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CASE REPORT

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Atezolizumab in combination with carboplatin plus nab-paclitaxel for managing combined large-cell neuroendocrine carcinoma: A case report

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Abstract

Large-cell neuroendocrine carcinomas (LCNECs), categorized as high-grade neuroendocrine carcinomas, account for approximately 3% of resected lung cancers. LCNECs containing other components are called 'combined LCNECs' and have no standard treatment. A 73-year-old male with a metastatic brain tumour from a combined LCNEC of the lung containing adenocarcinoma and sarcomatoid components was referred to our department. The patient was treated with chemotherapy consisting of carboplatin and nanoparticle albumin-bound (nab)-paclitaxel in combination with atezolizumab, which was decided in accordance with the histological evaluation of the components. This treatment resulted in partial response and remained durable for 12 months with an ongoing regimen. The current case suggests that the constituents of chemoimmunotherapy should be selected in accordance with the reported efficacy of relevant regimens for each component of the combined LCNEC.

KEYWORDS
atezolizumab, chemoimmunotherapy, combined large-cell neuroendocrine carcinoma (combined LCNEC), nab-paclitaxel, pleomorphic carcinoma

INTRODUCTION

Large-cell neuroendocrine carcinomas (LCNECs), categorized as high-grade neuroendocrine carcinomas, account for approximately 3% of resected lung cancers.[1] LCNECs, which contain other components such as adenocarcinoma, squamous cell carcinoma and pleomorphic carcinoma, are called 'combined LCNECs'. Currently, there is no standard treatment for advanced combined LCNECs.

This study reports the case of a patient with combined LCNEC whose symptoms were due to brain metastasis. Because the histological findings of the resected brain tumour and transbronchial biopsy specimen suggested combined LCNEC with a mixture of adenocarcinoma and sarcomatoid components, atezolizumab in combination with carboplatin and nanoparticle albumin-bound (nab)-paclitaxel was selected as the first-line treatment regimen. This treatment resulted in partial response and remained durable for 12 months with an ongoing regimen.

CASE REPORT

A 73-year-old man was referred to the Department of Neurosurgery with a complaint of a visual field defect. He was a past smoker with 94 pack-years of smoking and no apparent exposure to asbestos. Brain magnetic resonance imaging with contrast enhancement (CE) showed a brain tumour in the left occipital lobe (Figure 1A), and chest computed tomography (CT) revealed lung cancer in the right middle lobe accompanied by necrotic lesions, atelectasis (Figures 1B and 2B) and mediastinal lymph node metastases (Figure 2A). The brain tumour was surgically resected, and histological evaluation confirmed the diagnosis of a metastatic brain tumour that originated from lung cancer.

