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Case report

A case of impaired consciousness due to large cystic metastatic brain tumors from lung adenocarcinoma successfully controlled with Ommaya reservoir placement

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ABSTRACT

Large cystic brain metastases from lung cancer are rare but cause substantial central nervous system symptoms that often deprive patients of opportunities to receive anticancer therapy. There are no standard therapeutic strategies against this relentless condition. Here we report a patient with large cystic brain metastases from lung adenocarcinoma successfully controlled with Ommaya reservoir placement and subsequent gamma knife surgery (GKS). A 62-year-old Japanese man presented with left upper extremity paresis. Magnetic resonance imaging revealed large cystic masses in both cerebral hemispheres and multiple brain nodules. Computed tomography of the chest showed irregular nodular shadows in the lower lobe of the right lung with multiple swollen lymph nodes. His performance status (PS) and level of consciousness worsened rapidly. Thus, at that time, we could not perform bronchoscopy with the goal of establishing a pathological diagnosis. Intracystic placement of an Ommaya reservoir followed by GKS dramatically improved his PS and level of consciousness. We were subsequently able to perform bronchoscopy, which resulted in a diagnosis of lung adenocarcinoma with 100% positivity of programmed cell death-1 ligand-1 expression. The patient was started on a 3-week cycle of pembrolizumab. Substantial reduction in tumor size was observed after one course of pembrolizumab treatment. The patient had a partial remission. He has been still receiving pembrolizumab with long-term efficacy. In conclusion, our report suggests that aggressive Ommaya reservoir placement should be considered for large cystic metastatic brain tumors, even in patients with undiagnosed cancer, poor PS, and impaired consciousness.

1. Introduction

Large cystic brain metastases from cancers including lung cancer are extremely rare, but they cause sudden deterioration of performance status (PS) and impaired consciousness because of their rapid growth [1]. Acute deterioration of systemic condition deprives patients with lung cancer of opportunities for pathological diagnosis and subsequent treatment. There are no widely accepted standard therapies for this unrelenting pathology.

The Ommaya reservoir is an intraventricular catheter system designed to aspirate cerebrospinal fluid from cerebral ventricles or cystic lesions in the brain or administer drugs into these lesions [2,3]. This device is composed of two parts: a silicon-based capsule placed under the scalp and a catheter whose tip is positioned in the cerebral ventricle or cystic lesion. Here we describe a patient with an initially undiagnosed large cystic metastasis in the brain that was successfully controlled with intracystic placement of an Ommaya reservoir followed by gamma knife surgery (GKS).

2. Case report

A previously healthy 62-year-old Japanese man with a 10-day history of paresis of the left extremity visited a primary care physician. He was a former smoker and a social drinker. He did not take any medications or dietary supplements routinely. He consulted a neurosurgeon for evaluation of the paresis. Brain magnetic resonance imaging (MRI)

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revealed large cystic masses in both motor areas and multiple brain nodules in both hemispheres (Fig. 1A). Chest computed tomography (CT) showed a 28-mm irregular nodule in the right lower lobe as well as right hilar and mediastinal lymphadenopathy (Fig. 2A and B). He was referred to our hospital with acute onset of impaired consciousness that developed 2 days before hospitalization.

Physical examination at the time of hospitalization showed that his body temperature was 37.1 °C, blood pressure was 107/67 mmHg, pulse was 78 beats per minute, oxygen saturation was 95% while breathing ambient air, and respiratory rate was 20 breaths per minute. His Glasgow Coma Scale (GCS) score was 11 (3 for eye, 3 for verbal, 5 for motor). Breath sounds were clear. Manual muscle testing showed 4/5 strength in the upper and lower extremities. His Eastern Cooperative Oncology Group PS was 4. Serum carcinoembryonic antigen levels were high (16.1 ng/ml). Together with the imaging findings of the lungs and brain, we suspected advanced lung cancer with multiple brain metastases as possibly the main cause of his impaired consciousness.

