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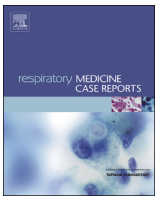

Case Report

A case of complete pathological response after comprehensive treatment in a patient with pulmonary adenocarcinoma with synchronous solitary brain metastasis

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ABSTRACT

Systemic chemotherapy is the standard treatment for non-small cell lung cancer with distant metastases. However, additional local treatment for brain and thoracic lesions is recommended for patients with synchronous solitary brain metastases (SSBM). We report the case of a 71-year-old male diagnosed with pulmonary adenocarcinoma and SSBM. Pathological examination of the brain metastasis showed positive immunostaining for programmed cell death ligand 1 expression. After four cycles of chemotherapy with immune checkpoint inhibitors, right upper lobectomy with ND2a-1 was performed. Pathological examination revealed complete pathological response, and this patient is expected to experience long-term survival.

1. Introduction

Non-small cell lung cancer (NSCLC) with distant metastases is classified as Stage IV disease [1]. Stage IV disease is considered a systemic disease that leads to poor prognosis, and the standard treatment is systemic chemotherapy. Stage IV NSCLC exhibits heterogeneity, including various forms of metastasis. In the case of limited metastatic lesions that are defined as "oligometastatic disease," additional local treatment could improve prognosis [2–4]. Therefore, NSCLC with a solitary metastasis is classified as Stage IVA (M1b) disease that is distinguished from Stage IVB (M1c) according to the current TNM classification [1]. According to the National Comprehensive Cancer Network (NCCN) guidelines, systemic chemotherapy after local treatment for brain metastasis is recommended for patients with NSCLC and synchronous solitary brain metastasis (SSBM). Surgical resection of the primary thoracic lesions is also considered after reevaluation of staging [5].

Regarding chemotherapy regimens, although immune checkpoint inhibitors (ICIs) have been widely proven effective and used in clinical settings [6], few reports have examined the effect of comprehensive treatment with ICIs on oligometastatic diseases. Therefore, herein, we report a case of pathological complete response (pCR) in a patient treated with preoperative chemotherapy, including ICIs.

Abbreviations: ICIs, immune checkpoint inhibitors; NSCLC, non-small cell lung carcinoma; pCR, pathological complete response; PD-L1, programmed cell death ligand 1; SSBM, synchronous solitary brain metastasis.

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2. Case presentation

A 71-year-old male with no relevant medical history presented with increased cognitive dysfunction and left paraplegia. The patient was a current smoker (18 cigarettes per day) and had been smoking for the past 51 years. At a previous hospital, the patient was diagnosed with pulmonary adenocarcinoma in the right upper lobe with SSBM and cT1bN0M1b Stage IVA disease. In accordance with NCCN guidelines, resection of the brain tumor and appropriate chemotherapy regimen based on the immunohistochemical examination results and genetic mutation status were planned. Surgical resection of the brain tumor in the right frontal lobe was performed by a neurosurgeon, and the patient received intensity-modulated radiotherapy of 50 Gy/25 Fr (Fig. 1).

Pathological examination of the resected brain tumor revealed that it was an adenocarcinoma, diagnosed as a metastasis of lung cancer. The samples were negative for driver gene mutations and translocations. Immunostaining revealed that 75 % of the tumor was positive for programmed cell death ligand 1 (PD-L1) (Fig. 2).

After four cycles of chemotherapy with carboplatin (AUC = 6, day 1), pemetrexed (500 mg/m^2, day 1), and atezolizumab (1200 mg/body, day 1), the thoracic lesion decreased in size on chest computed tomography (Fig. 3), and the treatment response was partial response (PR) according to the Response Evaluation Criteria in Solid Tumors (RECIST).

