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Case report

Invasion of small cell lung cancer into the limbic system from leptomeningeal metastases

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ABSTRACT

The diagnosis of leptomeningeal metastases is sometimes difficult when the cytology of cerebrospinal fluid is negative. We report a rare case of leptomeningeal metastases that required differentiation from paraneoplastic limbic encephalitis. A 67-year-old man with extensive-stage small cell lung cancer was admitted for a sudden decrease in the level of consciousness. He suffered memory disturbances that began the day before admission. Diffusion-weighted and fluid-attenuated inversion recovery images of brain magnetic resonance imaging (MRI) showed bilateral symmetric areas of hyperintensity in the hippocampus, amygdala, insular cortex, and medial temporal lobe; contrast enhancement was positive. Cytology of the cerebrospinal fluid (CSF) was negative. Anti-*N*-methyl-D-aspartate receptor antibody and herpes simplex virus DNA were not detected in the CSF. Paraneoplastic Limbic encephalitis was suspected due to his symptoms and brain MRI scan. The patient developed generalized seizures after admission. High-dose methylprednisolone and intravenous immune globulin were administered, but his condition did not improve. Uncontrollable seizures persisted and he died in the hospital at day 13. Autopsy revealed leptomeningeal metastasis and invasion of cancer cells into the limbic system. Contrast-enhanced MRI should be performed even if limbic encephalitis is suspected, and leptomeningeal metastases should be suspected if the lesions are enhanced.

1. Introduction

Leptomeningeal metastasis refers to the spread of malignant cells through the subarachnoid space. The 2-year cumulative incidence of leptomeningeal metastases of small cell lung cancer was estimated to be 10% [1]. The primary diagnostic indicator of leptomeningeal metastases is the presence of malignant cells in cerebrospinal fluid (CSF) cytology. The sensitivity of CSF cytology has been reported to be only 75% [2], and the diagnosis of leptomeningeal metastases is sometimes difficult when CSF cytology is negative. Here, we report a case of leptomeningeal metastases of small cell lung cancer that required differentiation from paraneoplastic limbic encephalitis.

2. Case report

A 67-year-old man was admitted for a sudden decrease in the level of consciousness. He suffered memory disturbances that began the day before admission. He had been diagnosed with small cell lung cancer with distant metastases in the liver, bone, and bone marrow 6 months before admission. Brain metastasis had not been detected by gadolinium-enhanced MRI. Hoarseness and left ptosis had been observed before chemotherapy with cisplatin and irinotecan, but these symptoms had improved after the treatment. After six courses of the chemotherapy, a slight enlargement of the hepatic metastasis had been observed on computed tomography (CT) at 3 days before his admission. Therefore, he had been scheduled for an administration of a new anti-cancer drug.

The patient's vital signs on admission were as follows: temperature,

Abbreviations: CSF, cerebrospinal fluid; CT, computed tomography; DWI, diffusion-weighted image; FLAIR, fluid-attenuated inversion recovery; MRI, magnetic resonance imaging.