Due to his severely impaired consciousness, we could not perform bronchoscopy for pathological diagnosis of lung cancer. At the time, we decided to provide best supportive care. To relieve brain edema associated with large cystic metastases, we started intravenous dexamethasone (13.2 mg/day) and 20% mannitol (600 ml/day). His level of consciousness improved gradually; his GCS score improved from 11 to 13 on day 8. However, he could not walk by himself. He was transferred to a neurosurgery hospital on day 9 to undergo radiosurgery for the brain metastases.

To reduce the radiation area, an Ommaya reservoir was placed stereotactically in both large cystic lesions in both motor areas. As a result, the cystic lesions decreased in size from 25 mm to 7.3 mm on the right side, and from 35 mm to 20 mm on the left side (Fig. 1B). GKS was performed subsequently for 15 metastatic lesions in bilateral cerebral hemispheres and the right midbrain. The margin dose to the tumor was 13–20 Gy (mean 16.5 Gy), and maximum dose was 26–40 Gy (mean 33 Gy). He was transferred to our hospital again on day 26. At that time, his GCS score was 14 (4 for eye, 5 for verbal, and 5 for motor). His PS score improved from 4 to 1, and he was able to perform activities of daily living by himself.

We performed bronchoscopy with sufficient sedation (fentanyl 0.04 mg and midazolam 4 mg) to avoid elevation of intracranial pressure. Histopathological findings of specimens obtained via endobronchial ultrasound-guided transbronchial needle aspiration from right hilar lymph nodes (11s and 11i) revealed adenocarcinoma of the lung with thyroid transcription factor-1 positivity and mucin production. The tumor cells were negative for *EGFR* mutations and *ALK* and *ROS1* gene rearrangements. Immunohistochemistry results showed that the programmed cell death-1 ligand-1 tumor proportion score of the tissue sample was 100%. We started intravenous pembrolizumab (200 mg/day every 3 weeks). After one course of pembrolizumab treatment, the lung nodule in the right lower lobe and multiple hilar and mediastinal lymph nodes were all decreased in size (Fig. 2C and D). He was discharged from our hospital on day 79. At present, he is asymptomatic and undergoing pembrolizumab treatment with continued partial response for 17 months and 21 courses.

3. Discussion

An Ommaya reservoir is a polyfunctional device with a capsule placed under the scalp and the catheter tip positioned in the ventricle or an intracranial cystic lesion. The capsule is punctured with a needle, allowing for repeated drainage of the cerebrospinal fluid or contents of the cystic lesion. In addition, intraventricular administration of drugs such as amphotericin B or methotrexate can be conducted through this device to treat fungal meningitis or meningioma [1,2]. In this report, we presented a case of large cystic brain metastases from lung adenocarcinoma successfully controlled with Ommaya reservoir placement. During the first admission, our management strategy for this patient was best supportive care because of poor PS and impaired level of consciousness. However, Ommaya reservoir placement and subsequent GKS dramatically improved the patient's clinical status, which led to achievement of pathological diagnosis, implementation of the treatment, and prolongation of survival. Our report suggests that even in patients with undiagnosed cancer, poor PS, and impaired consciousness, aggressive Ommaya reservoir placement for large cystic metastatic brain tumors should be considered.

Cystic metastatic brain tumors is a rare condition; patients with cystic metastatic brain tumors account for 1.7–4.8% of all patients with metastatic brain tumors [4–6]. The most common primary site of cystic metastatic brain tumors is breast followed by lung [3,6]. Yamanaka and

