 doi: 10.2176/jns-nmc.2022-0113

NMC Case Report Journal 9, 323-328, 2022

Solitary Leptomeningeal Metastasis from Lung Cancer: A Case Report

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Abstract

Leptomeningeal metastasis (LM) is a rare but devastating cancer complication. LM occurs when cancer spreads into the leptomeningeal layer or cerebrospinal fluid. Intracranial magnetic resonance (MR) images of LM are characterized by the diffuse enhancement of the leptomeninges along the cerebral sulci, cerebellar folia, and cranial nerves. Here, we report an extremely rare case of LM with an atypical MR image revealing tumor mass confinement to the arachnoid membrane. The case involves an 85-year-old man who was referred to our hospital with a three-day history of dysarthria. Radiological examination revealed a solid lesion with heterogeneous enhancement and a cystic component in the extra-axial region of the right parietal lobe. Upon subsequent general examination, multiple lung cancer metastases were suspected. The patient underwent gross total resection of the brain mass in the right parietal region. Although the tumor slightly adhered to the dura mater, it was sharply demarcated from the surrounding parenchyma and pia mater. Based on pathological examination, the tumor was diagnosed as small cell lung cancer metastasis. This metastatic brain tumor was exclusively confined to the arachnoid membrane and, except for a few blood vessels, the dura mater was not infiltrated by metastatic tumor cells. To our knowledge, this is the first reported case of LM in which the tumor mass is confined only to the arachnoid membrane. Thus, in cases with atypical MR images, a general examination considering the possibility of LM is important for prompt and accurate diagnosis.

Keywords: leptomeningeal metastasis, metastatic brain tumor, lung cancer

Introduction

Brain metastasis is the most common malignant brain tumor in adults, affecting approximately 30% of patients with solid cancers.[1)] Brain metastases occur in the brain parenchyma, the leptomeningeal layer (arachnoid mater, subarachnoid space, and pial surface), and the pachymeningeal layer (dura mater).[2)] While central nervous system metastases mainly occur in the brain parenchyma, metastatic cancer cells can also spread to the pia mater and arachnoid membrane, which is referred to as leptomeningeal metastases (LM).[3)] LM affects approximately 4%-15% of patients with solid cancers, and LM patients have a poor prognosis, with a mean survival time of 2-6 months, even with treatment.[4,5)] Considering its devastating impact on the quality of life, a prompt and accurate diagnosis of LM is crucial. Magnetic resonance imaging (MRI) is a gold standard for comprehensive neuroradiological evaluation and LM diagnosis.[4,6)] The hallmark of intracranial MRI abnormality in LM is the diffuse enhancement of the leptomeninges along the cerebral sulci, cerebellar folia, and cranial nerves.[7,8)] To our knowledge, there are no reports of LM forming an intracranial solid tumor. Here, we report an extremely rare case of LM with a solid tumor confined only to the arachnoid membrane.

