Case Report

A case of novel coronavirus disease after combination therapy with nivolumab and ipilimumab for metastatic renal cell carcinoma

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Abbreviations & Acronyms
COVID-19 = coronavirus disease
ICI = immune checkpoint inhibitor
RCC = renal cell carcinoma
RT-PCR = reverse transcription-polymerase chain reaction
TKI = tyrosine kinase inhibitor

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Introduction: We present a case of novel coronavirus disease-2019 that underwent combination therapy with nivolumab and ipilimumab for metastatic renal cell carcinoma.
Case presentation: A 50-year-old man complained of anorexia and weight loss. Contrast-enhanced computed tomography revealed a solid mass of 57 mm in diameter with cysts in the right kidney, along with liver, lung, and multiple bone metastases. Computed tomography-guided biopsy of the right kidney was performed, and a diagnosis of clear cell renal cell carcinoma was made. Three weeks after nivolumab and ipilimumab administration, the patient contracted coronavirus disease-2019. Anticoagulation therapy (dalteparin) was administered for 4 days once infection was confirmed, after which dexamethasone was administered for 10 days. The patient survived without experiencing worsened respiratory symptoms.
Conclusion: We administered nivolumab and ipilimumab combination therapy as treatment for metastatic renal cell carcinoma. No side effects or immune-related adverse events were observed for a short time.

Key words: anticoagulants, COVID-19, drug-related side effects and adverse reactions, ipilimumab, nivolumab.

Keynote message

We report a case of a novel coronavirus disease (COVID-19) following combination therapy with nivolumab and ipilimumab for metastatic renal cell carcinoma. Anticoagulant therapy (dalteparin) was started as soon as the infection was confirmed. Four days later, dexamethasone was administered for 10 days. The patient survived without experiencing worsened respiratory symptoms, and no immune-related adverse events occurred.

Introduction

Nivolumab and ipilimumab combination therapy has been approved as treatment for metastatic renal cancer. However, a shift from the use of one or two ICIs to the increased use of single TKIs occurred during the COVID-19 pandemic.[1] We report a case of COVID-19 that underwent ICI combination therapy with nivolumab and ipilimumab for metastatic RCC.

Case presentation

A 50-year-old man complained of anorexia and weight loss. Screening ultrasonography revealed a right kidney tumor and liver metastasis 6 months later. Contrast-enhanced computed tomography revealed a solid mass 57 mm in diameter with cysts in the right kidney, along with liver metastasis, multiple bone metastases, and lung metastasis. Paralysis progressed after irradiation therapy was performed to treat the bone metastases, after which the patient underwent laminectomy and spinal fusion. A computed tomography-guided tumor biopsy of the right kidney was performed, and the patient was diagnosed with clear cell RCC, G3 (Fuhrman grade 3, WHO/ISUP grade 3). Nivolumab and ipilimumab combination

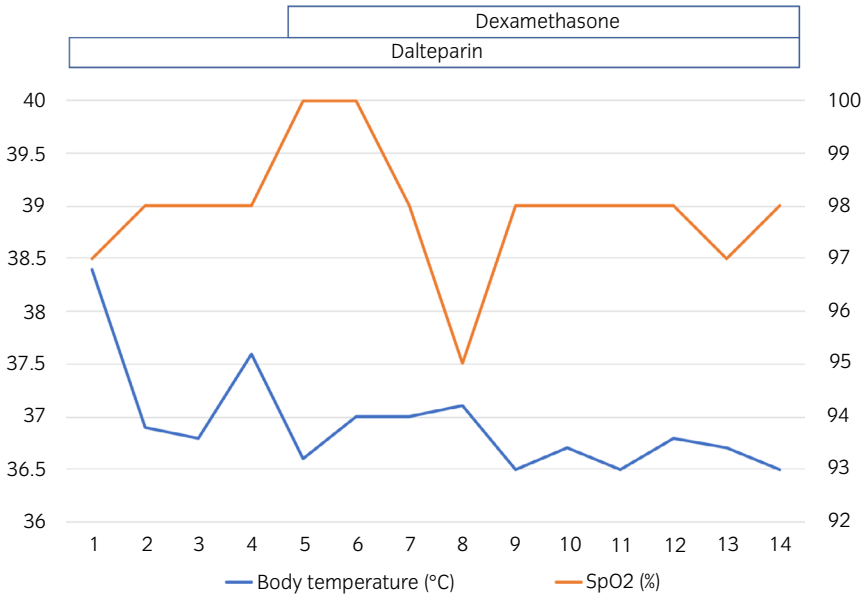

Fig. 1 Figure showing the clinical course after infection with SARS-CoV-2 in a 50-year-old man undergoing combination therapy with nivolumab and ipilimumab for metastatic renal cell carcinoma.

therapy was selected as the first-line therapy for poor-risk metastatic RCC based on the International Metastatic RCC Database Consortium risk classification.[2]

A COVID-19 outbreak occurred in the hospital during the patient's hospital stay. Three weeks after the administration of nivolumab and ipilimumab, the patient was infected with SARS-CoV-2. Three positive SARS-CoV-2 antigen and/or RT-PCR tests were performed before a COVID-19 diagnosis was made. The clinical course of this case after SARS-CoV-2 infection is shown in Figure 1. Anticoagulant therapy (dalteparin) was administered for 4 days once the infection was confirmed, after which dexamethasone was administered for 10 days. Computed tomography performed after COVID-19 diagnosis (day 16 of infection) showed ground-glass opacity in the bilateral lower lobes of the lungs (Fig. 2). The patient survived without experiencing worsened respiratory symptoms and did not require oxygen, was discharged approximately 2 months after testing negative for COVID-19 by RT-PCR. A second course of nivolumab and ipilimumab was administered 1 month after discharge; however, the patient died 1 month later due to progression of the metastatic RCC.

