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CASE REPORT

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Improving visual acuity with nivolumab plus ipilimumab plus two cycles of chemotherapy following a diagnosis of lung adenocarcinoma with choroidal metastasis: A case report and literature review

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Abstract

A 75-year-old woman presented at our hospital with bilateral visual impairment. Ophthalmological examination revealed multiple choroidal tumours. Chest computed tomography revealed a tumour shadow in the right lower lobe and multiple lymph node metastases in the mediastinum and pulmonary hilum. Following a detailed examination, the patient was diagnosed with primary lung adenocarcinoma (cT1cN3M1c Stage IVB) with choroid metastases. The tumour proportion score of programmed death ligand 1 (PD-L1) was 1% and EGFR exon 20 insertion mutations were also detected. The patient was administered combination chemotherapy with nivolumab and ipilimumab. Primary lung and metastatic tumours, including the choroid, were reduced, and visual disturbances improved completely. Herein, we describe a rare case in which a combination of chemotherapy with nivolumab and ipilimumab significantly reduced vision loss due to choroidal metastasis.

KEYWORDS
choroidal metastasis, ipilimumab, nivolumab, non-small cell lung cancer, vision loss

INTRODUCTION

Choroidal metastasis is most commonly observed in primary breast and lung cancer.[1] Reports on the successful treatment of choroidal metastases from lung cancer are limited to molecular-targeted agents. In this report, a lung cancer patient with choroidal metastasis was treated with nivolumab plus ipilimumab combined with two cycles of platinum-based chemotherapy, resulting in a reduction of the primary tumour and choroidal metastases, and improvement of visual acuity and quality of life (QOL).

CASE REPORT

A 75-year-old woman was referred to our hospital because of a loss of visual acuity in both eyes. Her best corrected visual acuity (BCVA) was 20/25 on the right and light perception on the left. The bilateral fundus showed no vitreous opacity but showed multiple elevated choroidal lesions and serous retinal detachment. Three-dimensional fundus imaging revealed an elevated retinal pigment epithelium and subretinal fluid in the right fundus (Figure 1A). Funduscopic fluorescence revealed numerous dots of hyperfluorescence in the same area (Figure 1B). Consequently, metastatic

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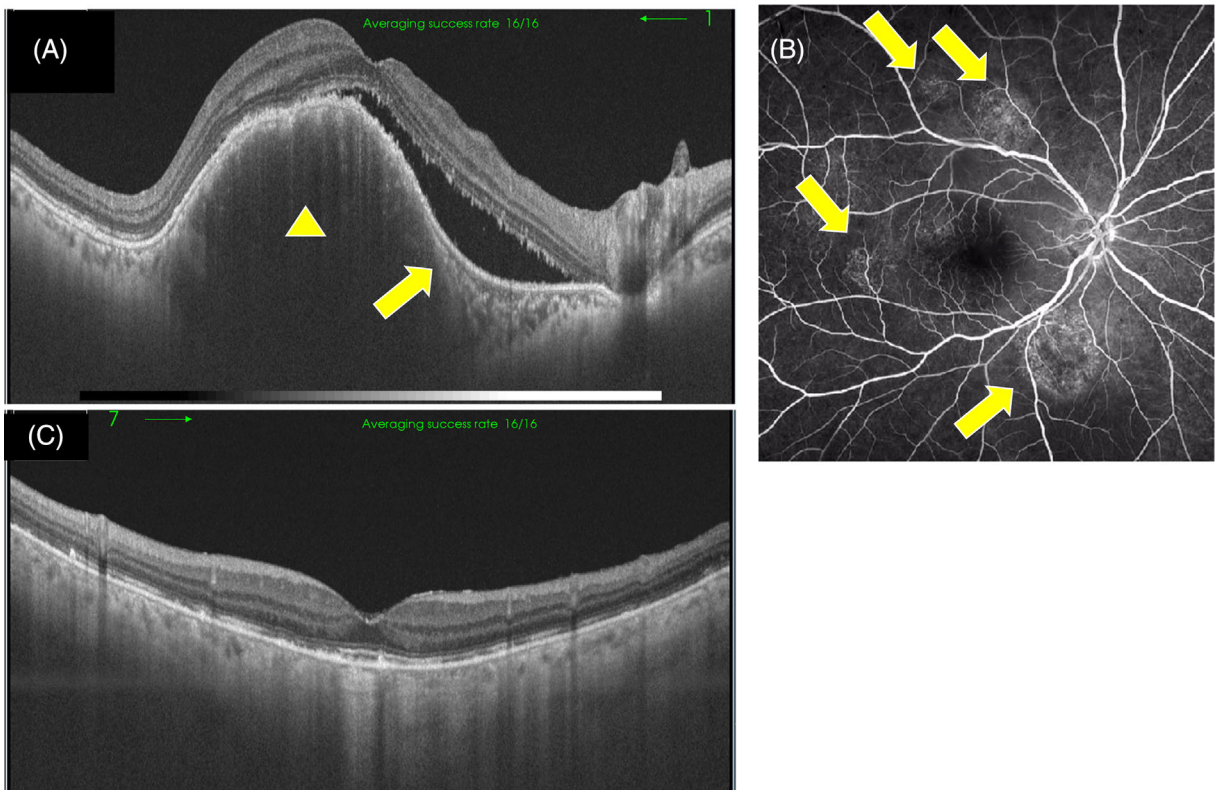

