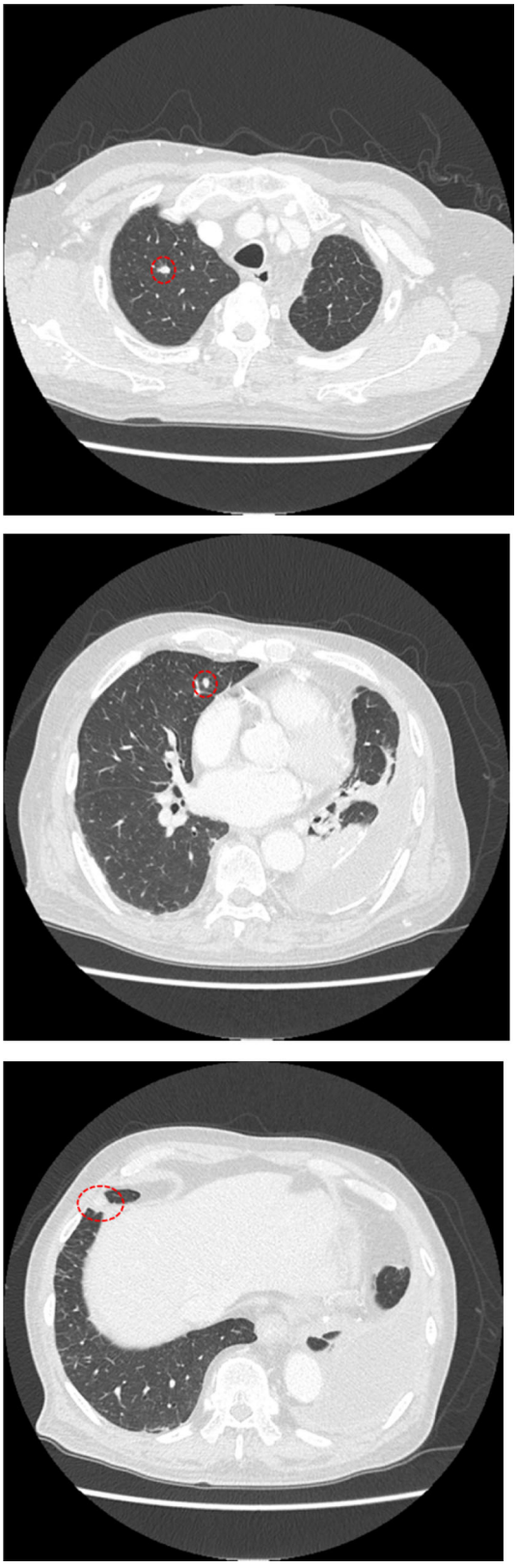

Fig. 3 Metastatic right lung tumor before Ave plus Axi combination therapy.

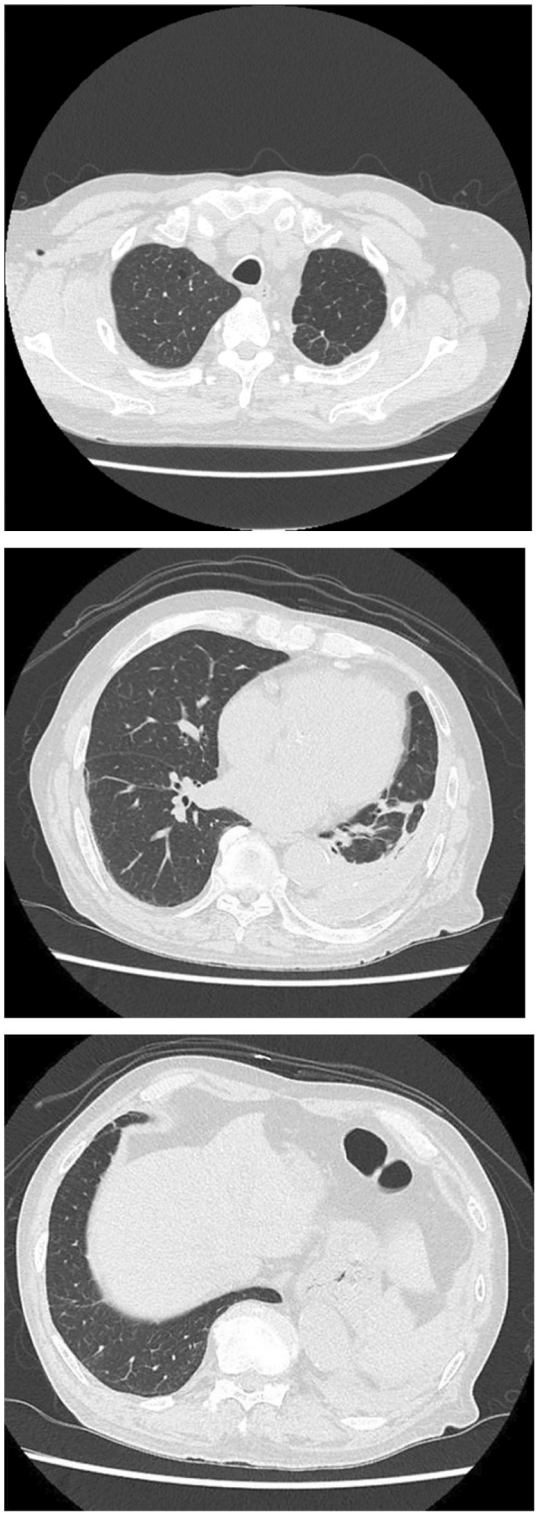

Fig. 4 Metastatic right lung tumor after Ave plus Axi combination therapy.

adverse events. However, if the drug withdrawal period would have been absent, a shorter time to CR could have been expected.

Ave plus Axi for patients undergoing dialysis is a safe treatment, our case recorded a complete response, which, to our knowledge, is the first report of Ave plus Axi. Based on this experience, we recommend the aggressive use of Ave plus Axi for metastatic renal cell carcinoma in those undergoing dialysis to gain further experience regarding its use.

Conclusion

We experienced a complete response after Ave plus Axi combination therapy for clear cell renal cell carcinoma of a dialysis patient. Ave plus Axi combination therapy may be useful and safe for dialysis patients.

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Author contributions

Ei Shiomi: Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; writing – original draft. Yuta Goto: Data curation. Mizuki Hisano: Data curation. Rento Ito: Investigation. Makoto Moriwaka: Investigation. Daiki Ikarashi: Investigation; methodology; project administration. Shigekatsu Maekawa: Investigation; methodology; project administration. Renpei Kato: Investigation; methodology; project administration; supervision. Mitsugu Kanehira: Investigation; methodology; project administration; supervision. Takashi Ujiie: Supervision; writing – review and editing. Wataru Obara: Supervision; writing – review and editing.

Conflict of interest

The authors declare no conflict of interest.

Approval of the research protocol by an Institutional Reviewer Board

Not applicable.

Informed consent

Written consent to publish was obtained from the patient for the publication of this case and any accompanying images.

Registry and the Registration No. of the study/trial

Not applicable.

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