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Case Report

Small-cell lung cancer metastasis to a meningioma: Case report and review of the literature ☆,☆☆,★

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ABSTRACT

Tumor-to-tumor metastasis is a rare event with meningioma as the recipient tumor accounting for 20% of the reported cases. The most common primary cancers showing this phenomenon are lung and breast cancer. Most lung cancers metastasizing to a meningioma are due to lung adenocarcinoma with the literature containing only 3 prior reports of small-cell lung cancer showing this pattern of spread. Herein, we present the case of a 67-year-old-patient with small-cell lung cancer that developed a metastasis to a meningioma.

Introduction

Two tumors coexisting in a single location is a rare phenomenon and occurs due to either a tumor-to-tumor metastasis or in a collision tumor. Unfortunately, although the 2 modes of tumor growth are distinct, the 2 terms are often inappropriately used interchangeably. Tumor-to-tumor metastatic spread occurs when a donor tumor shows hematogenous metastatic spread to a recipient tumor. A collision tumor consists of 2 histologically distinct tumors localized within a single organ growing into each other.

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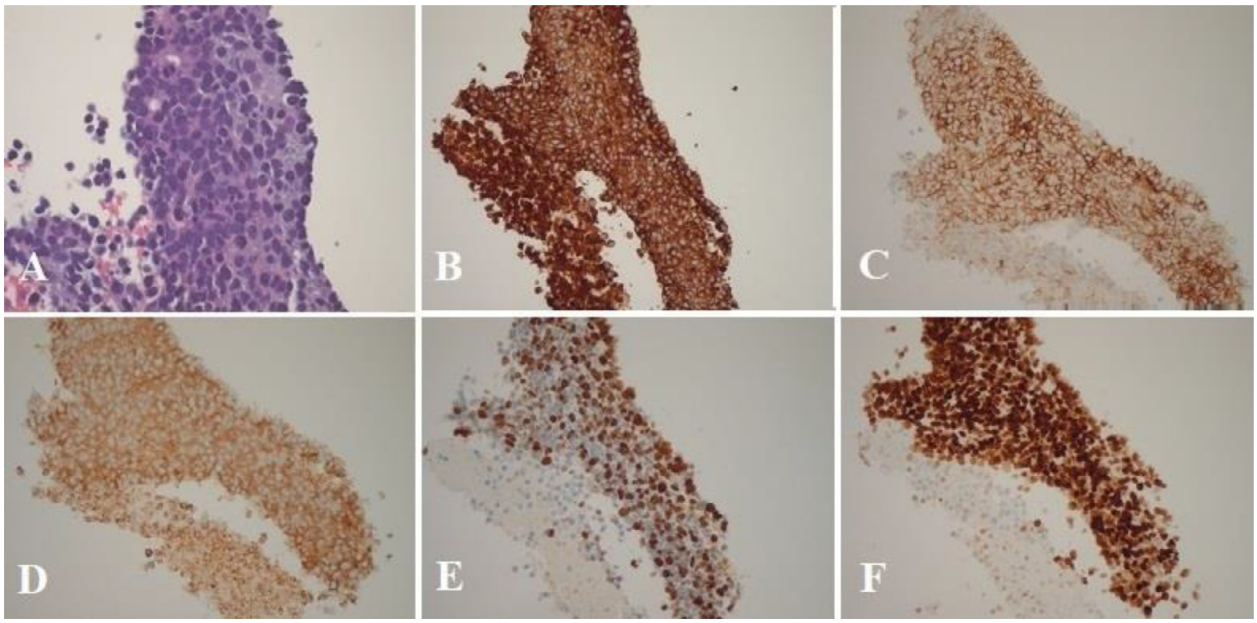

Fig. 1 – H&E as well as immunohistochemistry staining of the biopsy specimen from the left lung revealed small-cell lung cancer. (A) H&E staining reveals that the tumor is composed of small to medium sized round to oval blue cells with minimal cytoplasm. The nuclei exhibit a "salt and pepper" chromatin pattern with indistinct nucleoli, nuclear molding, smudge artifact, and frequent mitotic figures. Necrosis and individual cell apoptosis is evident (40× magnification). (B) The tumor cells demonstrate immunoreactivity to cytokeratin 8/18 (20× magnification). (C) Immunoreactivity is also seen with CD56 staining (20× magnification) and to (D) synaptophysin (20× magnification). (E) A Ki-67 stain shows a proliferation index of approximately 70% (20× magnification). (F) The tumor stains strongly for TTF-1 (20× magnification).

