CASE REPORT

Metachronous brain and intramedullary spinal cord metastases from nonsmall-cell lung cancer: A case report

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Abstract  A 44-year-old man had a brain tumor secondary to lung adenocarcinoma and underwent craniectomy to remove the brain tumor. After postoperative whole-brain radiation therapy, he underwent pneumonectomy followed by chemotherapy, mediastinal radiotherapy, and target therapy for lung cancer. Thirty-six months after the initial brain surgery, he suffered from neck pain and right upper limb numbness that rapidly progressed to upper extremity weakness and paralysis in 2 months. Magnetic resonance imaging demonstrated an intramedullary spinal cord lesion at the C4 level. Laminectomy and gross intramedullary tumor removal were performed. The patient’s neurological function improved after the operation. Nevertheless, 4 months after the intramedullary tumor removal, he began to show multiple metastases. Unfortunately, the patient died from respiratory failure 8 months after diagnosis with intramedullary spinal cord metastasis. In this case, early diagnosis and aggressive surgical treatment combined with postoperative radiotherapy and chemotherapy might have provided this patient with a prolonged survival and better quality of life.

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Introduction

Lung cancer is a common and fatal malignancy [1]. Metastases to the central nervous system such as the brain and meninges are often seen in patients with primary lung cancer [2]. However, intramedullary spinal cord metastasis (ISCM) from lung cancer is relatively rare compared with other system malignancies. Among cases of metastasis to the central nervous system (CNS), the frequency of ISCM is 4.2–8.5% in published autopsy reports [3–5].

The clinical features of ISCM have been described as a rapidly progressive neurological deficit [6]. Therefore, prognosis of ISCM is poor [7]. In a cohort study, individuals with brain metastases show a median survival time of 2.7 months after first admission with brain metastases. For lung cancer patients with brain metastasis, the survival time is even shorter. On average, these patients survive 2.5 months after their first admission with brain metastases [8].

Involvement of other sites within the CNS has been shown to be common in patients with ISCM. In Schiff and O’Neill’s report, 32.5% of patients with ISCM had a history of brain metastasis preceding the diagnosis of ISCM [9]. The published medical literature rarely shows a good long-term survival in patients with primary lung cancer and brain metastasis. Moreover, the prognosis of patients with primary lung cancer and brain metastasis deteriorating to ISCM is worse.

In this report, we present a patient with metachronous brain and ISCM from lung cancer.

Case report

A 44-year-old man was transferred to the neurosurgery department due to a 2-week history of headache, dizziness, and left leg numbness. He had a one-pack-a-day history of smoking lasting more than 20 years. His Karnofsky Performance Status (KPS) was 90%, without any adverse prognostic factors such as weight loss or laboratory abnormalities.

His preoperative chest X-ray film showed no definite diagnostic anomaly (Fig. 1A). Brain magnetic resonance imaging (MRI) found a heterogeneous nodule in the right postcentral gyrus (Fig. 2A). The cerebral lesion was completely surgically removed (Fig. 2B). Pathology revealed a metastatic adenocarcinoma, and immunohistochemical studies showed positivity for both TTF-1 and CK 7 (Fig. 3A–C), suggesting a pulmonary origin. Whole-brain radiation therapy (WBRT), consisting of a total dose of 3400 cGy in 200-cGy daily fractions, was administered postoperatively.

Chest computed tomography (CT) was performed and revealed metastatic disease in the middle mediastinum (see Fig. 1B). An endobronchial lesion was found on bronchoscopy, and the biopsy demonstrated bronchogenic adenocarcinoma. Left pneumonectomy was performed after WBRT. Pathology revealed a moderately differentiated, lung adenocarcinoma (pT2N1M1) (Fig. 3D).

After lung surgery, the patient’s KPS remained at 90%. He underwent five courses of chemotherapy with paclitaxel and cisplatin. Subsequently, positron emission tomography found multiple intense foci of fluodeoxyglucose-avid lesions in the mediastinal lymph nodes and left posterior cervical lymph nodes. As a metastatic lesion was highly suspected, radiotherapy with a total dose of 5220 cGy for a mediastinal metastasis was performed. In addition, the patient continued chemotherapy with two courses of paclitaxel alone, one course of intravenous vinorelbine, and six courses of pemetrexed. In addition, he had target therapy with gefitinib for 2 months.

Three years after the initial brain surgery, the patient began to suffer from neck soreness followed by right upper limb numbness. Two months later, these neurological symptoms rapidly progressed to upper extremity weakness and paralysis. At that time, his KPS was 60%. The cervical spine MRI showed an intramedullary tumor at C4 level (Fig. 4A). Therefore, he underwent C3–C5 laminectomy with gross removal of the C4 intramedullary tumor. The surgical pathology revealed a metastatic adenocarcinoma.

