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Case report

Successful treatment by pembrolizumab in a patient with end-stage renal disease with advanced non-small cell lung cancer and high PD-L1 expression

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ABSTRACT

We report a 66-year-old Japanese male with end-stage renal disease (ESRD) and advanced non-small cell lung cancer (NSCLC) who was on hemodialysis. The patient harbored high programmed death ligand 1 (PD-L1) expression and was successfully treated with pembrolizumab. Laboratory examination upon diagnosis showed elevated serum creatinine (6.58 mg/dL). We administered pembrolizumab (200 mg/body) and repeated every 3 weeks. His renal dysfunction gradually progressed, hemodialysis was initiated after eight courses of pembrolizumab, and the antitumor effect was maintained at five months after hemodialysis initiation. Therefore, pembrolizumab can be administered for patients with ESRD and advanced NSCLC, who harbor high PD-L1 expression, during preparation for hemodialysis.

1. Introduction

Patients with metastatic non-small cell lung cancer (NSCLC) with chronic kidney disease (CKD) or end-stage renal disease (ESRD) who are also on hemodialysis have poor prognoses and limited therapeutic options. An anti-programmed death-1 (PD-1) antibody was recently approved in Japan for the treatment of metastatic NSCLC. Pembrolizumab, an anti-PD-1 antibody, has shown favorable antitumor efficacy in metastatic melanoma and NSCLC [1,2]. Patients with untreated metastatic NSCLC with high levels of programmed death ligand 1 (PD-L1) expression (tumor proportion score [TPS] $\geq$ 50%) who were treated with pembrolizumab showed a significant survival benefit [3]. However, there have been no reports describing the safety and efficacy of pembrolizumab in patients with advanced NSCLC and CKD or ESRD who are also on hemodialysis. To our knowledge, this is the first report of successful pembrolizumab treatment in a patient with advanced NSCLC and ESRD who was on hemodialysis.

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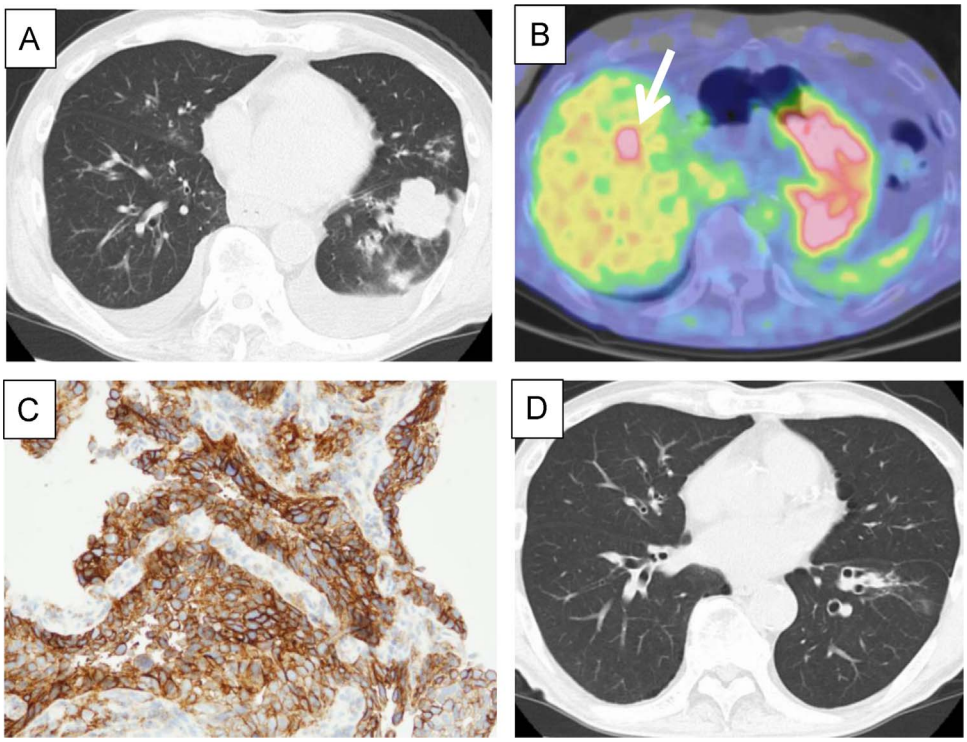

Fig. 1 – A: Chest CT demonstrating a mass in the patient's left lung and bilateral pleural effusion. B: PET-CT showing FDG accumulation in the liver mass (*arrow*). C: Histopathological findings of the mass obtained from the left lower lung, showing high expression of PD-L1: TPS 80% (≥ 50%). D: Chest CT demonstrating the antitumor effect at five months after the start of hemodialysis.

2. Case report

A 66-year-old Japanese male with a 4-year history of CKD, due to diabetes mellitus, was admitted to our hospital because of an abnormal chest shadow. He had a 40 pack/year smoking history, and his Eastern Cooperative Oncology Group performance status was 0. The results of laboratory examinations showed elevated serum creatinine (6.58 mg/dL; normal range <1.04 mg/dL) and blood urea nitrogen (53.6 mg/dL; normal range <22.0 mg/dL), and a reduced estimated glomerular filtration rate (e-GFR) (7 mL/min/1.73 m^2). We concluded that his renal function was end-stage, due to diabetic nephropathy.

A chest computed tomography (CT) scan revealed a 38-mm irregular tumor in the left lower lobe (Fig. 1A), a liver metastasis, and a bone metastasis in a lumbar vertebra. A transbronchial lung biopsy of the mass was performed, and the pathological diagnosis was squamous cell carcinoma. 18F-fluorodeoxyglucose (FDG) positron-emission tomography (PET) demonstrated FDG accumulation in the left lower lung mass and bone metastasis, and a liver mass (Fig. 1B). Magnetic resonance imaging of the head showed no metastasis to the brain. The clinical stage was IVB (cT2aN0M1c), and PD-L1 expression was assessed with an immunohistochemistry assay (Dako, Carpinteria, CA), with the murine 22C3 anti-human PD-L1 antibody, and the TPS was 80% (≥ 50%) (Fig. 1C).

We administered pembrolizumab (200 mg/body) and repeated treatment every three weeks. After six cycles of pembrolizumab administration, CT scan demonstrated marked tumor reduction and confirmed a partial response (PR), as defined by the Response Evaluation Criteria in Solid Tumors (RECIST) ver. 1.1. As for immune-related adverse events (irAEs), a grade 1 rash was observed on the trunk of the patient's body. There were no renal tubular injuries or other further irAEs. However, his renal dysfunction gradually progressed, and we initiated hemodialysis after the eighth course of pembrolizumab (Fig. 2A-C). The same pembrolizumab treatment regimen was continued throughout hemodialysis, without any other irAEs, and the antitumor effect was maintained, with a PR, at five months from the start of hemodialysis (Fig. 1D). Although the patient still receives pembrolizumab treatment, his progression-free survival (PFS) was 11.3 months, on the data cut-off date of 11 March 2018.

3. Discussion

Although the overall survival of patients with NSCLC has been markedly improved by new molecular targeted agents (such as tyrosine kinase inhibitors of the epidermal growth factor receptor, anaplastic lymphoma kinase, and c-ros oncogene 1) and new immune checkpoint inhibitor immunotherapies have been introduced, there are few evidence-based chemotherapy regimens for patients with metastatic NSCLC with CKD or ESRD, in part because it is difficult to conduct clinical trials for these patients.

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