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Case Report

Leptomeningeal carcinomatosis from breast cancer initially mimicking cerebral infarction on MRI ☆

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ABSTRACT

A female patient in her early 50s with breast cancer underwent breast-conserving surgery, followed by radiation therapy. She developed multiple lung and bone metastases and was started on chemotherapy with bevacizumab and paclitaxel 3 years later. After 6 months of chemotherapy, she developed a decline in conversation and memory. Magnetic resonance imaging (MRI) was conducted and showed multiple cortical and subcortical lesions and nodules with restricted diffusion but with no contrast enhancement on gadolinium (Gd) enhanced T1-weighted image, raising a suspicion of Trousseau's syndrome. A follow-up MRI revealed unchanged signal intensity of the lesions but with minimal enlargement. The cerebrospinal fluid cytology was negative for malignancy. Consequently, an open biopsy of the cortical lesion was conducted. Histopathology showed that the tumor cells were morphologically similar to the primary breast cancer extending from the brain surface along the Virchow–Robin spaces, which yielded a diagnosis of leptomeningeal carcinomatosis from breast cancer. Contrast enhancement on Gd-MRI may be impaired in case of tumor spread along the perivascular space or in patients treated with bevacizumab.

Introduction

Leptomeningeal carcinomatosis (LC) is an advanced stage of cancer; however, with early diagnosis and appropriate therapeutic strategies, patient's prognosis can be improved [1,2]. Furthermore, contrast-enhanced magnetic resonance imaging (MRI) is a useful tool for LC diagnosis, which demonstrates leptomeningeal enhancement [1]. Conversely, cancer-related thromboembolism, such as deep vein thrombosis, pulmonary embolism, and cerebral infarction, can occur in patients with cancer, referred to as Trousseau's syndrome [3].

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Here, we present a case of LC from breast cancer that was initially suspicious of Trousseau's syndrome owing to the lack of enhancement and the findings resembling cortical laminar necrosis, leading to a delay in diagnosis and treatment.

Case report

A female patient in her early 50s was diagnosed with breast cancer (cT2N1M0, stage IIB). Biopsy demonstrated invasive ductal carcinoma, negative for estrogen receptor (ER) and progesterone receptor (PgR), human epidermal growth factor receptor 2 (HER2) score of 2 (fluorescence in situ hybridization negative), and a Ki-67 index of 75%. Thereafter, she received preoperative chemotherapy, followed by breast-conserving surgery with axillary lymph node dissection. After surgery, she underwent radiotherapy and 6 months of adjuvant chemotherapy, and she was undergoing close monitoring for 2 years without further treatment.

Three years after the initial diagnosis of breast cancer, the patient was diagnosed with multiple lung and bone metastases on computed tomography. She was started on chemotherapy with bevacizumab and paclitaxel.

After 6 months chemotherapy initiation, she was referred to the outpatient department due to a decline in conversation and memory. MRI showed multiple cortical and subcortical lesions, which revealed restricted diffusion but failed to demonstrate contrast enhancement on gadolinium (Gd) enhanced T1-weighted image (Figs. 1A–E). Trousseau's syndrome was suspected, and aspirin was initiated. A month after, a repeat MRI was conducted due to lightheadedness. The signal intensity of the lesions on DWI remained unchanged with minimal increase in size, which was atypical for Trousseau's syndrome. However, due to the lack of contrast enhancement, further examination was not performed to examine suspicious brain metastases. She developed dysphagia and neurological dysfunction, including impaired consciousness and paralysis, which gradually progressed. On the MRI performed 2.5 months after the initial one, further enlargement was observed and a minimal increase in lesions with a similar signal (Figs. 1F and G).

