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Case report

Good response with durvalumab after chemoradiotherapy for epidermal growth factor receptor exon 20 insertion adenocarcinoma: A case report

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ABSTRACT

Epidermal growth factor receptor (EGFR) exon 20 insertion is not associated with sensitivity to EGFR tyrosine kinase inhibitors and chemotherapy. Here, we report the case of a 41-year-old man who presented a right lower lobe nodule and mediastinal lymph node enlargement diagnosed as EGFR exon 20 insertion adenocarcinoma with high-expression programmed cell death ligand 1 (PD-L1). He showed stable disease to chemoradiation treatment at the primary tumor site. However, durvalumab treatment has good response. Non-small cell lung cancer with EGFR exon 20 insertion and high PD-L1 expression may be treated with immunotherapy exposure.

1. Introduction

Non-small cell lung cancers (NSCLC) harboring the epidermal growth factor receptor (EGFR) exon 20 insertion mutations are generally thought to be unresponsive to EGFR tyrosine kinase inhibitor (TKI) therapy [1,2]. Chemotherapy was superior to the currently approved EGFR TKIs as treatment for EGFR exon 20 insertion mutations [3]; however, the benefit of EGFR TKIs or chemotherapy to patients with NSCLC who harbor exon 20 insertion remains unclear.

Immune checkpoint inhibitors (ICIs) are currently changing the treatment approach for patients with NSCLC. Durvalumab is a novel ICI that blocks programmed cell death ligand 1 (PD-L1) and is approved for unresectable stage III NSCLC [4]. However, current data suggest that its efficacy in EGFR-induced cancers is limited [5,6].

Here, we report a case of a patient with NSCLC with EGFR exon 20 insertion who did not respond to chemoradiation but responded well to durvalumab treatment.

2. Case

A 41-year-old man presented with an abnormal shadow on chest radiography during a regular health check-up. He has been smoking cigarettes, 1 pack/day for the last 21 years. His medical history included hypertension and diabetes. Chest computed tomography (CT) showed only the nodular shadow in the lower right lobe (Fig. 1 A–C), but CT at 6 months showed rapidly enlarging mediastinal lymph nodes (Fig. 1 D–F). He was referred to our hospital because of a suspected lung cancer. Tumor marker levels such as carcinoembryonic antigen, cytokeratin-19 fragments, and pro-gastrin-releasing peptide were not elevated. Since the diagnosis of small peripheral pulmonary nodule is difficult by transbronchial biopsy, we performed endobronchial ultrasound-guided transbronchial needle aspiration of the lymph node (Station 7). Pathologic anatomy showed lymph node adenocarcinoma involvement. Moreover, immunohistochemical staining indicated positive results for thyroid transcription factor 1 (TTF-1) and cytokeratin 7 (CK7) and negative results for CK20 (Fig. 2A–D). The tumor proportion score (TPS) of PD-L1(IHC 22C3, Dako North America) was 90%. Furthermore, molecular testing (Cobas EGFR Mutation Test ver2.0, Roche Molecular Systems Inc.) revealed an EGFR exon 20 insertion mutation. No distant metastasis was observed, and thus, he was diagnosed with clinical stage IIIC adenocarcinoma. Osimertinib or chemoradiotherapy was also considered. Since it is unclear whether EGFR TKIs is effective in managing adenocarcinoma with EGFR exon 20 insertion, a complete response to chemoradiotherapy was expected. Six courses of chemotherapy with carboplatin and paclitaxel and radiotherapy of 66 Gy were completed. He showed stable disease at the primary tumor site (Fig. 3 A–C). Durvalumab as consolidation therapy was started 2 weeks after the completion of chemoradiotherapy. Routine CT 2 months after the start of durvalumab showed a good response (Fig. 3 D–F). Radiation pneumonitis occurred 14 weeks after starting radiotherapy, but it was asymptomatic with a slight shadow. Six months after durvalumab administration for a period of 1 year, no recurrence was noted (Fig. 3G–I).