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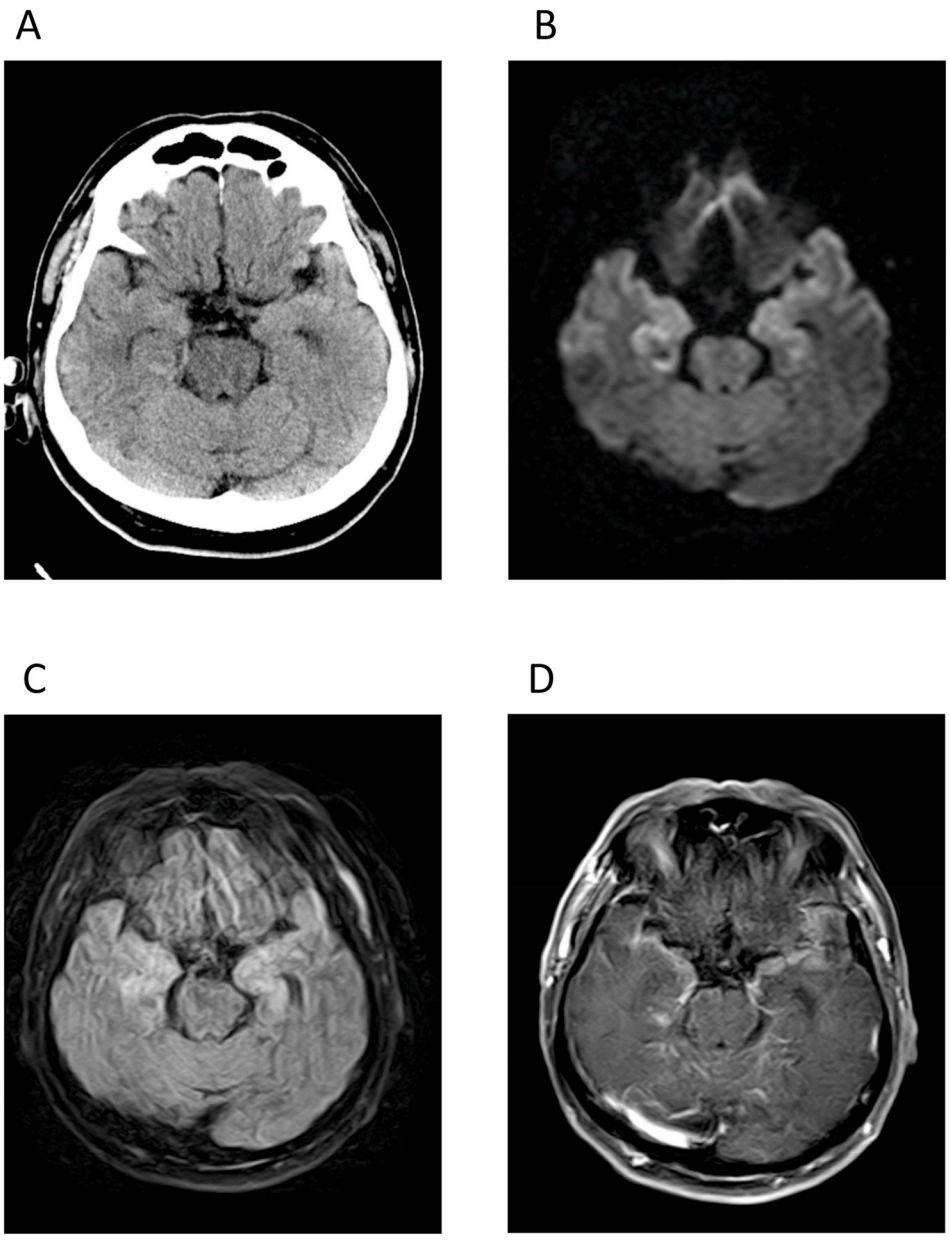

Fig. 1. Neuroimaging studies on admission. (A) Non-contrast brain computed tomography scan shows no abnormalities. (B) Diffusion weighted, (C) fluid-attenuated inversion recovery, and (D) gadolinium-enhanced Tl-weighted images of brain MRI. MRI reveals bilateral symmetric high intensity areas in the hippocampus, amygdala, and temporal lobe. These lesions are enhanced by gadolinium on Tl-weighted image. MRI, magnetic resonance imaging.

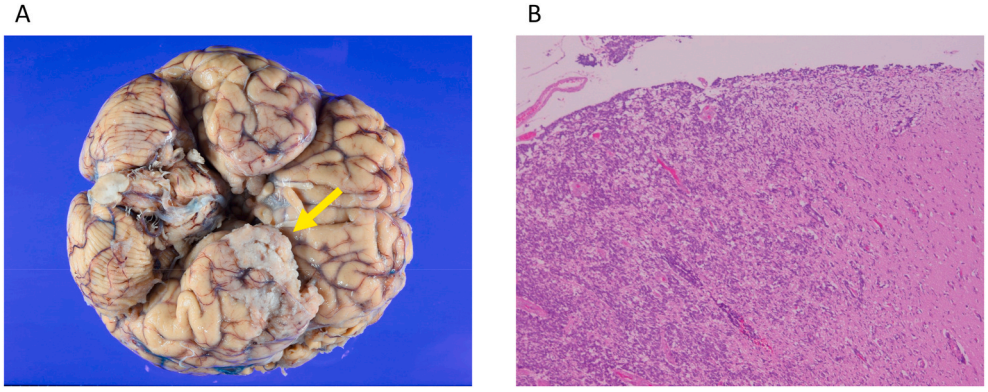

Fig. 2. Brain autopsy. (A) The medial temporal lobe is covered with a white opaque lesion (arrow). (B) Cancer cells invade into the brain parenchyma from the subarachnoid space in the medial temporal lobe.

