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CASE REPORT

Long-term response with durvalumab after chemoradiotherapy for pulmonary pleomorphic carcinoma: A case report

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Abstract

Pulmonary pleomorphic carcinoma (PPC) is a non-small-cell lung cancer, resistant to chemotherapy and no standard therapy has as yet been established. We herein report the case of a 59-year-old man with PPC who showed a long-term response with durvalumab after chemoradiotherapy. He was referred to our hospital with a mass shadow at the right upper lung. PPC clinical stage IIIB was diagnosed, and the tumor proportion score of programmed death-ligand 1 (PD-L1) was 100%. Six days after transbronchial biopsy, he had difficulty walking owing to sensory abnormalities. We found that the primary tumor had invaded the spinal cord and compressed the cord at T1–T4, resulting in the abnormalities. He underwent tumor resection and received chemotherapy involving cisplatin (CDDP) + S-1 and concurrent radiotherapy (66 Gy). Subsequently, durvalumab treatment as consolidation therapy was commenced. After one year of durvalumab treatment had been completed, he had no apparent signs of relapse or severe adverse events. This case suggests that a long-term response can be achieved with durvalumab after chemoradiotherapy for stage III inoperable PPC showing high PD-L1 expression.

Key Points

Significant findings of the report

A long-term response might be achieved with durvalumab after chemoradiotherapy in patients with stage III inoperable pulmonary pleomorphic carcinoma showing high expression of programmed death-ligand 1.

What this study adds

It is possible to continue durvalumab treatment for one year without any severe adverse events. Although pulmonary pleomorphic carcinoma is considered to have a poor prognosis, the combination therapy of immune checkpoint inhibitors and radiotherapy may be an effective treatment option.

Introduction

Pulmonary pleomorphic carcinoma (PPC) is rare and represents less than 1% of all lung cancers. A standard treatment for PPC has not been established because of its rarity. PPC is resistant to chemotherapy and has a poor prognosis. Recently, several studies have highlighted that PPC highly expresses programmed death-ligand 1 (PD-L1), and several cases of successful treatment with immune checkpoint inhibitors (ICIs) have been reported. We herein report a rare case of a patient with stage III inoperable PPC showing high PD-L1 expression, who experienced a long-term response with durvalumab after chemoradiotherapy.

Case report

A 59-year-old man experienced pain in his right back for two months previously. He was subsequently referred to our hospital with a mass shadow visible on chest x-ray of the his right upper lung (Fig 1). He had a history of paroxysmal supraventricular tachycardia, and was an ex-smoker with a Brinkman index of 800. Transbronchial biopsy (TBB) was performed, and he was diagnosed with PPC in August 2018 (Fig 2). Epidermal growth factor receptor (*EGFR*) gene mutations and the anaplastic lymphoma kinase gene were not detected. The tumor proportion score (TPS) of PD-L1 was 100%. Six days after TBB, he experienced difficulty walking because of sensory abnormalities on the inside of the upper arm and from the abdomen to the lower legs. We found that the primary tumor had invaded around the spinal cord and compressed the cord at T1–T4, resulting in the abnormalities. There was no lymph node metastasis or distant metastasis, and he was diagnosed with clinical stage IIIB PPC.

He was admitted to the hospital, and tumor resection around the spinal cord and thoracic posterior vertebral fusion were performed. Chemotherapy with cisplatin (CDDP) + S-1 was performed on day 10 of hospitalization, and concurrent radiotherapy was started from day 16. Two courses of chemotherapy with CDDP + S-1 and radiotherapy of 66 Gy were completed. Durvalumab treatment as consolidation therapy was started nine weeks after the first chemotherapy day. At the start of durvalumab treatment, the tumor size was 61 × 47 mm (Fig 3), which was approximately 22% smaller than the size at diagnosis. Radiation pneumonitis occurred 14 weeks after the start of radiotherapy, but the shadow was slight and asymptomatic, and durvalumab treatment was continued. One year of continuous durvalumab treatment was completed, and he did not show apparent signs of relapse or severe adverse events. The tumor size was 46 × 39 mm at the end of durvalumab treatment (Fig 4).

Discussion

According to the 2015 World Health Organization classification,[1] PPC is defined as a poorly differentiated NSCLC, namely a squamous cell carcinoma, adenocarcinoma, or undifferentiated NSCLC with at least 10% spindle and/or giant cells or a carcinoma with only spindle and giant cells.

Bae *et al*. reported cytotoxic chemotherapy was administered for postoperative relapse and inoperable cases and 11 of 13 cases involved progressive disease, with a median overall survival (OS) of approximately five months.[2] Similarly, some PPC cases treated with cytotoxic chemotherapy have been reported,[3,4] but the median OS was only 7–8 months. Some reports have mentioned that a regimen involving gemcitabine[2–7] or taxanes[8,9] is effective. Tamura *et al*. reported chemoradiotherapy for postoperative relapse and locally advanced cases, in which one of three cases had a long-term response, with progression-free survival of over 65 months.[4] Similar cases have been reported,[5] and combination radiotherapy and cytotoxic chemotherapy might achieve a long-term response.