Berent first reported a case of tumor-to-tumor metastasis in 1902 [1]. Fried reported the first case of tumor-to-meningioma (TTM) metastasis in 1930 [2]. To date, a total of 152 cases of TTM metastasis haven been reported in the literature with the most common donor tumor showing this type of spread being breast and lung accounting for 34% and 28% of the cases, respectively [3]. However, only 3 prior cases of small-cell lung cancer exhibiting TTM spread have been reported [4–6].

Case presentation

A 67-year-old patient presented with left chest wall pain that progressed in severity over a course of several weeks. Computed tomography (CT) imaging of the chest revealed an 11cm left upper lung mass with multiple non-calcified bilateral pulmonary nodules. At least twelve non-calcified lung nodules were noted with the largest measuring 1.5cm. The findings were highly suggested of a primary lung malignancy given the patient's history of smoking one pack of cigarettes per day for 45 years. A CT-guided needle-core biopsy of the left lung mass was performed. The hematoxylin and eosin (H&E) staining as well as the immunohistochemical staining revealed small-cell lung cancer (Fig. 1). The tissue showed strong immunoreactivity to cytokeratin 8/18, CD56, and synaptophysin. As to be expected for small-cell lung cancer, the tissue showed significant immunoreactivity with a thyroid-transcription-factor-1 (TTF-1) stain.

At the time of presentation, the patient had neither neurologic-related complaints nor findings on physical exam to suggest central nervous system (CNS) metastasis. Nonetheless, magnetic resonance imaging (MRI) of the brain was performed that did not reveal any evidence of brain metastases. However, an extra-axial mass measuring 5cm in maximal dimension was noted arising from the left frontal lobe region and extending across the midline associated with the falx cerebri (Fig. 2). The MRI signal characteristics of the incidentally identified brain tumor were consistent with a meningioma. The tumor uniformly enhanced upon gadolinium (Gd) administration, contained a dural tail, and on T2-weighted images showed a "cleft sign" with a rim of high intensity cerebral spinal fluid (CSF) confirming its extra-axial origin and fulfilled the standard radiologic criteria of a meningioma [7,8]. In addition, brain metastases from small lung cancer are rapidly growing and it was highly unlikely that a metastatic lesion of this size would produce no neurologic symptoms.

The patient underwent a course of combined modality therapy consisting of systemic therapy with intravenous carboplatin and etoposide along with 60 Gray (Gy) of thoracic radiation therapy to the large left lung mass. Upon completion of his combined modality therapy, the patient began a course of immunotherapy with intravenous atezolizumab (Tecentriq, Genentech).

Imaging with a CT of the chest, abdomen, and pelvis performed 3 months after completion of the patient's combined modality therapy revealed a very good response with contraction of the left lung mass and disappearance of the majority of the lung nodules. There was no evidence to suggest progres-