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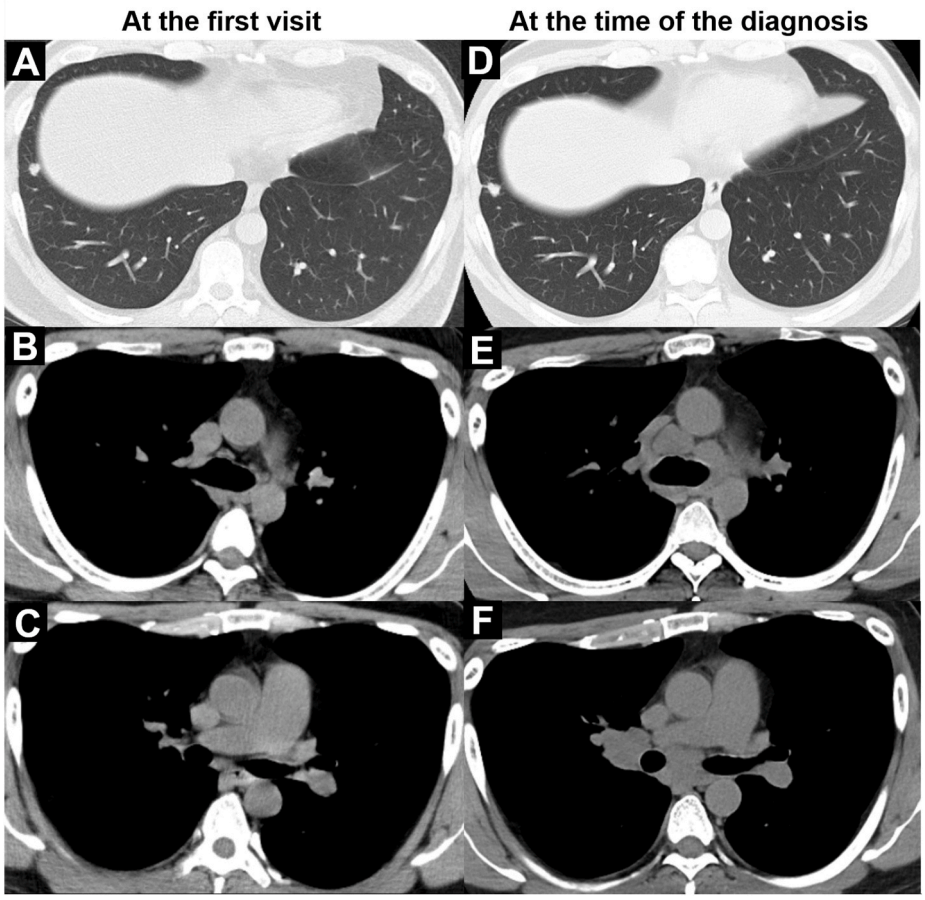

Fig. 1. Findings of the chest computed tomography imaging during the patient's course: (A, B, and C) at the first visit and (D, E, and F) at the time of diagnosis; mediastinal/hilar lymph nodes had rapidly enlarged at 6 months.

3. Discussion

Exon 20 insertion was reported to contribute to approximately 2–2.5% of all patients with NSCLC and 4–9% of all EGFR mutations [7,8]. Second-generation EGFR TKIs demonstrated durable responses in some patients with EGFR exon 20 insertions [9]. Several retrospective studies reported that EGFR TKIs are ineffective in patients with NSCLC with EGFR exon 20 insertions [1,2], which may generally be treated with upfront chemotherapy. However, in our patient with NSCLC with EGFR exon 20 insertion, the efficacy of chemoradiotherapy was limited. The benefit of EGFR TKIs or chemotherapy for patients with NSCLC who harbor EGFR exon 20 insertions remains uncertain.

Clinical evidence suggests that common EGFR mutant lung cancers rarely derive benefit from the treatment with ICIs [5,6]. PD-L1 expression is recognized as a predictor of the ICI effect, and the TPS of PD-L1 of ≥50% in NSCLC has been reported to be 23.2% [10]. PD-L1 expression was significantly higher in patients with wild-type EGFR than those with EGFR mutations [11]. Cardona et al. reported that 81.7% of patients with EGFR exon 20 insertions had TPS of PD-L1 of ≥1% expression [12]. PD-L1 expression may be associated with different types of EGFR mutation status. Therefore, patients with EGFR exon 20 insertion and high PD-L1 expression may benefit from immunotherapy exposure.

Our patient had stable disease after chemoradiotherapy. In patients with locally advanced lung cancer, the effects of chemoradiotherapy may be delayed. Tanaka et al. reported that tumor shrinkage rate after chemoradiotherapy in patients with locally advanced EGFR-positive lung adenocarcinoma is 72%, with 10% of such patients exhibiting stable disease; however, 2-year recurrence free rates are 92.3% and 71.9% in patients harboring EGFR mutations and patients with wild-type disease, respectively [13]. Even though our patient had stable disease after chemoradiotherapy, no recurrence was observed for 1 year after durvalumab treatment following chemoradiotherapy. A retrospective study reported that the efficacy of ICIs in patients harboring an uncommon EGFR mutation is significantly better than that in those harboring common EGFR mutations [14]. We speculate that in our patient with EGFR exon 20 insertion, durvalumab, rather than chemoradiotherapy, was effective.

In conclusion, this patient may not be treated with chemoradiotherapy. However, durvalumab may have a better effect than chemoradiotherapy alone.

Declaration of competing interest

The authors declare that they have no conflicts of interest.