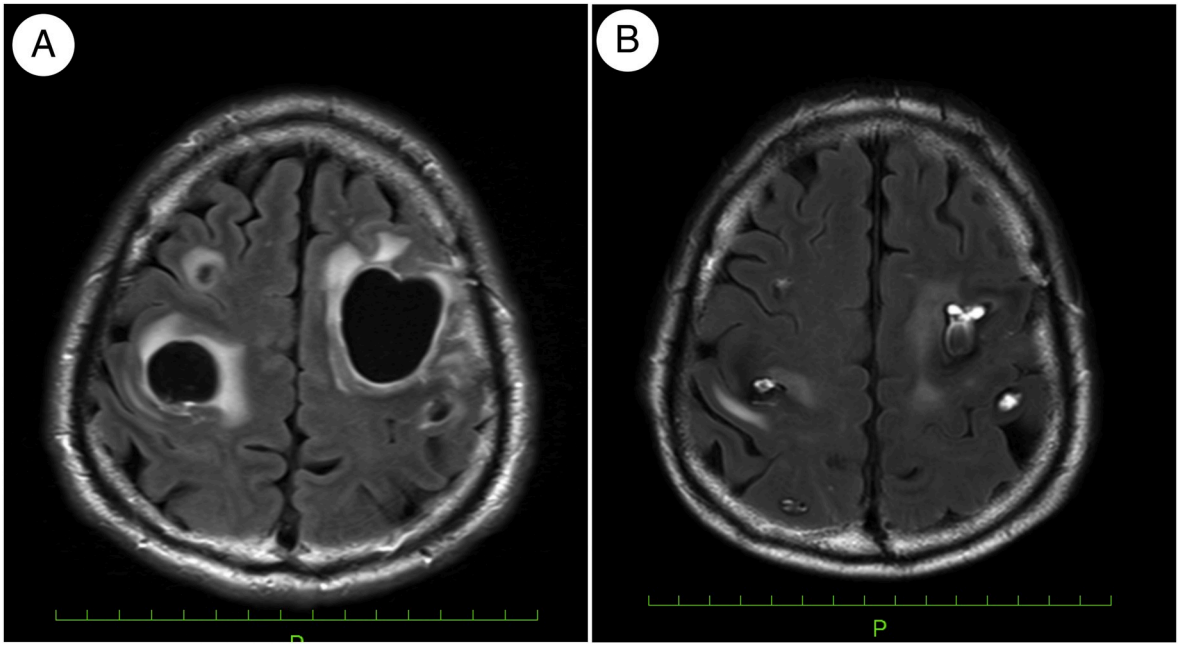

Fig. 1. Brain MRI images on admission (A) and after the placement of Ommaya reservoirs (B). A: FLAIR imaging shows large cystic brain tumors and multiple small cystic nodules. B: After Ommaya reservoir placement, the giant cysts on both sides decreased in size.

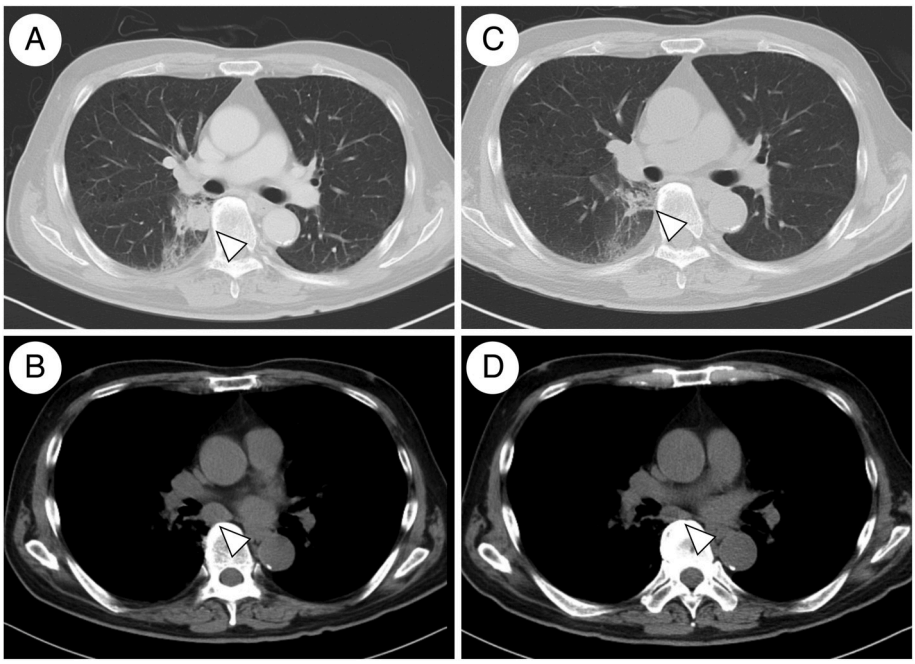

Fig. 2. Chest CT images on admission (A, B) and 15 days after one course of pembrolizumab (C, D). A, B: Chest CT on admission shows an irregular lung nodule in the right lower lobe and lymphadenopathy in the mediastinum (arrowheads). C, D: After one course of pembrolizumab, the lung nodule and mediastinal lymph nodes decreased in size.

