

# Meningitis as a Hidden Cause of Neurological Deterioration in Patients With Known Brain Metastases: A Report of Two Cases

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## Abstract

When a patient with known brain metastases presents to the emergency department with neurological deterioration, an overt diagnosis exists. However, alternative diagnoses should also be considered in the appropriate clinical context. A correct diagnosis is critical for the appropriate treatment, especially in cases, in which a reversible cause of illness exists. In this report, we describe two cases of cancer patients with known brain metastases in whom the neurological deterioration was due to carcinomatous meningitis and viral meningitis, respectively. A lumbar puncture was performed based on the fact that neurological deterioration was in contrast with the absence of new findings in brain CT scans. As it is emphasized by these two cases, patients with brain metastases, unchanged at CT imaging, and recent neurological deterioration must undergo lumbar puncture before their symptoms are considered a progression of their already existing brain metastases. In some cases, the deterioration might be due to a potentially reversible illness or due to an illness requiring specific treatment.

**Keywords:** Cancer; Brain metastases; Fever; Altered mental status; Headache; Meningitis

## Introduction

Brain metastases occur in about 25% of all cancer patients during the course of their illness. In adults, most brain metastases originate from lung cancers (50-60%), followed by breast cancers (15-20%), melanomas (5-10%) as much as cancers of the gastrointestinal tract and renal cell carcinomas [1].

Neurological manifestations occur in more than two-thirds

of patients with brain metastases. The clinical presentations include headache and vomiting (with or without nausea), altered mental status, ataxia, seizures, dizziness, hemiparesis, aphasia, visual reduction, cranial nerve impairment, etc. In some cases, the onset of neurological manifestations is abrupt like a stroke attack [2]. Moreover, fever may coexist both as a manifestation of cancer and also from the brain metastases itself [3].

When a patient with known brain metastases presents to the emergency department (ED) with one, or some, of these symptoms, an overt diagnosis exists. However, alternative diagnoses should also be considered in the appropriate clinical context. For example, symptoms like headache, nausea and vomiting, seizures, motor or sensory focal deficit and altered mental status may also occur in patients with meningitis [4]. Consequently, a correct diagnosis is critical for the appropriate treatment, especially in cases, in which a reversible cause of illness exists.

In this report, we describe two cases of cancer patients with known brain metastases in whom the neurological deterioration was due to meningitis.

## Case Reports

### Case 1

A 53-year-old female patient was brought to the ED due to excessive vomiting, headache, confusion and generalized malaise during the last few days. From her past medical history, she was diagnosed with invasive ductal carcinoma (IDC) stage 4 with bone metastases for which she received chemotherapy. A few days later, she underwent a brain magnetic resonance imaging (MRI) and she was diagnosed to have a mild ventricular distention and multiple small sized parenchymal metastases. From her neurological examination on admission, nuchal stiffness and altered mental status were observed while her inflammatory markers were the following: C-reactive protein (CRP) < 3.27 mg/L (0 - 5 mg/L), erythrocyte sedimentation rate (ESR) 2 mm/h (2 - 20 mm/h) and white blood cells (WBCs)  $21.760 \times 10^3/\mu\text{L}$  ( $4.000 - 11.000 \times 10^3/\mu\text{L}$ ), and polymorphonuclear neutrophils (PMNs)  $18.460 \times 10^3/\mu\text{L}$  ( $2.500 - 7.500 \times 10^3/\mu\text{L}$ ). She underwent a brain CT with intravenous contrast medium that revealed a mild ventricular distention without any widening of the peripheral subarachnoid spaces.

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As the brain computed tomography (CT) could not explain completely the clinical picture, she underwent lumbar puncture, which revealed a clear and colorless cerebrospinal fluid (CSF) with the presence of six cells, glucose of 25 mg/dL (serum glucose of 97 mg/dL), lactate dehydrogenase (LDH) of 504 U/L and protein of 250 mg/dL. From the CSF cytology, the presence of tumor cells was confirmed. She was treated with dexamethasone with gradual improvement of her clinical symptoms and finally she was referred to her oncologist for further treatment.