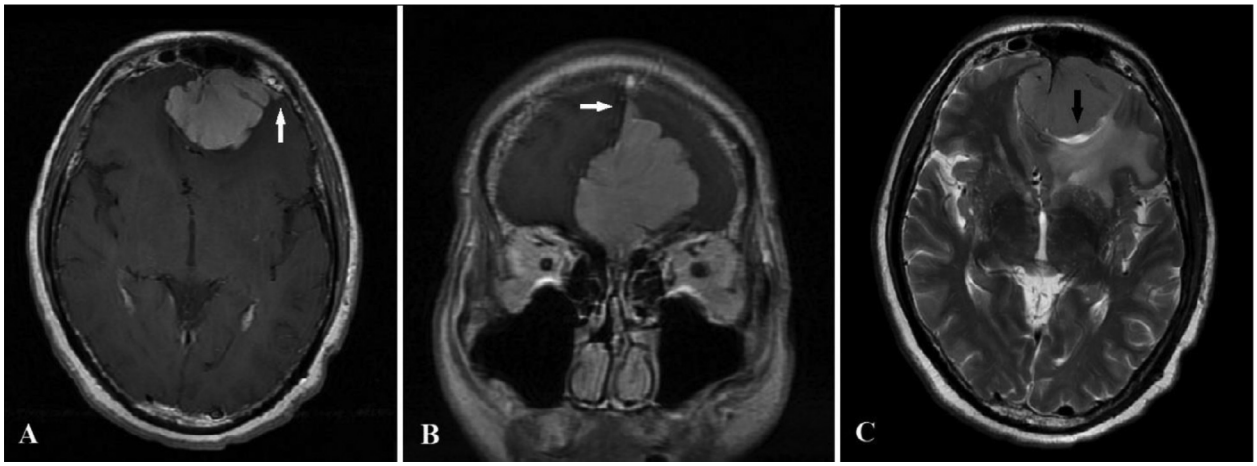

Fig. 2 – MRI of the brain obtained at the time of diagnosis revealing a bifrontal meningioma. (A) Gd-enhanced T1-weighted axial image showing a homogeneously enhancing bifrontal lobe mass with a dural tail (white arrow). (B) Gd-enhanced T1-weighted coronal image showing a homogeneously enhancing bifrontal lobe mass with a dural tail (white arrow). (C) A T2-weighted axial image showing surrounding vasogenic edema with a "cleft" sign consisting of a rim of CSF (black arrow).

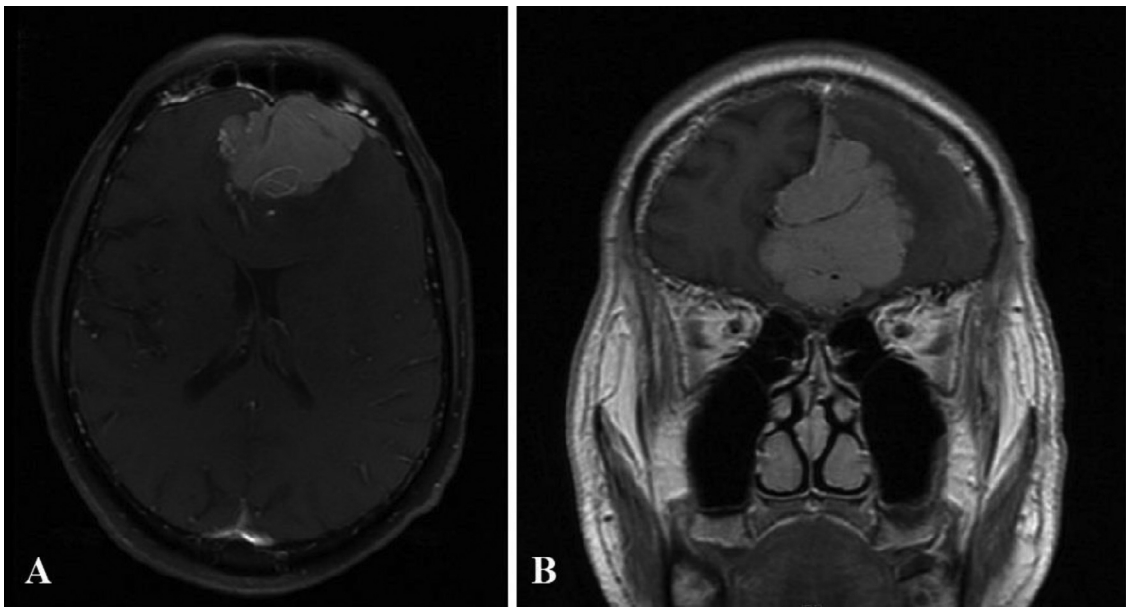

Fig. 3 – Images obtained 3 months after completion of combined modality therapy of the lung malignancy showing stability of the meningioma. (A) Gd-enhanced T1-weighted fat-saturated axial image. (B) Gd-enhanced T1-weighted coronal image.

sion of disease. A surveillance MRI of the brain performed 4 months after the patient's initial presentation showed no evidence of brain metastases and no change in the previously seen meningioma (Fig. 3). This was further evidence that the mass in the frontal lobe region was not a metastasis as it is unlikely that the extracranial disease responded to systemic therapy but an untreated brain metastasis from small-cell lung cancer would show neither a decrease nor increase in size.

Although, the immunotherapy was continued, CT imaging of the chest, abdomen and pelvis 3 months later unfortunately revealed progression of disease with enlargement in the size and number of numerous bilateral pulmonary nodules.

Four weeks later, the patient presented with a 2-day history of confusion and left arm weakness. A non-contrast CT of the head revealed the meningioma to be stable in size but there now was development of several intraparenchymal brain lesions consistent with hemorrhagic metastases. An MRI of the brain confirmed the presence of multiple intraparenchymal hemorrhagic metastases. In addition, within the meningioma, there was development of a 3 cm hemorrhagic metastasis (Figs. 4 and 5). Increasing vasogenic edema surrounding the meningioma was also identified.