After local treatment for brain metastasis and systemic chemotherapy, including ICIs, the brain metastases disappeared and the surrounding edema improved (Fig. 4). And the primary thoracic lesion was well controlled and new distant metastasis was not detected. Positron emission tomography revealed that the maximum standardized uptake value of the primary thoracic lesion before chemotherapy was 4.3, decreasing to 1.2 after chemotherapy. However, the uptake value remained constant. Based on the results of reevaluation of staging, the disease was determined to be ycT1bN0M1b Stage IVA. Thus, robot-assisted right upper lobectomy was performed for local control of the pulmonary lesions. Pathological examination revealed no viable tumor cells, indicating pCR (Ef.3) (Fig. 5). The final pathological staging was ypT0N0M1b Stage IVA. The patient was discharged without complications. He is currently undergoing 13 cycles of maintenance therapy with atezolizumab (1200 mg/body, every 3 weeks), and after 1 year of treatment, no recurrence was observed.

3. Discussion

We have been treating NSCLC patients with SSBM according to the NCCN guidelines and previously reported the case of a patient with NSCLC with SSBM who achieved 5-year tumor-free survival after aggressive trimodality therapy [7]. NCCN guidelines recommend systemic chemotherapy, but the optimal chemotherapy regimen has not been strictly defined. ICIs are effective in patients with high PD-L1 expression rates [6]. In Japan, the use of PD-1/PD-L1 inhibitors is recommended for stage IV NSCLC with negative driver gene mutations/translocations and PD-L1 tumor proportion score (TPS) of 50 % or higher [8]. We selected a regimen that included ICIs based on the immunohistochemical examination results of resected brain tumors that showed a PD-L1 TPS of 75 %. After four cycles of chemotherapy with ICIs, no serious adverse events occurred, and no new metastatic lesions were detected.

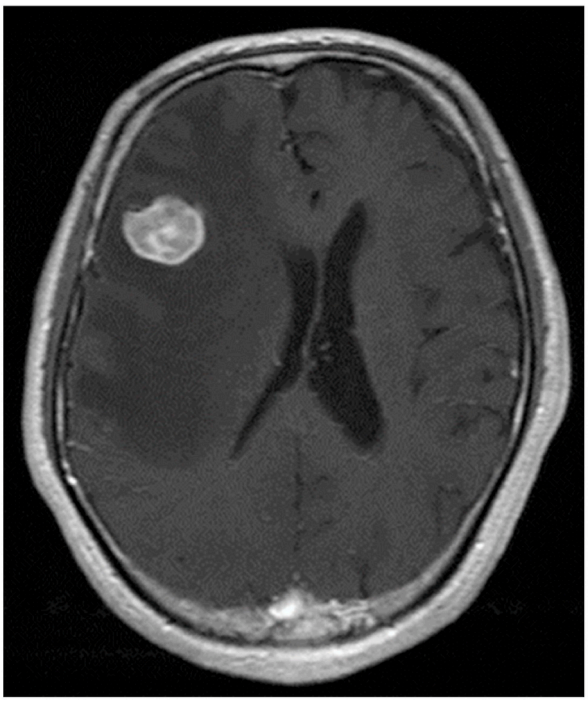

Fig. 1. Brain magnetic resonance image demonstrating a solitary 25 × 20-mm tumor with heterogeneous contrast enhancement in the right frontal lobe; edema around the tumor is shown on the T1-weighted image.