## Case 2

A 56-year-old male patient was admitted due to generalized malaise, headache, altered mental status, vomiting, nausea and fever (38.5 °C) for the last few days. On admission, his laboratory findings were the following: WBCs  $5.900 \times 10^3/\mu\text{L}$  ( $4.000 - 11.000 \times 10^3/\mu\text{L}$ ), PMNs  $5.500 \times 10^3/\mu\text{L}$  ( $2.500 - 7.500 \times 10^3/\mu\text{L}$ ), CRP 7.68 mg/L (0 - 5 mg/L) and ESR 102 mm/h (2 - 20 mm/h). From his past medical history, he was diagnosed with squamous cell lung carcinoma with brain metastases for which he received both chemotherapy and radiotherapy. The last days, before his current neurological deterioration and until the time of admission, he started dexamethasone in order to treat the brain peritumoral edema. Based on his medical history, he underwent a brain CT scan, which revealed brain metastases (the bigger one was located near cerebellum) with accompanied vasogenic edema. He was treated with dexamethasone and mannitol. Because of persistent headache and fever, in the absence of an obvious site of infection, coexisting meningitis was suspected. He underwent a lumbar puncture with the following CSF characteristics: clear and colorless, negative Gram and Ziehl-Neelsen stains, CSF cell count: 80 cells (54% PMNs and 46% lymphocytes), LDH of 69 U/L, glucose of 60 mg/dL (serum glucose of 139 mg/dL), and protein of 180.81 mg/dL. In the absence of titers for virus-specific antibodies in CSF, he was empirically treated with acyclovir. His symptoms improved rapidly and fever receded. After 5 days, he underwent a new lumbar puncture with the following results: CSF cell count of two cells, LDH of 46 U/L, glucose of 130 mg/dL (serum glucose of 203 mg/dL), and protein of 183.11 mg/dL. Two weeks after his admission, while the patient was asymptomatic, he underwent a brain MRI scan that revealed the already known metastases with accompanied peritumoral edema.

## Discussion

In the first case, the neurological deterioration was due to a non-reversible cause. The infiltration of the leptomeninges by malignant cells, as a complication of cancer, is called carcinomatous meningitis and breast cancer is the most common solid tumor complicated by meningeal carcinomatosis at a proportion of approximately 5% [5]. Although the overall prognosis remains poor, the expansion of the repertoire of available drugs for intrathecal administration, systemic chemotherapy,

gene therapy and the use of immunotoxins for the management of leptomeningeal metastases can prolong life expectancy and improve the health-related quality of life in these patients [6]. To these treatment options, the craniospinal radiotherapy should also be added, which is feasible and effective for palliative treatment of leptomeningeal metastases [7].

In the second case, the neurological deterioration was due to a self-limiting, potentially reversible [8] and, in cases of bacterial meningitis, treatable illness (especially if the appropriate treatment initiates in time) [9].

Our patients had both negative Kernig's and Brudzinski's sign, while only the first one had nuchal rigidity. Nevertheless, it has been reported that nuchal rigidity was found during clinical examination in 35% and 13% of the acute care geriatric and younger patients, respectively, despite the absence of meningitis [10]. Anyway, the three classic meningeal signs (Kernig's sign, Brudzinski's sign and nuchal rigidity) were not able to accurately discriminate patients with meningitis from those without [4] and individual items of the clinical history have low accuracy for the diagnosis of meningitis [11]. However, in patients with suspected meningitis, rapid and accurate clinical evaluation is required in order to determine the need for lumbar puncture [4].

The main reason that leads to the decision to perform a lumbar puncture in our patients was the fact that their neurological deterioration was in contrast with the absence of new findings in the performed brain CT scans. This fact, combined with the presence of headache and altered mental status, raised the suspicion of meningitis.

As it is emphasized by these two cases, patients with brain metastases, unchanged at CT imaging, and recent neurological deterioration must undergo lumbar puncture before their symptoms are considered a progression of their already existing brain metastases. In some cases, the deterioration might be due to a potentially reversible illness or due to an illness requiring specific treatment.

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## Conflicts of Interest

None of the authors has any conflicts of interest.

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