Received April 9, 2022; Accepted July 21, 2022

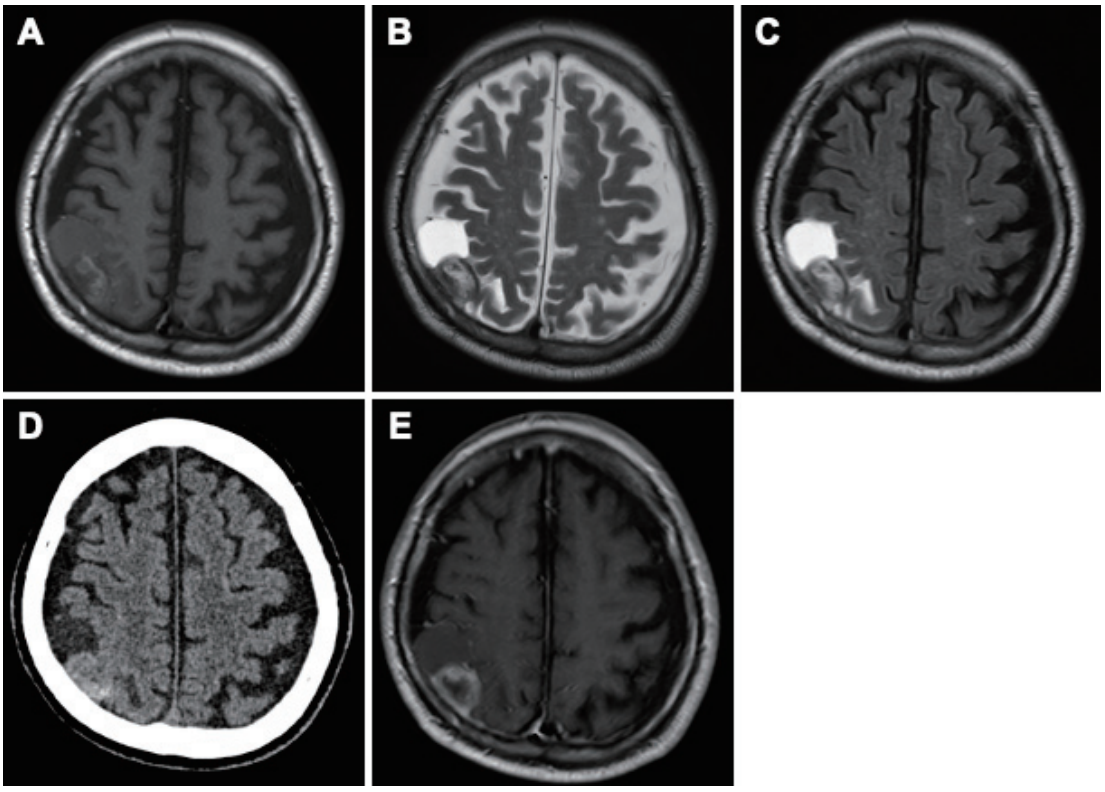

Fig. 1 (A) T1-weighted MR image showing the heterogeneous hyperintense solid lesion and the isointense cystic lesion in the right parietal region. (B and C) T2-weighted (B) and FLAIR MR (C) images showing the heterogeneous hyperintense solid and the hyperintense cystic lesions. (D) Head CT showing no calcification in the mass. (E) Gadolinium contrast-enhanced, T1-weighted MR image showing the solid lesion with heterogeneous enhancement and the cystic lesion in the right parietal region. CT: Computed tomography; FLAIR: fluid-attenuated inversion recovery; MR: magnetic resonance

Case Report

An 85-year-old man with a history of Hansen's disease and hypertension presented with dysarthria that lasted three days. Head MRI revealed a mass of 4.2 cm in diameter in the right parietal region. The mass comprised a solid lesion and a cystic lesion. Subarachnoid hemorrhage was observed around the mass, but there was no brain edema. The solid lesion was heterogeneous hyperintense on T1- and T2-weighted images, while the cystic lesion was isointense on T1- and hyperintense on T2-weighted and fluid-attenuated inversion recovery images (Fig. 1A-C). Head computed tomography (CT) revealed no calcification in the mass (Fig. 1D). We, therefore, suspected an extra-axial brain tumor, such as meningioma, and performed a gadolinium contrast-enhanced MRI, which revealed a heterogeneous enhancement of the solid lesion (Fig. 1E). Thus, a whole-body iodine contrast-enhanced CT was carried out to rule out the possibility of a metastatic brain tumor. This examination revealed an irregularly shaped nodule in the left lung (Fig. 2A) and left pleura, multiple ring-enhancing lesions in the liver, and multiple swollen lymph nodes (LNs) in the left hilum, mediastinum, bilateral axillae, para-aortic region, and mesentery. The hilar and mediastinal LNs were swollen, predominantly on the left side (Fig. 2B and C). The patient underwent axillary LN biopsy and two days later underwent a gross total resection of the brain mass in the right parietal extra-axial region. The brain tumor adhered to the dura mater (Fig. 2D). The cyst wall was very thin, and the cyst was attached to the solid lesion. After puncturing the cyst, the solid lesion was resected. The solid lesion was sharply demarcated from the surrounding parenchyma and pia mater (Fig. 2E), and gross total resection was achieved (Fig. 2F). Postoperative MRI showed gross total removal of the tumor (Fig. 2G).