Figure 1. (A) Chest plain film showing no definite diagnostic anomaly. (B) A chest computed tomography scan shows metastatic disease in the middle mediastinum (white arrow) with partial atelectasis of the left lingular lobe (black arrows).
Figure 2. (A) Contrast-enhanced T1-weighted imaging shows a heterogeneous nodule with mild gadolinium enhancement in the right postcentral gyrus (arrow). Perinodular hyperintensity can be noted. (B) Two years after brain surgery, contrast-enhanced fast fluid-attenuated inversion-recovery (FLAIR) imaging shows that the tumor has been completely removed without recurrence.

Figure 3. (A) The brain shows metastatic adenocarcinoma composed of hyperchromatic nuclei and pleomorphic tumor cells arranged in a papillary glandular or cribriform pattern. H&E, 200×. (B) The tumor cells of the metastatic lesion (brain) are immunopositive for TTF-1. TTF-1 immunohistochemical stain, 200×. (C) The tumor cells of the metastatic lesion (brain) are immunopositive for CK7. CK-7 immunohistochemical stain, ×200. (D) Histologically, the left lung shows features of adenocarcinoma. H&E, 200×. (E) The cervical cord shows metastatic adenocarcinoma composed of cancerous cells with moderate pleomorphism arranged in a glandular or villoglandular pattern. H&E, 200×.
The patient was then transferred to rehabilitation department. His neurological symptoms and signs subsided, and his KPS returned to 80%.

Four months later, the patient's follow-up chest CT found several osteoblastic metastatic lesions in the spine and ribs bilaterally. A bone scan revealed multiple bone metastases from lung cancer. Brain MRI revealed multiple metastatic brain tumors in the cerebrum, cerebellum, and subependymal area. Hence, chemotherapy with two courses of gemcitabine was given concurrently with radiotherapy consisting of a total dose of 3000 cGy in 300-cGy daily fractions, for lumbar spine and sacroiliac joint metastases. In addition, he underwent radiotherapy, consisting of a total dose of 3060 cGy in 340-cGy daily fractions, for brain metastases.

The patient became weaker and developed shortness of breath. He was admitted to the hospice ward for palliative treatment and unfortunately died from respiratory failure 8 months after the diagnosis of ISCM.

Discussion

Patients with lung cancer and brain metastasis have a poor prognosis. Surgery plus postoperative WBRT provides a favorable prognosis for patient with a single metastatic brain tumor [10,11]. Many studies have recommended surgery for the primary lung tumor, suggesting a longer functional survival than without surgical intervention [12,13]. Nevertheless, Billing et al. [14] suggested that surgical resection provides benefit only in patients without lymph nodes metastases. They reported that no patient with mediastinal lymph node involvement survived longer than 3 years. In our report, this 4-year survivor underwent dual resection of both the lung primary and brain metastases followed by radiotherapy, chemotherapy, and target therapy. We deem that aggressive treatment for lung cancer with brain metastasis is an optimal approach that would lead to a favorable prognosis.

ISCM represents a rare evolution of cancer from systemic cancer, and it is a challenge in terms of diagnosis and treatment. Prior to the advent of MRI, many diagnoses were established post mortem [3–5]. Gadolinium-enhanced MRI shows a high sensitivity and has become the gold standard in diagnosis of this disease [9,15,16]. Nowadays, other diagnostic tests, such as plain radiographs of spine and cerebrospinal fluid analysis, have comparatively less value in the diagnosis of ISCM [9].

Lung cancer and breast cancer represent the most common primary sources of extra-CNS ISCM, with lung cancer accounting for almost half of the cases [7,9,17]. ISCM may occur at any level of the spinal cord. In a review article [7], 147 patients with ISCM were analyzed. Metastasis to the cervical cord was most common (42%), which might relate to the greater bulk and richer vascular supply in the cervical cord [18].

Previous studies illustrated three pathways of ISCM, including hematogenous spread [7,19], direct intramedullary invasion by meningeal carcinomatosis [20], and direct invasion from a contiguous structure [3,20]. With the evidence of multiple CNS metastases from lung cancer, we postulate that the most likely pathway is via the arterial route, as well as direct extension via cerebrospinal fluid distribution from the central canal into the intramedullary space.

From a treatment perspective, we consider surgical resection to be the optimal treatment for patient with ISCM. In the medical literature [16,20], radiotherapy is often indicated for patients with ISCM; even so, surgical resection for intramedullary spinal cord tumor can also be
performed in selected cases and has been associated with a favorable prognosis [21–24]. In the present case, the patient’s neurological function improved after surgery. We believe that surgery would provide a favorable internal decompression, which is helpful to relieve the rapid neurological deterioration.

The duration between a patient’s initially diagnosed tumor and ISCM has been shown to be 25 months on average, the mean period between the occurrence of the patient’s symptom and the diagnosis with ISCM being 52 days [7]. In our case, this patient was diagnosed with ISCM 38 months after the diagnosis of his primary lung cancer. We believe that the prolonged survival of this patient is the result of increased awareness of the condition and an improvement in investigative techniques, as well as aggressive surgical treatment with postoperative adjuvant chemotherapy and radiotherapy.

References