Recently, ICIs have been approved for the treatment of NSCLC. PD-L1 expression is recognized as a predictor of the ICI effect,[10] and the TPS of PD-L1 of ≧50% in NSCLC has been reported to be 23.2%.[11] Conversely, in PPC, the TPS of PD-L1 of ≧50% has been reported to be 60% and that of ≧1% has been reported to be 91.4%.[12] Based on

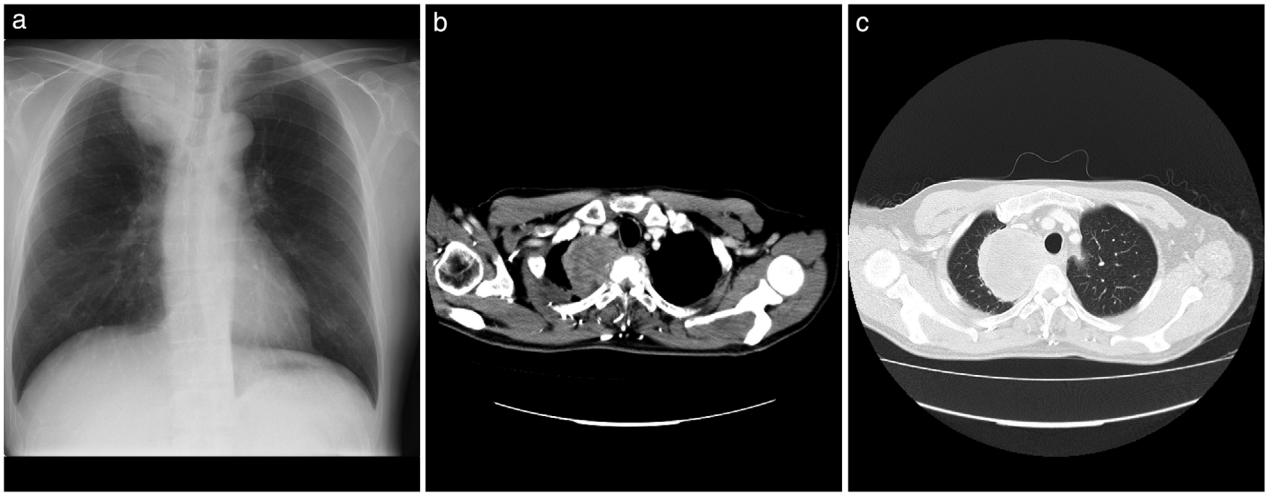

Figure 1 (**a**) The chest radiography revealed a mass shadow in the right upper lung. (**b**,**c**) The chest high resolution computed tomography (CT) scan showed a tumor in the right upper lobe. The tumor size was 70 × 69 mm with a necrotic center.

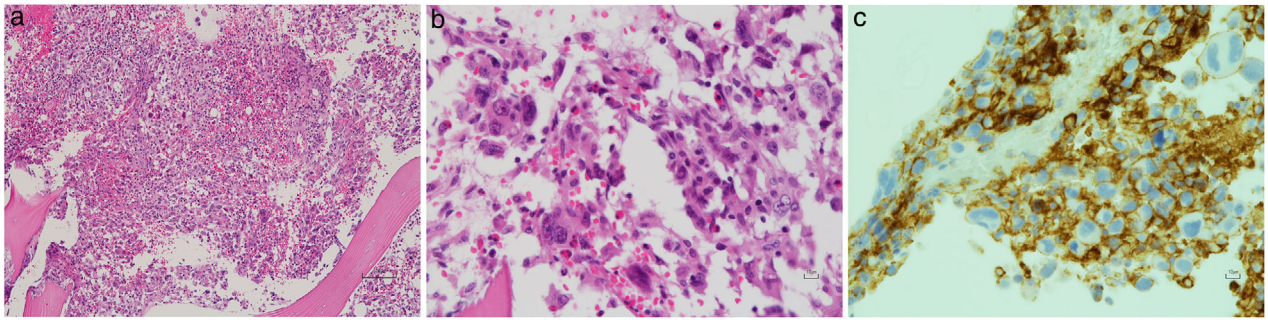

Figure 2 (**a**) Histopathology showed a pleomorphic carcinoma with spindle and giant cells. Hematoxylin and eosin staining, ×100 magnification and (**b**) ×400 magnification. (c) The PD-L1 expression was 100% (×400 magnification).