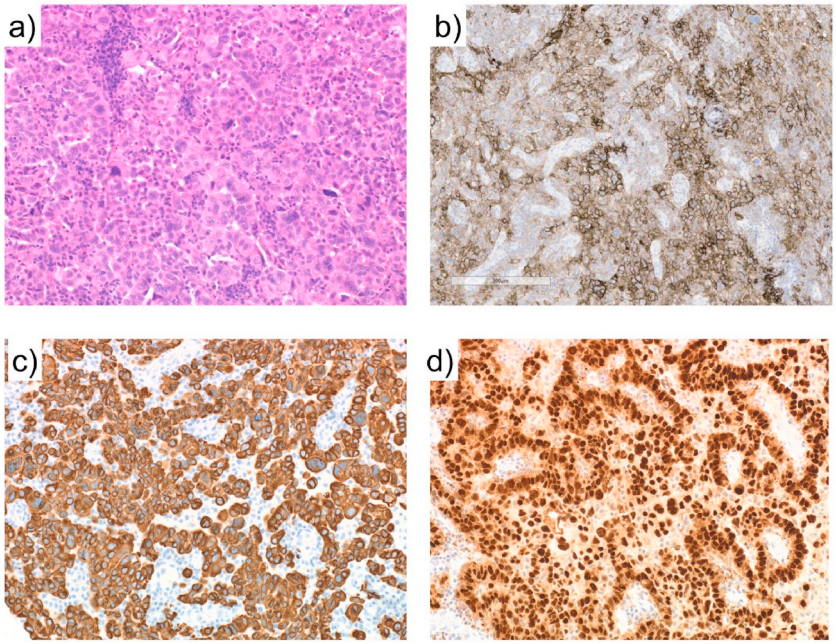

Fig. 2. Histopathological findings of the brain tumor (× 200 magnification)
a) Hematoxylin-eosin staining demonstrates atypical cells; proliferated papillary, papillary-tubularly, and multinucleated cells; and megakaryocytes with mitosis and necrosis. Immunohistochemistry results are as follows: b) PD-L1 positivity at 75 %, c) CK7 positivity at 100 %, d) TTF-1 + Napsin A positivity at 100 %. CK7, cytokeratin 7; PD-L1, programmed cell death ligand 1; TTF-1, thyroid transcription factor-1.

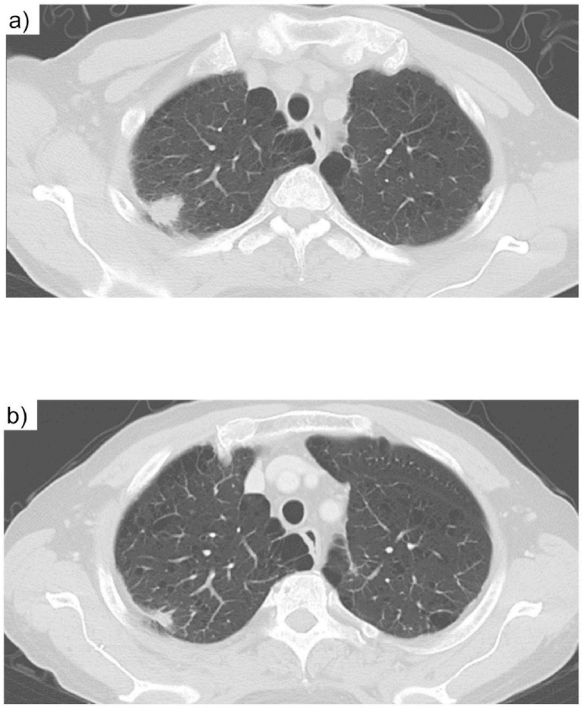

Fig. 3. Chest computed tomography (CT) scans
a) Before chemotherapy, the scan demonstrates a 15 × 13-mm lobulated nodule in the peripheral aspect of the right upper lobe (S_1). b) Chest CT scan after chemotherapy demonstrates a 11 × 6-mm nodule that decreased in size.