As metastatic lesions were suspected, a CSF examination was conducted. The CSF examination demonstrated mild elevations in protein and interleukin 6; however, the CSF cytology was negative for malignancy. Consequently, an open biopsy of the brain lesion was conducted to confirm the diagnosis. The lesion in the right temporal lobe (Fig. 1H) including the cortex and white matter was sampled in a 1.5-cm block. Histopathology revealed tumor cells extending from the brain surface along the Virchow–Robin spaces (Figs. 2A and B) but with no invasion in the surrounding brain parenchyma. Within the parenchyma, no apparent mass was formed. The tumor cells were morphologically similar to the primary breast cancer and

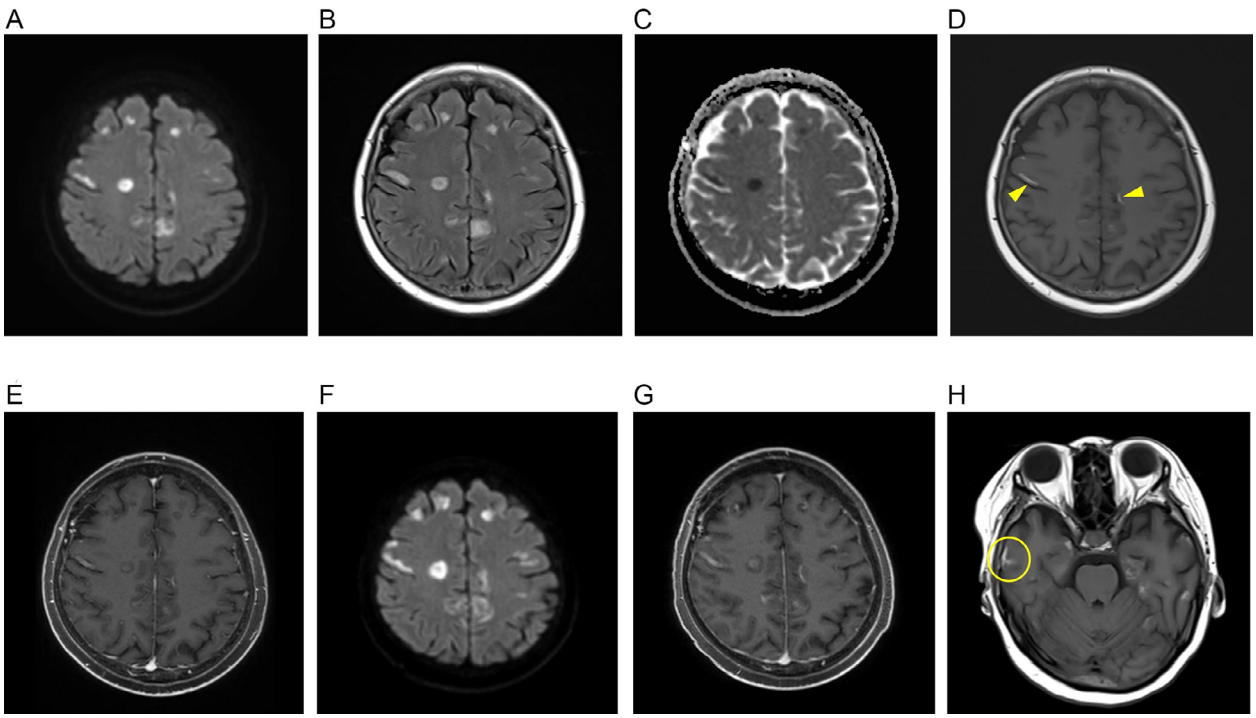

Fig. 1 – Initial brain MRI (A-E) and follow-up MRI (F-H). Multiple cortical and subcortical high signal intensity on diffusion-weighted image (DWI) (A) and fluid-attenuated inversion recovery sequences (B), and low values on apparent diffusion coefficient map (C). Scattered high signal intensity along the cortex on T1-weighted images (D, arrowheads). No contrast enhancement on gadolinium (Gd) enhanced T1-weighted image was observed (E). On follow-up DWI, the signal of lesions remained unchanged with slight increase in size (F). No contrast enhancement was observed on Gd-enhanced T1-weighted image (G). A linear lesion with high signal intensity on T1-weighted images was also observed in the biopsied site (H, circle).