37.0 °C; heart rate, 109 beats/min; blood pressure, 185/106 mmHg; respiratory rate, 14 breaths/min; and oxygen saturation, 98% on room air. Slight anisocoria (rt: 2.5 mm, lt: 3.0 mm) and sluggish light reflex of the left pupil were observed. He could tell his name but could not indicate where he was. Paralysis of the limbs was not observed.

A non-contrast brain CT scan did not reveal any abnormality (Fig. 1A). Although image quality was degraded due to motion artifact, diffusion-weighted image (DWI) and fluid-attenuated inversion recovery (FLAIR) image of brain magnetic resonance imaging (MRI) showed bilateral symmetric areas of high intensity in the hippocampus, amygdala, insular cortex, and medial temporal lobe (Fig. 1B and C). These lesions were enhanced by gadolinium on Tl-weighted imaging (Fig. 1D). CSF analyses revealed lymphocytic pleocytosis (20/μL) and elevation of protein (172 mg/dL). CSF glucose concentration was 58 mg/dL. Cytology of the CSF was negative. CSF culture was also negative. Anti-*N*-methyl-D-aspartate receptor antibody and herpes simplex virus DNA were not detected in the CSF.

The patient developed generalized seizures after admission. Limbic encephalitis was suspected due to his symptoms and brain MRI scans showing high intensity areas in the bilateral limbic system and medial temporal lobe. High-dose methylprednisolone and intravenous immune globulin were administered, but his condition did not improve. Uncontrollable seizures persisted and he died in the hospital at day 13. Autopsy revealed that the medial temporal lobe was covered with white opaque lesions (Fig. 2A). Cancer cells filled the subarachnoid space and invaded deep into the brain parenchyma in the limbic system and medial temporal lobe (Fig. 2B). Leptomeningeal metastasis was also found in other part of the cerebrum, cerebellum, and brainstem.

3. Discussion

We reported a rare case of leptomeningeal metastases in which bilateral high intensity areas were localized to the limbic system on MRI. Autopsy revealed that these abnormalities consisted of cancer cells filling the subarachnoid space and infiltrating into the limbic system. Invasion into the limbic system was thought to have induced the patient's memory disturbance, decreased level of consciousness, and seizures.

We needed to differentiate his condition from paraneoplastic limbic encephalitis because he had some features indicating this disease. First, he had small cell lung cancer, which is likely to be accompanied by limbic encephalitis [3]. Second, the patient had memory disturbance, decreased levels of consciousness, and seizures, which are typical symptoms of limbic encephalitis [3]. Third, brain MRI scan showed bilateral symmetric areas of high intensity on DWI/FLAIR in the limbic system and medial temporal lobe; these findings are typical in limbic encephalitis [4]. Contrast enhancement of affected lesions on MRI is relatively rare in autoimmune encephalitis other than anti-Ma2-associated encephalitis [5], whereas it is common in leptomeningeal metastases [6]. In a previous study, contrast enhancement was seen in only 5 of 25 patients with paraneoplastic limbic encephalitis [3]. Although the distribution of the high intensity areas on MRI was compatible with limbic encephalitis, we should have suspected leptomeningeal metastasis because of the contrast enhancement.

The diagnosis of leptomeningeal metastases was delayed by negative finding on CSF cytology. Although Identification of malignant cells by CSF cytology is the diagnostic standard for leptomeningeal metastases, the sensitivity of CSF cytology has been reported at 75% and a negative finding cannot rule out leptomeningeal metastases [2]. Because the sensitivity is increased by repeated CSF sampling [7], the lumber puncture should have been repeated in the present case.

In conclusion, we reported a case of leptomeningeal metastasis of small cell lung cancer that required differentiation from paraneoplastic limbic encephalitis. Contrast-enhanced MRI should be performed even if limbic encephalitis is suspected, and leptomeningeal metastases should be suspected if the lesions are enhanced.

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Declaration of competing interest

I declare on behalf of my co-authors and myself that we do not have any conflict of interest to declare.

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