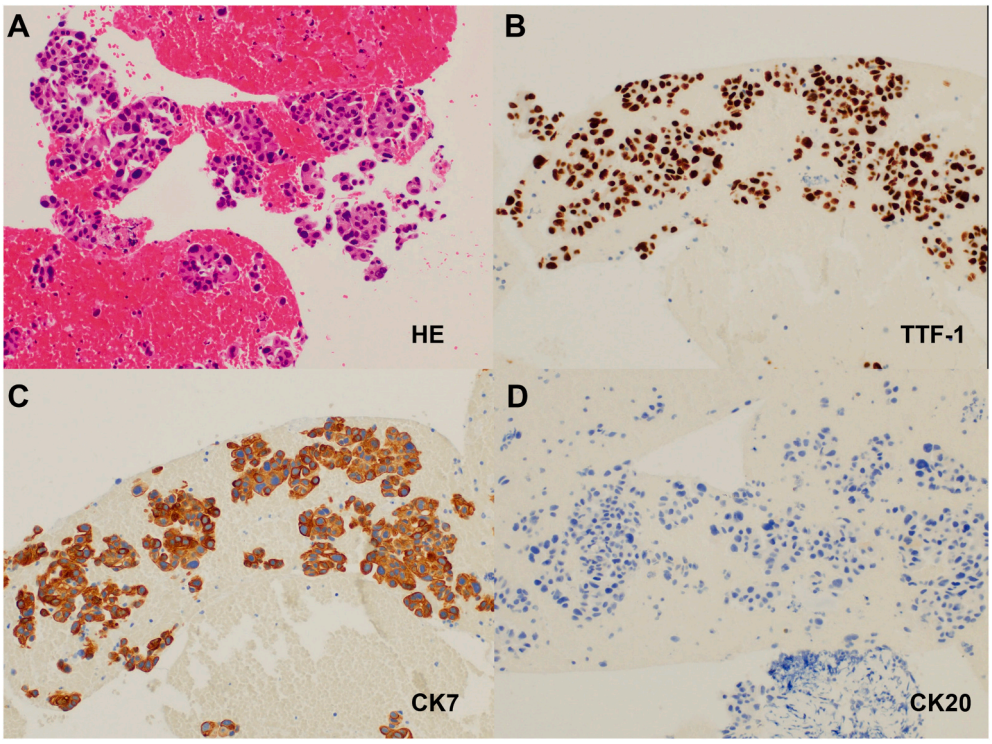

Fig. 2. Histopathological features. (A) Histological examination of ultrasound-guided biopsy specimens obtained from the mediastinal lymph nodes revealed adenocarcinoma. (HE staining). (B, C) Immunohistochemical staining of TTF-1 and CK7 was positive. (D) CK20 staining was negative. HE: hematoxylin and eosin, TTF-1: thyroid transcription factor 1, CK: cytokeratin.

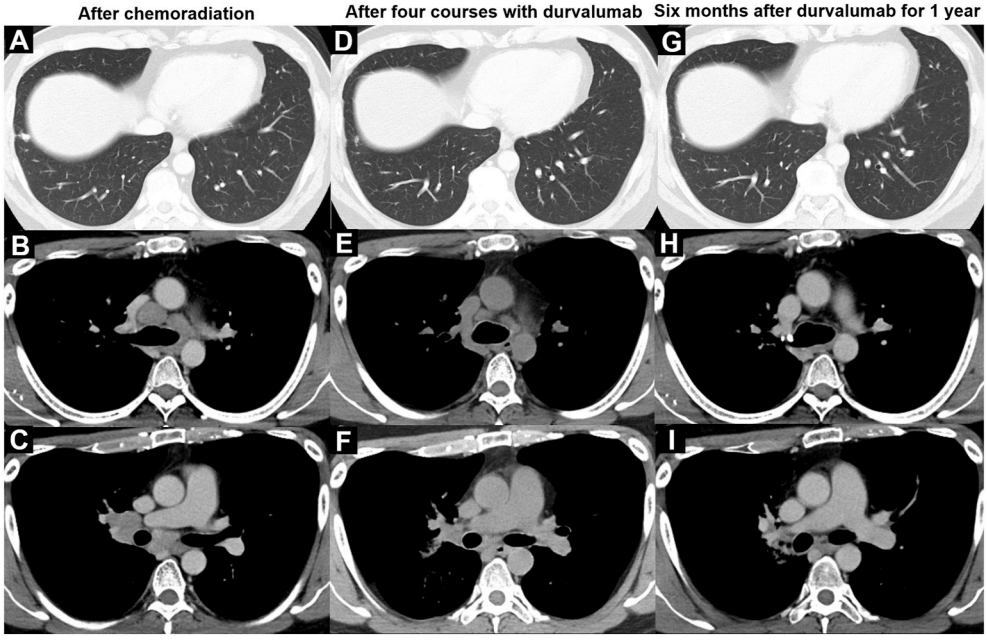

Fig. 3. Findings of the chest computed tomography imaging during the treatment course: (A, B, and C) after chemoradiotherapy, the left pulmonary lesion and mediastinal/hilar lymph nodes showed stable disease; (D, E, and F) after the fourth round of durvalumab, the left pulmonary lesion and mediastinal/hilar lymph nodes exhibited a partially good response; (G, H, and I) 6 months after durvalumab administration for 1 year, the left pulmonary lesion and mediastinal/hilar lymph nodes did not show recurrence.

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