The patient completed a course of a palliative whole brain radiotherapy receiving a total of 30 Gy. Unfortunately, the pa-

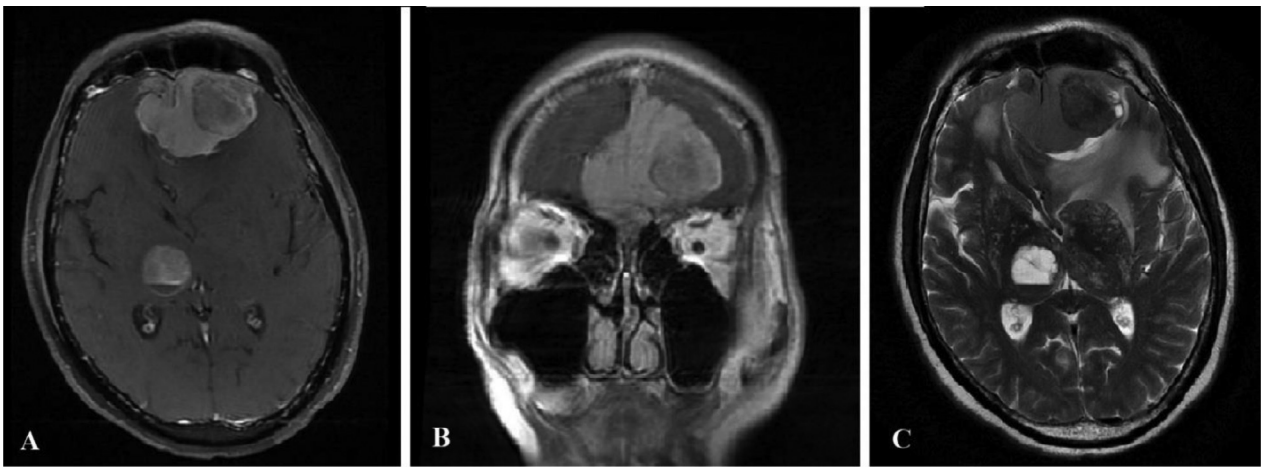

Fig. 4 – MRI images of the brain showing development of brain metastases with a metastatic deposit within the meningioma. (A) A Gd-enhanced T1-weighted fat-saturated axial image showing a heterogeneously enhancing mass within the left portion of the meningioma. A right thalamic hemorrhagic metastasis is also seen. (B) A Gd-enhanced T1-weighted coronal image showing the heterogeneously enhancing mass within the left portion of the meningioma. (C) A T2-weighted axial image showing increasing vasogenic edema surrounding the meningioma in comparison to the prior images (Fig. 2).