Histopathological examination of the axillary LN revealed proliferation of atypical cells with a high nuclear-to-cytoplasmic ratio (Fig. 3A). Immunohistochemistry showed that the tumor cells were positive for CD56, chromogranin A, synaptophysin, and thyroid transcription factor-1 (TTF-1) (Fig. 3B-E), and negative for Napsin A (Fig. 3E), p40, and CK14 (data not shown), leading to the diagnosis of small cell lung cancer LN metastasis. Histopathological analysis of the brain tumor gave similar morphology to those of axillary LN analysis, leading to the diagnosis of small cell lung cancer brain metastasis. Intriguingly, the metastatic brain tumor was exclusively confined to the arachnoid membrane (Fig. 4A-D), without dural infiltration by metas-

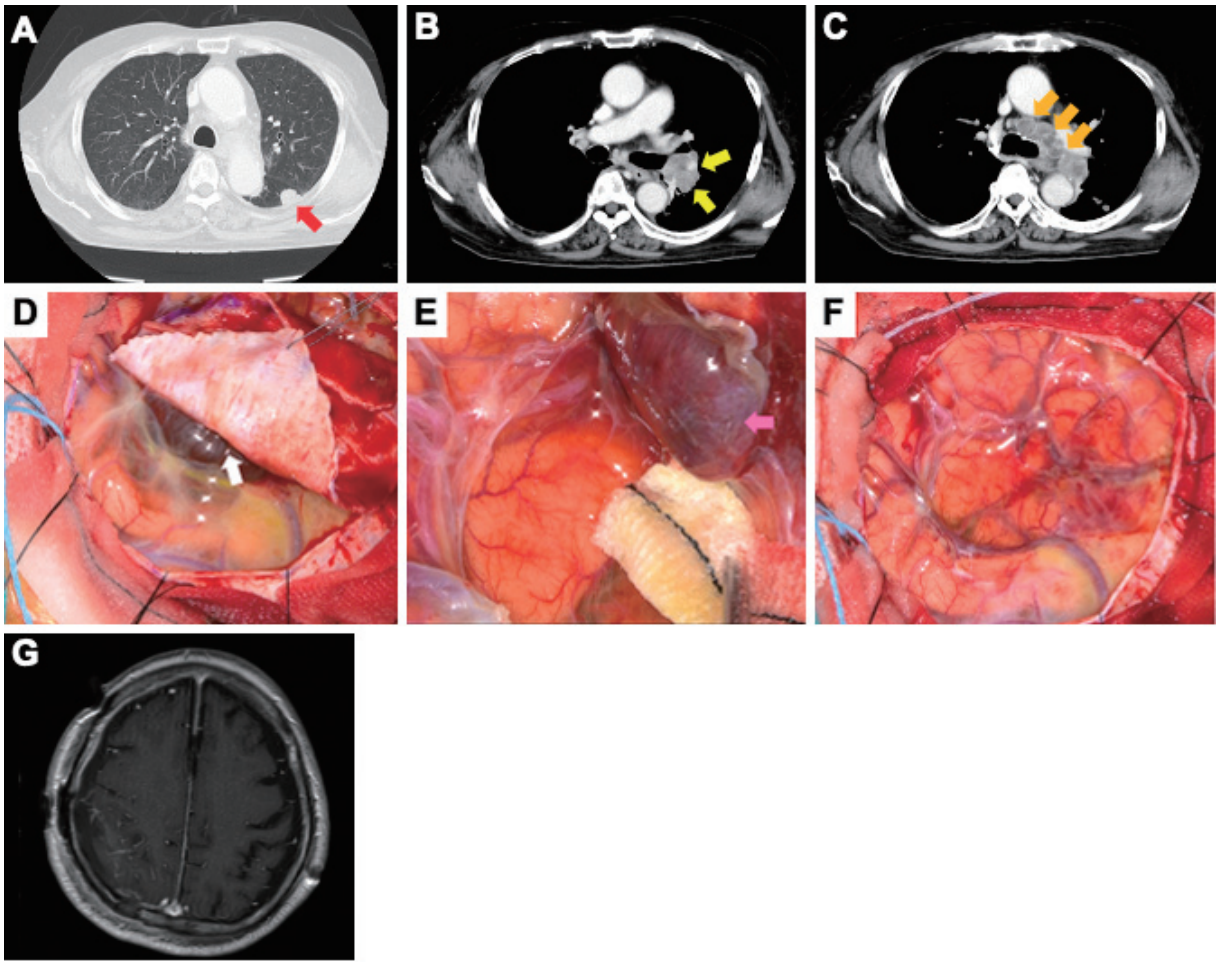

Fig. 2 (A-C) Whole-body iodine contrast-enhanced CT showed an irregularly shaped nodule in the left lung (A; red arrow). The lymph nodes of the pulmonary hilum (B; yellow arrow) and mediastinum (C; orange arrow) were swollen, predominantly on the left side. (D-F) Intraoperative photographs. The brain tumor was adherent to the dura mater (D). The solid lesion was resected after puncturing the cystic lesion (D; white arrow), and the solid lesion (E; pink arrow) was sharply demarcated from the surrounding parenchyma and pia mater (E). Gross total resection was achieved (F). (G) Postoperative MR image showing gross total removal of the lesion. CT: computed tomography; MR: magnetic resonance

tatic tumor cells, except for very few vessels in the dura mater (Fig. 4D).