colleagues [6] reported that 3.5% (11/317) of GKS-treated breast cancer cases involved cystic lesions, whereas only 0.6% (7/1099) of GKS-treated lung cancer cases involved cystic lesions. Therefore, the number of reported lung cancer cases in which an Ommaya-Reservoir was used for cystic metastatic brain tumors is quite limited; to date, there have been 10 cases, including the present case [6–8]. The pathogenesis of cyst formation in brain metastases remains unknown. Our patient had adenocarcinoma histology with mucus production. Taking into consideration that the most common primary sites of cystic brain metastases are breast cancer and lung cancer, excess mucus production from adenocarcinoma cells may contribute to cyst formation in brain metastases.

Cystic brain tumors are usually large in size and volume; the mean maximum diameter and tumor volume are 40.1 mm and 20.3 cm^3, respectively [5,6]. They are resistant to radiation treatment. In particular, larger than 3 cm is more likely to be associated with radiation necrosis and other critical adverse events [9]. An Ommaya reservoir can be used to decrease the size of cystic brain tumors, thereby enhancing the therapeutic response to stereotactic radiation therapy and improving quality of life via prompt normalization of intracranial pressure [10]. Drainage of a fluid collection by an indwelling Ommaya reservoir achieves a 20% reduction in tumor diameter and a 50% shrinkage in tumor volume [5,6]. In this case, Ommaya reservoir placement resulted in 70% reduction of tumor diameter. Invasive intracranial interventions in patients with poor PS are usually avoided. Ommaya reservoir placement is a short procedure that takes usually less than 1 hour and is performed under local anesthesia. Large cyst-forming metastatic brain tumors usually occur in subcortical areas near the cerebral cortex, making it possible to place an Ommaya reservoir relatively safely [6]. One factor that determines the success or failure of drainage is the viscosity of the fluid. T1-weighted imaging showing hyperintensity suggests intracystic hemorrhage or fluid with high protein concentration, often making effective drainage impossible. In this case, brain MRI demonstrated that the intracystic lesion had low intensity on T1-weighted imaging, so effective fluid drainage was possible.

Due to the large cystic brain metastases, this case was associated with a high risk of critical of bronchoscopy-related complications related to the central nervous system such as cerebral hernia and cerebral hemorrhage. Kerwin and colleagues reported that 81% of patients with brain injury suffer from rapid and transient increases in intracranial pressure at the time of bronchoscopy [11]. They also showed that cerebral pressure rises more than 3 times during endoscopic examinations [11]. Therefore, it is extremely important to control intracranial pressure before and during bronchoscopy, especially in patients with large cystic metastatic brain tumors. In this case, we confirmed that there was considerable shrinkage of the cystic tumor and decreased cerebral edema on brain MRI before bronchoscopy. During bronchoscopy, we used a sufficient dose of sedative drugs and maintained tight control of blood pressure that prevented intracranial pressure elevation. Previous reports of large cystic metastatic brain tumors from lung cancer were all cases in which an Ommaya reservoir was placed after the diagnosis of lung cancer [6–8]. This is the first case report of a patient with a large cystic metastatic brain tumor who successfully underwent bronchoscopy with Ommaya reservoir placement before pathological diagnosis of lung cancer.

In summary, we have described a case involving a large cystic metastatic brain tumor from lung cancer that was successfully controlled with Ommaya reservoir placement and GKS. Consideration of aggressive Ommaya reservoir placement for large cystic metastatic brain tumors is vital for an excellent outcome, even in patient with undiagnosed lung cancer complicated with poor PS and impaired consciousness.

Declaration of competing interest

The authors declare that there were no conflicts of interest.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.rmcr.2020.101069.

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