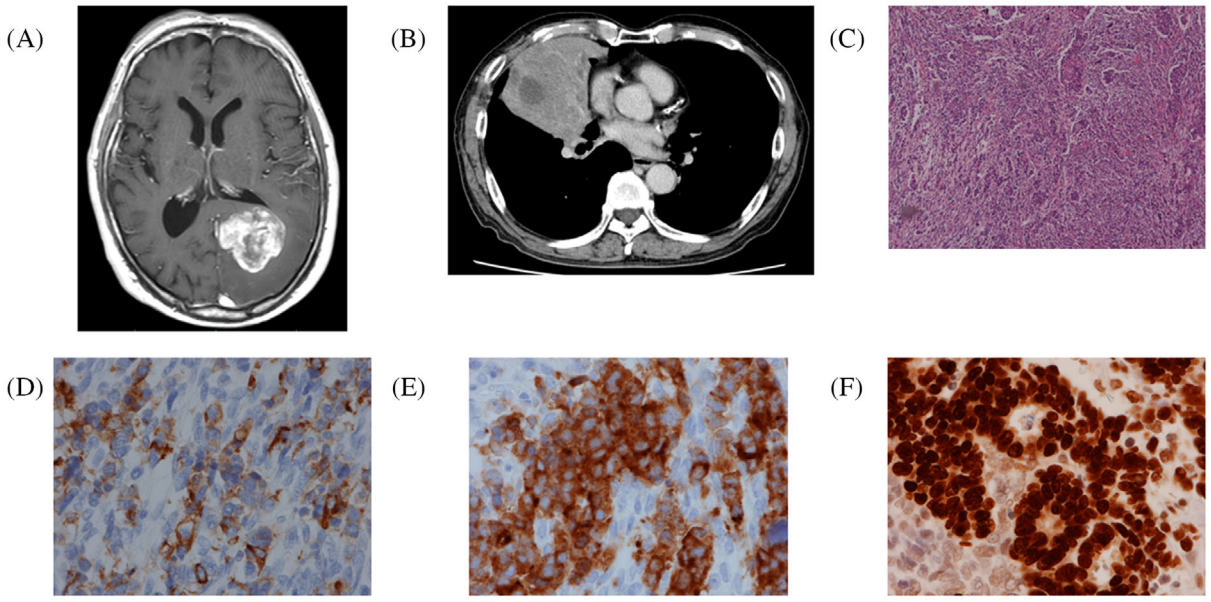

FIGURE 1 Brain magnetic resonance imaging with contrast enhancement (CE) showing a brain tumour with ring enhancement in the left occipital lobe (A). Chest computed tomography (CE) revealing a mass in the right middle lobe with necrotic lesion and partial atelectasis (B). Haematoxylin–eosin staining of the brain tumour showing rosette-like structures suggesting a neuroendocrine feature, which is accompanied by adenocarcinoma and pleomorphic carcinoma including spindle and giant cells (C). Immunohistochemistry is positive for chromogranin A (D), synaptophysin (E) and thyroid transcription factor-1 (F).

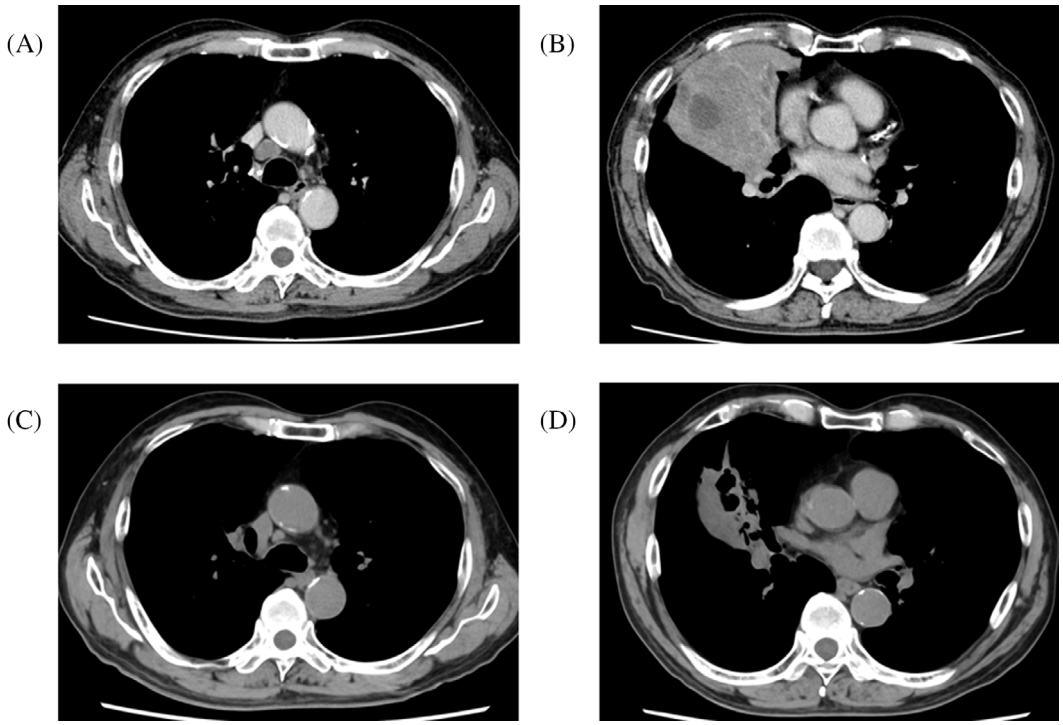

FIGURE 2 Chest computed tomography images with contrast enhancement of the primary tumour in the right middle lobe (B) and mediastinal lymph node metastasis to #4R (A) are shown. Both lesions appear reduced in size after two cycles of chemoimmunotherapy (C, mediastinal lymph node; D, primary tumour)