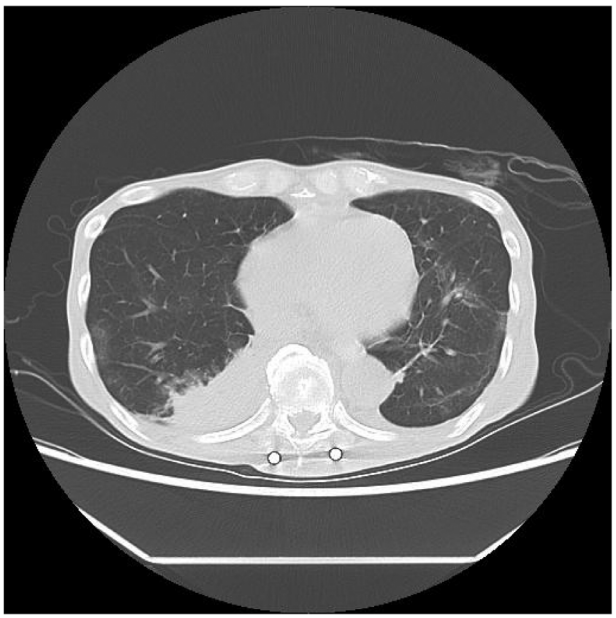

Fig. 2 Computed tomography image taken 16 days after infection with SARS-CoV-2 in a 50-year-old man after combination therapy with nivolumab and ipilimumab for metastatic renal cell carcinoma. Ground-glass opacity can be observed in the bilateral lower lobes of the lungs.

Discussion

We report a case of COVID-19 after nivolumab and ipilimumab combination therapy for a metastatic renal tumor. According to the International Metastatic RCC Database Consortium risk classification, nivolumab and ipilimumab are first-line therapies for poor-risk metastatic RCC.[2] A randomized trial, CheckMate 214, recently established the efficacy of combining ICI treatment with nivolumab and ipilimumab.[2–4] For patients with advanced RCC who have not undergone prior systemic therapy, nivolumab plus ipilimumab combination therapy improves overall survival more than sunitinib.[2–4] However, the most common adaptation that occurred during the pandemic has been the replacement of one or two ICIs with TKI monotherapy.[1] Although drugs that inhibit PD-1/PD-L1 interactions may enhance the CD8 T-cell response and thereby reduce the viral load, they may also overstate primary T-cell responses and exacerbate acute infections.[5,6] In addition to possible exacerbation of COVID-19 by ICIs, the controversy regarding SARS-CoV-2 and ICI-based anticancer therapy is driven by the concern that coronavirus-induced interstitial pneumonia may be complicated by pulmonary toxicity caused by anti-PD-1/PD-L1 agents.[7] Most experts change the regimen by either extending the treatment cycle or withholding one or even both ICIs.[1] However, whenever possible, it is recommended to continue ICI administration for cancer control.

SARS-CoV-2 infection status should be considered when choosing anticancer treatment. In this case, an infection cluster occurred in the hospital during the patient's hospitalization, and the patient was diagnosed with COVID-19 after undergoing treatment with nivolumab and ipilimumab. False-negative SARS-CoV-2 RT-PCR test results have been reported when hospitalized patients with clinically diagnosed COVID-19[8,9] tested positive after two consecutive negative tests.

No treatment for COVID-19 currently exists, although adjunctive therapies such as corticosteroids, anti-cytokines, immunosuppressive drugs, and immunoglobulins exist.[10] Anticoagulant therapy is reportedly the most important treatment for reducing COVID-19-related mortality.[11] In conclusion, we administered nivolumab and ipilimumab as treatment for metastatic RCC to a patient with COVID-19. In this case, steroids and anticoagulant therapy were also administered, and the latter was considered particularly effective.

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Author Contributions

Yu Kijima: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Software; Validation; Visualization; Writing – original draft; Writing – review & editing. **Tomokazu Shimizu:** Conceptualization; Methodology; Project administration; Supervision; Writing – review & editing. **Shinya Kato:** Project administration. **Eri Sekido:** Project administration. **Kana Kano:** Project administration. **Makoto Toguchi:** Project administration. **Toshihide Horiuchi:** Project administration. **Hiroshi Toma:** Supervision. **Shoichi Iida:** Supervision. **Toshio Takagi:** Supervision.

Conflict of interest

The authors declare no conflict of interest.

Approval of the research protocol by an institutional review board

Not applicable.

Informed consent

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

Registry and the registration no. of the study/trial

Not applicable.

Data availability statement

All data generated or analyzed during this study are included in this published article.

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