FIGURE 1 Optical coherence tomography reveals retinal pigment epithelium elevation (arrowhead) and retinal detachment (arrow) in the right eye at (A) admission and at (C) 9 months after treatment. (B) Fluorescence angiography on admission reveals granular hyperfluorescence in the early phase (arrow).

choroidal tumours were suspected. Chest computed tomography revealed nodular lesions in the right lower lobe, multiple small nodules in both lung fields, and multiple lymph node metastases in the mediastinum and hilar regions (Figure 2A). Magnetic resonance imaging showed no abnormalities in the head, eyes, or optic nerves. A bronchoscopic biopsy revealed an adenocarcinoma of the right lower lung. Based on the imaging and pathological findings, she was diagnosed with cT1cN3M1c stage IVB lung adenocarcinoma. Programmed cell death ligand-1 (PD-L1) testing showed low expression, with a tumour proportion score (TPS) of 1%. Next-generation sequencing revealed EGFR exon 20 insertion mutations (p.S768_D770dup).

The patient was treated with carboplatin (area under curve 5 every 3 weeks for two cycles), pemetrexed (500 mg/m^2 every 3 weeks for two cycles), nivolumab (360 mg every 3 weeks), and ipilimumab (1 mg/kg every 6 weeks), based on the CheckMate 9LA regimen.[2] This treatment resulted in a reduction in the primary tumour and lymph node metastasis (Figure 2B). Moreover, the choroidal tumours and retinal detachment improved markedly on fundus examination (Figure 1C), and the ocular symptoms gradually improved. Eighteen months after starting therapy, her BCVA improved to 20/20 on the right and 20/40 on the left, and she could continue treatment without relapse (Figure 2C).

DISCUSSION

Although intraocular metastases of lung cancer are rare, choroidal metastases are relatively common among intraocular metastases. A systematic review reported that 82% of the patients with intraocular metastases from lung cancer had choroidal metastases.[3] The symptoms of choroidal metastases include decreased vision, ocular pain, photopsia, floaters, and visual field defects. In the previous study of 17 cases of primary lung cancer with choroidal metastasis, 16 cases have been shown to have ocular symptoms as the initial manifestation. In our case, vision loss was the initial symptom and lung cancer was later identified.[4] However, when ocular symptoms are observed, choroidal metastases, in addition to metastatic brain tumours and cancerous meningiomas, should also be considered in the differential diagnosis by examining aggressive ophthalmologic evaluations.

The treatment for choroidal metastases includes systemic chemotherapy, radiation therapy, photocoagulation, and enucleation.[5] The standard treatment is palliative radiation therapy, and the rates of complete remission and visual acuity improvement are reported to be 80% and 57%–89%, respectively.[6] However, there are concerns regarding the late effects of radiation therapy, such as cataracts and glaucoma. In a phase III CheckMate 9LA trial comparing nivolumab