The patient's dysarthria improved before surgery. The postoperative course was uneventful and the patient was discharged 13 days after surgery. However, an MRI examination carried out after the patient started to experience limb weakness showed that the cervical spinal cord was compressed by an extradural mass that was considered to be a metastatic tumor. Multiple asymptomatic cerebellar metastases were also observed. The patient was then placed in palliative care and passed away 2 months after surgery.

Discussion

Here, we report an extremely rare case of LM, resulting in a tumor mass that was confined only to the arachnoid membrane. Although the magnetic resonance images of this case were quite unusual, LM was promptly and accurately diagnosed on the basis of a preoperative, systemic search after suspecting a metastatic brain tumor.

LM, which is also known as carcinomatous meningitis, is a devastating cancer complication with diverse clinical manifestations and few therapeutic options. Tumor-cell invasion into the leptomeninges may occur through hematogenous spread via arterial or venous circulation, or through endoneural, perineural, perivascular, or lymphatic spread. Additionally, direct invasion may occur by brain or spinal cord parenchymal metastases in contact with the cerebrospinal fluid (CSF).[6] In this case, there was no tumor invasion into the dura mater; however, tumor cells were found in a very small number of blood vessels running in the dura mater, which might have contributed to the LM. Among solid tumors, breast cancer, lung cancer,