Haematoxylin–eosin (H–E) staining of the brain tumour revealed neuroendocrine features accompanied by a mixture of adenocarcinoma and spindle and giant cells, suggesting a sarcomatoid component (Figure 1C). Immunohistochemistry was positive for CD56, chromogranin A (Figure 1D), synaptophysin (Figure 1E) and thyroid transcription

factor-1 (Figure 1F). Therefore, he was referred to our department, and transbronchial biopsy was subsequently performed. H–E staining of the lung specimen showed rosette-like structures similar to those of the resected brain tumour. Chest and abdominal CT (CE) and positron emission tomography/CT demonstrated no distant metastases. Therefore, the final diagnosis was combined LCNEC with a mixture of adenocarcinoma and pleomorphic carcinoma that originated from the lung and metastasized to the brain (cT3N2M1b [BRA], stage IVA). The programmed cell death-ligand 1 expression in the tumour cells was 1%–10% and no oncogenic driver was detected by next-generation sequencing (Oncomine Dx Target Test Multi-CDx system, Life Technologies Corporation Japan).

Although the neuroendocrine component was dominant in the histological evaluation, chemoimmunotherapy consisting of carboplatin and nab-paclitaxel in combination with atezolizumab was selected because the histology included various components of LCNEC, adenocarcinoma and pleomorphic carcinoma. Chemoimmunotherapy resulted in a partial response with shrinkage of the primary tumour (41% in longer diameter; Figure 2D) and mediastinal lymph nodes (32% in shorter diameter [non-measurable lesion]; Figure 2C), accompanied by an improvement in atelectasis after two cycles of induction therapy. After four cycles of induction chemoimmunotherapy, atezolizumab maintenance therapy was administered for 11 cycles, and the response remained durable for 12 months with an ongoing regimen. The brain metastasis, which was fully resected, also remained recurrence-free.

DISCUSSION

LCNECs are defined as high-grade neuroendocrine carcinomas accounting for 2.1%–3.5% of resected lung cancers, accompanied by lymph node metastases in 60%–80% and distant metastases in 40% of cases.[1] LCNECs used to be treated with platinum plus etoposide similar to that in the standard small-cell lung cancer (SCLC) regimen. On the other hand, platinum plus paclitaxel showed a good response rate as high as 78%.[2] Taxane-based platinum-doublet chemotherapy has also shown outcomes similar to those of the SCLC regimen.[3] Although the usefulness of immune checkpoint inhibitors (ICIs) in LCNECs has not been confirmed, chemoimmunotherapy has been shown to improve overall survival.[4] Therefore, chemoimmunotherapy with taxanes could be a promising option for LCNECs.

Approximately 10% of LCNECs contain other components and are called combined LCNECs.[1] As there is no standard treatment for combined LCNECs, the chemotherapy regimen should be decided considering each specific component.

In the current case, histological evaluation demonstrated a variety of components, including LCNEC, adenocarcinoma and pleomorphic carcinoma with spindle and giant cells. Although pemetrexed is effective in managing adenocarcinoma, pemetrexed plus carboplatin has reportedly shown unfavourable outcomes in the treatment of LCNECs.[3] However, the usefulness of both taxanes[3] and ICI[4] for pleomorphic carcinomas has been reported. In addition, the following three regimens are also effective for adenocarcinoma: nab-paclitaxel in combination with carboplatin; chemoimmunotherapy including atezolizumab in combination with carboplatin plus nab-paclitaxel[5]; and atezolizumab in combination with bevacizumab, carboplatin and solvent-based paclitaxel. In the current case, a bevacizumab-containing regimen was avoided because of the presence of necrotic lesions in the main tumour (Figure 1B). Thus, atezolizumab in combination with carboplatin and nab-paclitaxel was adopted, resulting in a partial but durable response. The current case suggests that the constituents of chemoimmunotherapy should be selected in accordance with the reported efficacy of the relevant regimens for each component of combined LCNEC.

To our knowledge, this is the first report of combined LCNEC that was successfully treated with chemoimmunotherapy. The regimen was decided in full consideration of the histological evaluation, in which a variety of components were detected.

AUTHOR CONTRIBUTION

Rei Tsutsumi designed the work and wrote the manuscript. Nobutaka Kataoka and Takayuki Nakano were the treating physicians. Nobutaka Kataoka, Yusuke Kunimatsu and Mai Tanimura collected the data. Izumi Sato and Keiko Tanimura took the initiative in the analysis and interpretation of the clinical course. All authors participated in the discussion. Takayuki Takeda supervised the entire work and revised the final manuscript.

CONFLICT OF INTEREST

None declared.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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