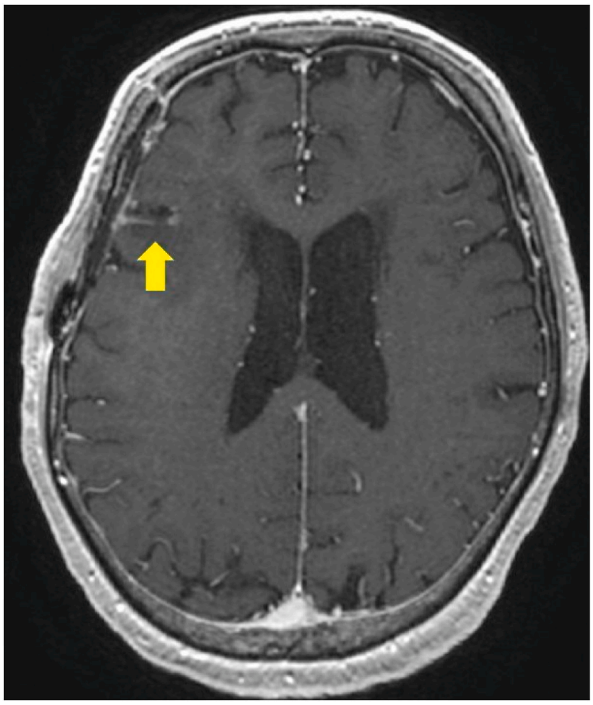

Fig. 4. Brain magnetic resonance image showed that after metastasectomy and radiotherapy, the brain metastases disappeared and the surrounding edema improved.

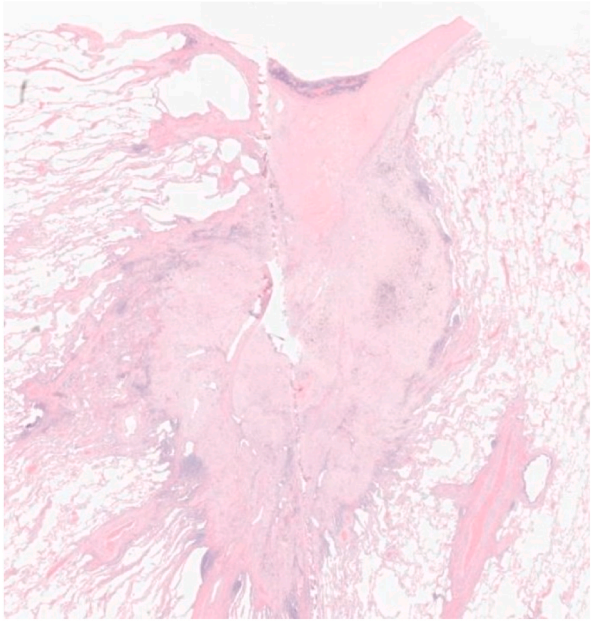

Fig. 5. Hematoxylin-Eosin staining of the primary lung tumor revealed fibrosis and hyalinization, but no viable tumor cells.

The treatment response for the primary thoracic lesion was evaluated as a PR by RECIST; however, pathological examination revealed a pCR. In previous studies, based on the pathological evaluation after preoperative treatment, pCR has been found to be a favorable prognostic factor [9]. Few studies have evaluated the effects of multidisciplinary treatment with ICIs for oligometastatic diseases. However, preoperative chemotherapy with ICIs or preoperative treatment with ICIs alone has shown good results, with high rates of pCR and major pathological remission (54 and 69 %, respectively) [10]. In this case, we selected a regimen that included ICIs based on the pathological results of the resected brain metastatic lesions. The result of preoperative treatment was pCR; hence, this patient is expected to experience long-term survival.

Oligometastatic diseases, including SSBM, are rare clinical conditions; therefore, conducting large-scale clinical trials is difficult. However, chemotherapy, including ICIs, could be effective for oligometastatic diseases, and it is hoped that more knowledge will be accumulated in the future.

4. Conclusions

Stage IV NSCLC has a poor prognosis, but our patient with NSCLC and SSBM achieved pCR with preoperative chemotherapy and ICI therapy. pCR is a considered favorable prognostic factor, and our patient is expected to experience long-term survival.

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CRediT authorship contribution statement

Tomoya Tajiri: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Keigo Sekihara:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Motohisa Shibata:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Takamitsu Hayakawa:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Akikazu Kawase:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Norihiko Shiiya:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Kazuhito Funai:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation.

Declaration of competing interest

None.

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