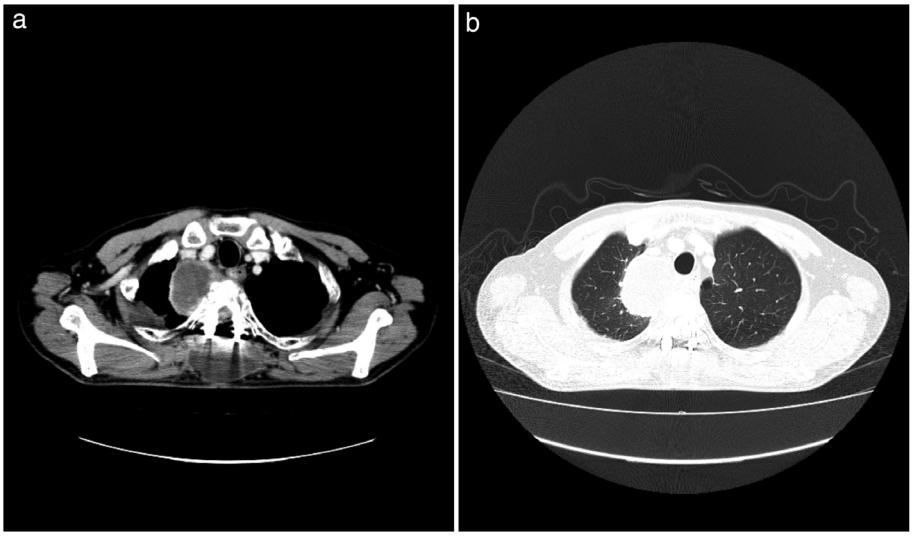

Figure 3 (**a**,**b**) At the start of durvalumab treatment, the tumor size was 61 mm × 47 mm, which was approximately 22% smaller than that at diagnosis.

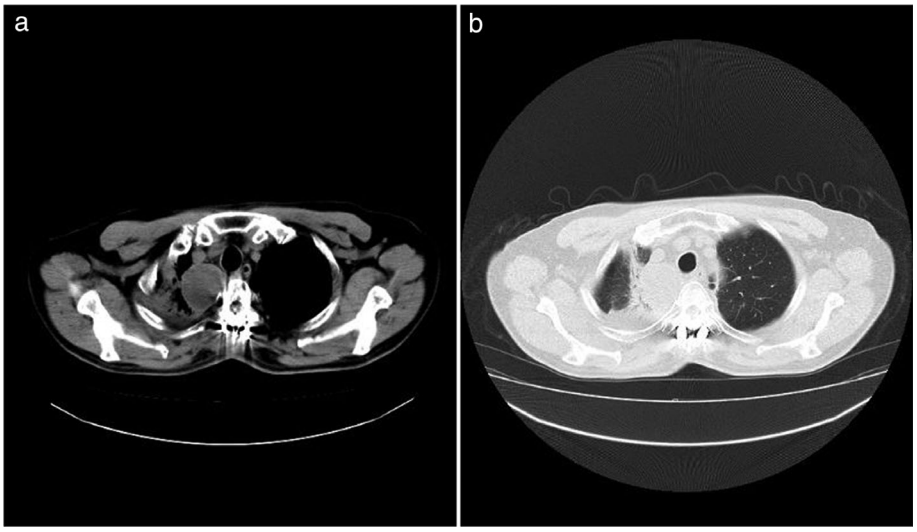

Figure 4 (**a**,**b**) At the end of durvalumab treatment, the tumor size was 46 mm × 39 mm, which was approximately 39% smaller than that at diagnosis.

these findings, PD-L1 expression is believed to be higher in PPC than in NSCLC. It has been reported that PD-L1 is frequently expressed around sarcoma components and necrotic tissues in PPC and that high PD-L1 expression is associated with a poor prognosis.[13,14] Some reports have mentioned that treatment with ICIs is effective in PPC with high PD-L1 expression.[15,16] However, in some patients, only a short-term response has been obtained, although PD-L1 expression was ≧95%.[15] Thus, a high PD-L1 expression is not necessarily a predictor of the ICI effect. According to a study by Kanazu *et al.* tumor mutation burden might be a predictor of the ICI effect, but this has not yet been applied in clinical practice.[15]

Durvalumab treatment has been approved as a consolidation therapy after chemoradiotherapy for inoperable stage III NSCLC. In many cases, radiation pneumonia develops during durvalumab treatment. In the PACIFIC study, 18.7% of cases in the durvalumab group developed grade 1–2 radiation pneumonia.[17] However, in the present case, the patient was asymptomatic and was able to continue durvalumab treatment.

In conclusion, this patient may be cured with chemoradiotherapy. However, the combination of the abscopal effect and ICIs has been previously reported,[18,19] and may have a better effect than radiotherapy alone. This case suggests a synergic effect of the combination therapy, and further accumulation of cases and formal clinical trials are expected.

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Disclosure

The authors state that they have no conflict of tnterests.

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