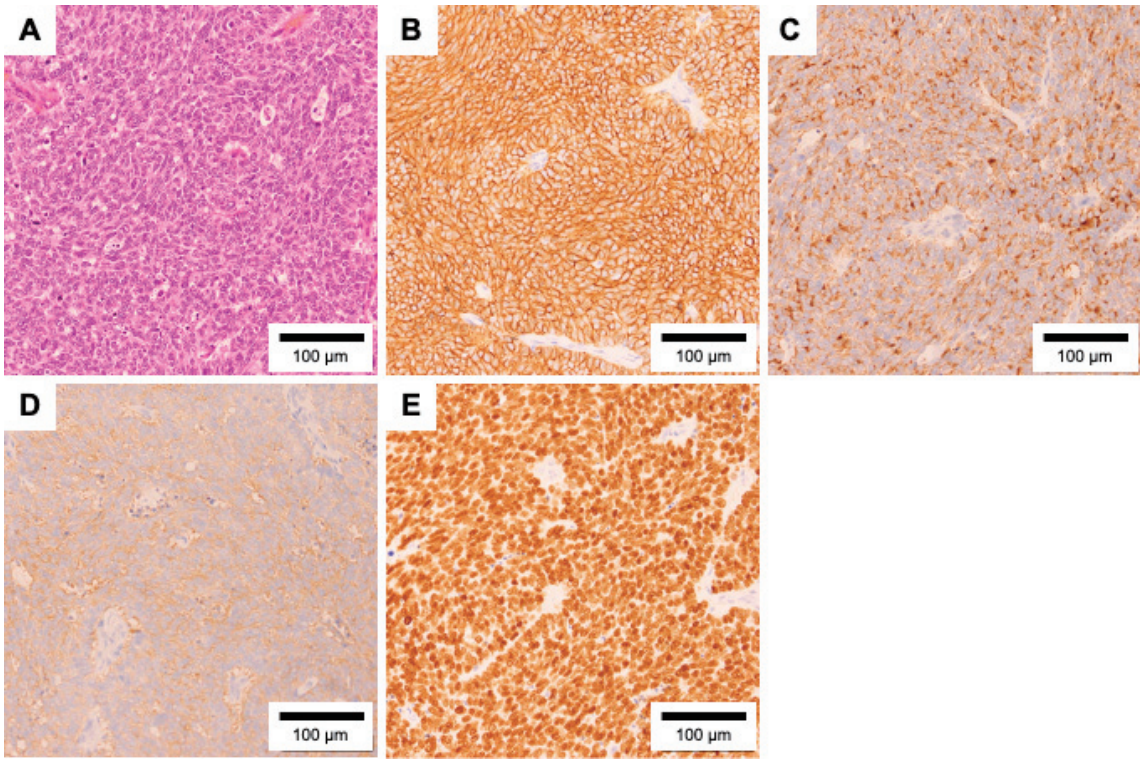

Fig. 3 (A) Hematoxylin and eosin staining of the axillary LN specimen revealed the proliferation of atypical cells with a high N/C ratio. (B-D) The tumor cells that metastasized to the axillary LN were positive for CD56 (B), chromogranin A (C), and synaptophysin (D). (E) Immunohistochemical two-antibody cocktail staining (TTF-1/Napsin A) of the tumor cells showed positivity for nuclear TTF-1 but negativity for cytoplasmic Napsin A. LN: lymph node; N/C ratio: nuclear-cytoplasmic ratio

and melanoma are the most common causes of LM. Most lung tumors that cause LM are adenocarcinomas.[9-11] Non-small-cell lung cancer cases that express mutant epidermal growth factor receptor or anaplastic lymphoma kinase rearrangement have been reported to exhibit specific tropism for the central nervous system.[12] LM prognosis is very poor, with an estimated median survival of only 2-6 months with treatment and 4-6 weeks without treatment.[13] Reflecting the diffuse nature of the lesion, LM has a myriad of clinical manifestations, including headache, nausea, vomiting, dysphagia, dysarthria, mental changes, seizures, gait difficulties, cranial nerve palsies, and spinal symptoms.[14] LM diagnosis is very challenging due to the high symptom variability among patients and lack of tests with sufficient sensitivity and specificity.

Cerebrospinal MRI with and without contrast enhancement, using a field strength of at least 1.5 T, is a gold standard imaging modality for LM diagnosis, with a sensitivity of 66%-98% and a specificity of 77%-97.5% in patients with suspected LM.[4,6] LM may present with diverse enhancement patterns on MRI, with linear and nodular enhancing lesions of the cranial nerves, spinal nerve roots, cerebral sulci, and cerebellar folia being the most common observations. Recently, the European Association of Neuro-Oncology (EANO)-European Society for Medical Oncology (ESMO) joint recommendations proposed the classification of LM based on MRI neuroimaging findings into the following four distinct categories: type A, LM with linear leptomeningeal disease; type B, LM with nodular leptomeningeal disease; type C, LM with both linear and nodular disease; and type D, LM without MRI abnormalities except possible hydrocephalus.[6] This case presented a solid mass lesion with a heterogeneous enhancement in the extra-axial region of the right parietal lobe, a very rare imaging observation of LM that has not been reported before.