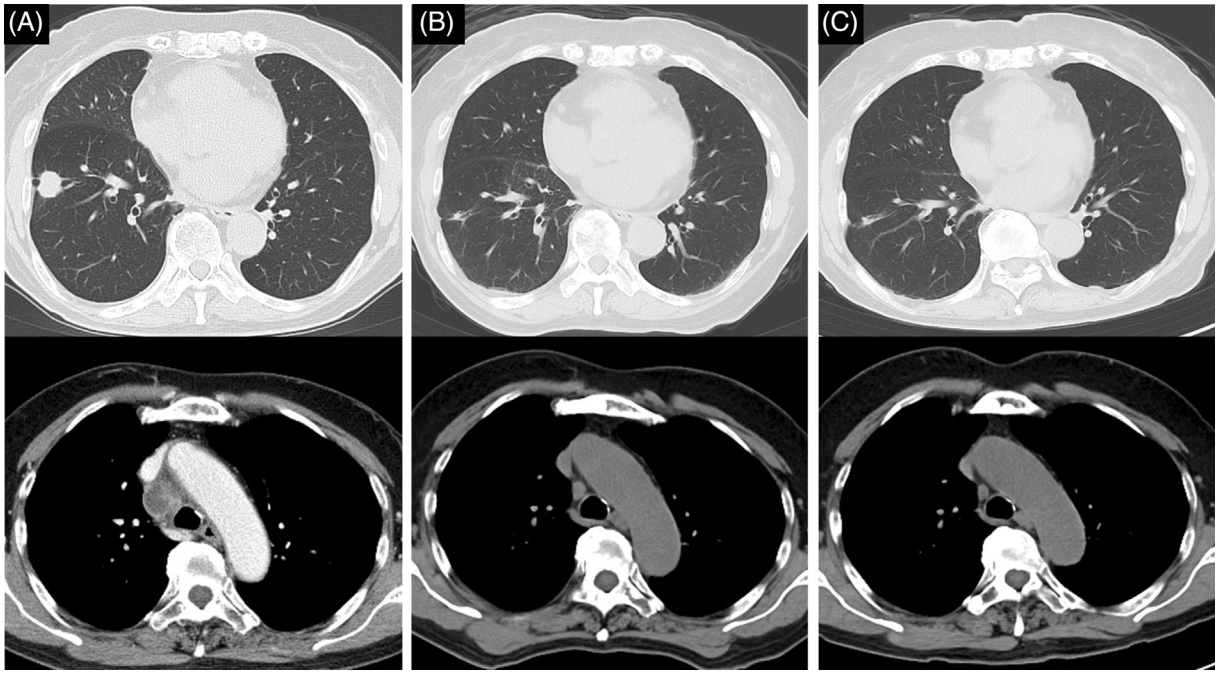

FIGURE 2 Chest computed tomography findings showing a tumour in the right lower lobe and enlarged lymph nodes in the mediastinum at (A) admission and (B) nine and (C) 18 months after treatment.

plus ipilimumab with two cycles of chemotherapy versus chemotherapy alone in patients with stage IV non-small cell lung cancer (performance status (PS) 0–1) without EGFR mutations or ALK translocations, overall survival (OS) and progression-free survival (PFS) were significantly longer in the nivolumab plus ipilimumab group than in those receiving chemotherapy. Furthermore, in the subgroup analysis of PD-L1 expression, OS was prolonged in the intervention group regardless of TPS.[2] Thus, nivolumab plus ipilimumab plus two cycles of chemotherapy is recommended for patients with stage IV non-small cell lung cancer (driver mutation/translocation negative) with a PD-L1 TPS <50% or unknown. Our patient was in good general condition despite being elderly, and her lung adenocarcinoma had no treatable driver genes and had low PD-L1 expression. Therefore, nivolumab, ipilimumab, carboplatin, and pemetrexed were selected for treatment.

In a systematic review of lung cancer patients with choroidal metastases, the median OS was not reached in patients treated with molecular-targeted agents, and good effects, including stable or improved visual function, were reported.[3] Nevertheless, non-small cell lung cancers with EGFR exon 20 insertion mutations have been indicated to be poorly responsive to EGFR-targeted agents.[7,8] On the other hand, as for immune checkpoint inhibitors, a case of lung cancer with choroidal metastases treated with pembrolizumab plus chemotherapy has been reported.[9] However, the case treated with nivolumab plus ipilimumab plus two cycles of chemotherapy has not been reported. The combination of systemic chemotherapy with immune checkpoint inhibitors might be an option for lung cancer patients with choroidal metastasis who have no treatable driver genes including EGFR exon 20 insertion mutations, because it is expected to not only prolong OS but also improve ocular symptoms caused by choroidal metastasis. The patient's clinical course was excellent, and visual function significantly improved, in addition to reducing the primary tumour and choroidal metastases.

In conclusion, we encountered a case of lung cancer with choroidal metastasis that achieved shrinkage of both primary and choroidal metastatic lesions, resulting in improved visual acuity and QOL, by combination therapy with nivolumab, ipilimumab, carboplatin, and pemetrexed. Currently, the evidence for immune checkpoint inhibitors for metastatic lesions, including choroidal metastases, is insufficient, and further accumulation of cases is required.

AUTHOR CONTRIBUTIONS

Takahiro Matsuyama, Masashi Oniwa, Kentaro Tsuruzono, and Shunsuke Yasuda conceived and wrote the article. Takayuki Suetsugu, Keiko Mizuno, and Hiromasa Inoue reviewed and supervised the manuscript. Takahiro Matsuyama, Masashi Oniwa, Kentaro Tsuruzono, Mikiko Yone, Yuya Tomioka, Akifumi Uchida, Hideo Mitsuyama, Shingo Kubota and Takayuki Suetsugu were attending physicians, involved in data collection. All the authors have read and approved the final version of manuscript.

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CONFLICT OF INTEREST STATEMENT

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DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no data were generated or analyzed in this study.

ETHICS STATEMENT

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

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