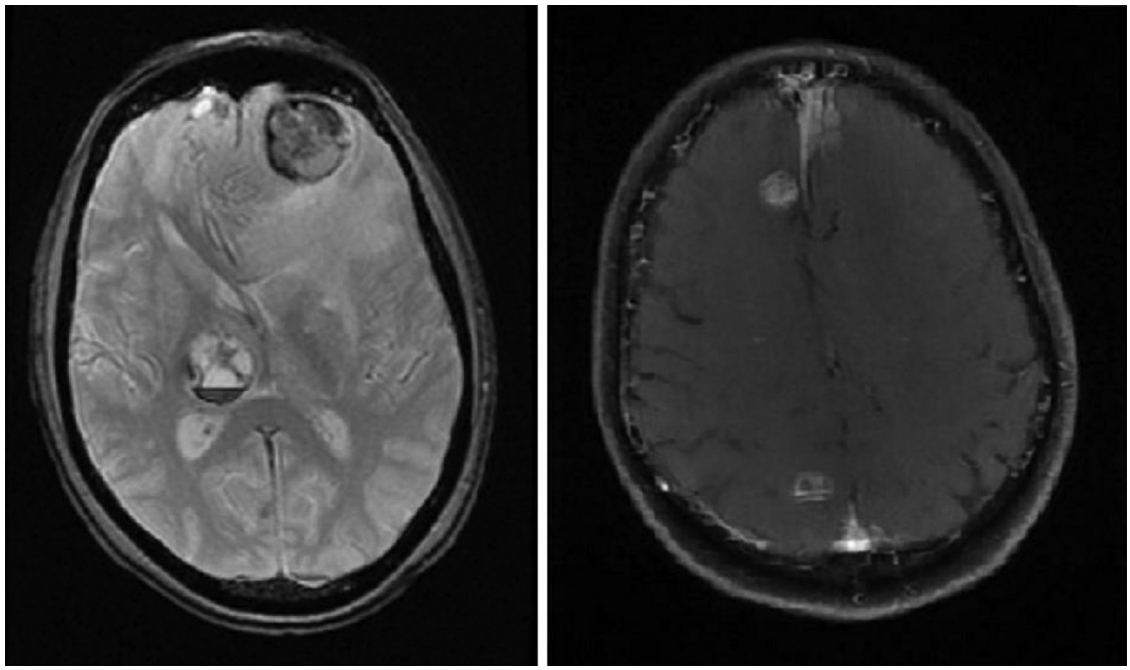

Fig. 5 – MRI images revealing the presence of the other metastases in addition to the tumor-to-meningioma metastasis. (A) Gradient MRI images of the brain showing the well circumscribed left frontal metastasis within the meningioma and a separate right thalamic metastasis. (B) A Gd-enhanced T1-weighted fat saturation axial image showing enhancing hemorrhagic metastases in other portions of the brain.

tient succumbed to metastatic small-cell lung cancer shortly thereafter.

Discussion

In 1968, Campbell et al. [9] proposed the following criteria for diagnoses of tumor-to-tumor metastasis: (1) there must be more than one primary tumor, (2) the recipient tumor is a true neoplasm, (3) the metastatic neoplasm is a true metastasis with evident growth within the recipient tumor, and (4) exclusion of tumors that have metastasized to the same lymph node. Later, Chambers et al. [4] proposed 2 other criteria for TTM metastasis: (1) the metastatic foci should be surrounded by tissue that is histologically different than the metastasis and (2) the existing primary tumor should be proven histologically.

The time course of the events with the patient presenting with an abrupt onset of neurologic deterioration is consis-

tent with hemorrhagic brain metastasis with an associated increase in the vasogenic edema surrounding the meningioma. The radiographic pattern is also consistent with development of multiple hemorrhagic brain metastases with the finding of several well circumscribed lesions with ring-like enhancement and associated increasing vasogenic edema (Figs. 4 and 5). This presentation is similar to that reported by Ranvik et al. [10] of a case of lung adenocarcinoma with a hemorrhagic metastasis to a meningioma presenting as an acute decline in neurologic status. In our case, the standard of care did not allow for biopsy confirmation of the brain metastases. However, the radiographic findings and their time course are compelling and sufficient to substantiate a finding of TTM metastasis as proposed by Campbell and Chambers.

The large majority of cases of TTM metastasis from lung cancer arise due to a lung adenocarcinoma serving as the donor tumor [11]. Only 3 cases have been previously reported in the literature in which the donor lung cancer was of small-cell histology [4–6]. This is a surprising result since brain metastases are estimated to occur in approximately 40% of patients with small-cell lung cancer during a patient's lifetime [12].

Meningiomas are the most common recipient tumor for intracranial tumor-to-tumor metastasis. [11]. Several factors have been proposed to account for this predisposition. In general, meningiomas grow indolently and have a slow metabolic rate [13], they contain a rich vascular supply with a low venous flow rate [14], and have a minimal host immune response rendering them as immunological sanctuaries for metastases [15]. The high lipid and collagen content of meningiomas may also predispose for the implantation of malignant cells [16]. With regards to breast cancer, both meningiomas and breast cancer have significant E-cadherin expression that may account for the finding of spread of breast cancer to a meningioma [17].

Interestingly, apart from the E-cadherin content of breast cancer, the other factors listed above are general in nature and should apply to small-cell lung cancer metastases as well. Yet, despite the high likelihood of a patient with small-cell lung cancer developing brain metastasis, only a handful of cases of small-cell lung cancer with TTM metastasis have been reported. It is interesting to note that almost all of the reports of non–small-cell lung cancer showing TTM metastasis have been adenocarcinomas which show a high staining for TTF-1. However, despite the large majority of small-cell lung cancers exhibiting strong TTF-1 expression as well, small-cell lung cancer with TTM spread is very rare. Therefore, there may be an unknown mechanism which inhibits this mode of spread which is specific to small-cell lung cancer.

Conclusion

The clinical and radiographic findings are compelling in showing metastatic spread of a small-cell lung cancer to a meningioma in our patient. Despite the high risk of small-cell lung cancer metastasizing to the brain, our patient represents only the fourth reported case of this mode of spread.

Patient consent

A written informed consent for this case report was obtained from the patient. All the images included are nonidentifiable images consistent with Elsevier policies.

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