CSF cytology is another gold standard for LM diagnosis[4,6] and is based on the presence of malignant cells in the CSF or leptomeningeal biopsy.[3,6] However, the sensitivity of CSF analysis is reported to be low.[15] Increased opening pressure, lymphocytic pleocytosis, elevated protein, and decreased glucose are the most frequent observations in the CSF of LM patients, but they are not specific to LM.[6] The results of CSF cytology may be inconclusive because non-definitive, atypical, or suspicious cells can be isolated.[3] Thus, multiple cytological CSF examinations are often needed to confirm LM diagnosis because the sensitivity increases to 80%-90% after the second or third lumbar puncture.[15] While recent advances in liquid biopsy technologies that detect circulating tumor cells and cell-free tumor DNA in the CSF have the potential to improve LM diagnosis, they have not yet been adopted into diagnostic guide-

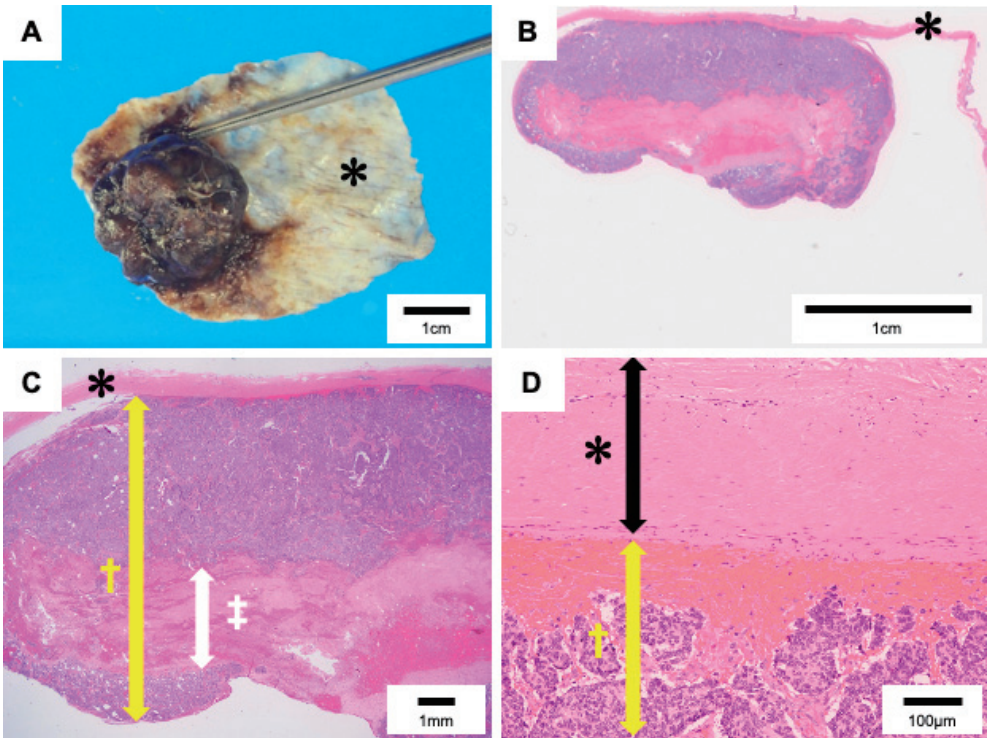

Fig. 4 (A-D) Histopathological findings of the brain tumor. (A) Gross findings of the excised brain lesion specimen. The tumor lesion was adherent to the dura mater. (B-D) Histopathological findings of the excised brain lesion specimen showing intratumoral hemorrhagic necrosis. There was no tumor invasion into the dura mater (D). *: dura mater; †: arachnoid mater; ‡: hemorrhagic necrosis

lines for clinical application.[3,16-21] In the present case, by performing tumor resection instead of CSF cytology, we promptly and accurately diagnosed LM.

Conclusions

Here, we report an extremely rare case of LM presenting as a tumor mass confined only to the arachnoid membrane. Thus, in cases where MRI images are atypical for LM or metastatic brain tumors, a general examination for suspected metastatic brain tumors is important for prompt and accurate diagnosis.

Acknowledgments

We thank F. Kobia, Ph.D., from Edanz (https://jp.edanz.com/ac) for editing a draft of this manuscript.

Informed Consent

Informed consent has been obtained from the patient for this report.

Conflicts of Interest Disclosure

The authors declare that they have no commercial or financial relationships that could be construed as a potential conflict of interest.

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