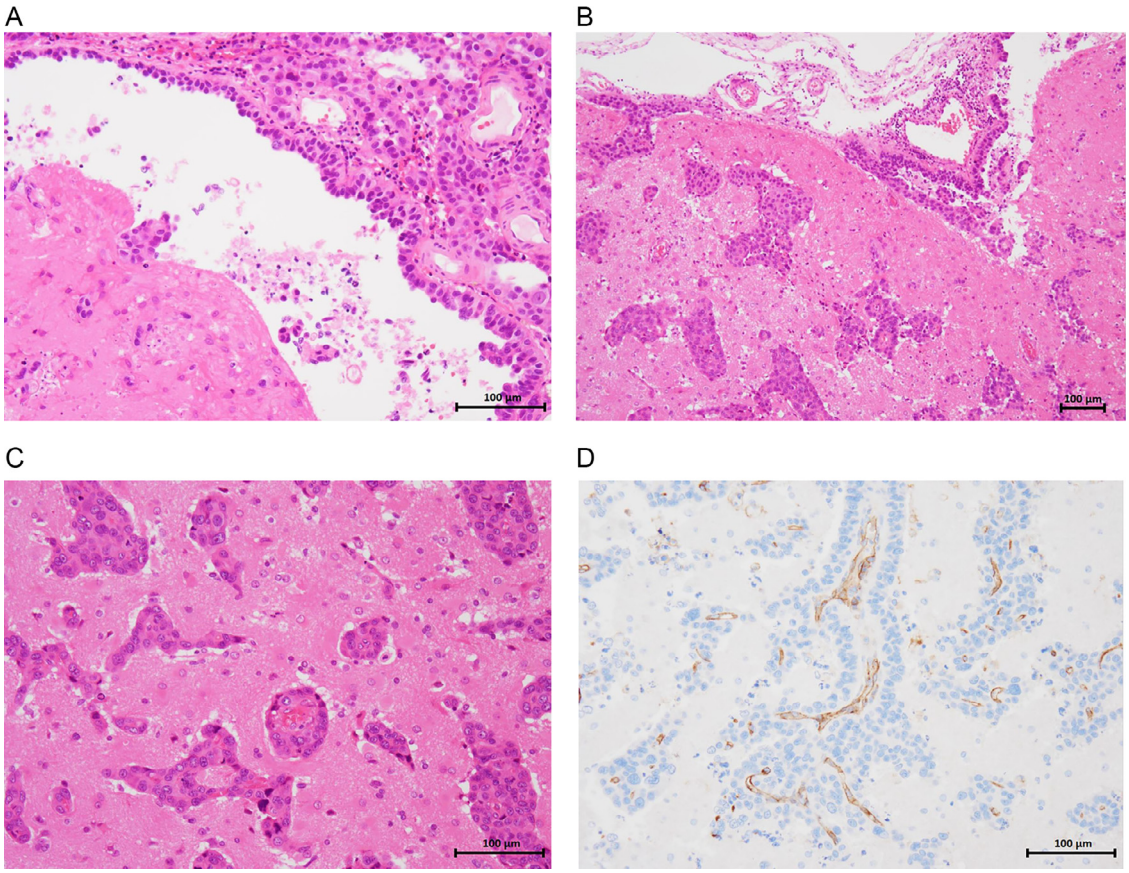

Fig. 2 – Histopathology of biopsied specimen from the right temporal lobe (A-C; hematoxylin and eosin stain, D; CD31 immunohistochemical staining, bars represent 100 μm). Atypical cells with enlarged nuclei along the arachnoid and in the subarachnoid space (A). Tumor cells extending from the brain surface along the Virchow–Robin space (B). Perivascular space of micro vessels was filled with tumor cells (C). The vessel lumen collapses due to compression by tumor cells (D).

immunohistochemically positive for CK7 and GATA3, but negative for CK20. Biomarker expression was ER and PgR negative, with a HER2 score of 2 and a Ki-67 index of 90%, closely resembling that of primary breast cancer. Thus, a diagnosis of Leptomeningeal carcinomatosis (LC) from breast cancer was established.

Whole-brain irradiation of 20 Gy in five fractions was performed; however, symptoms such as impaired consciousness and paralysis failed to improve. The patient was placed on palliative care and was deceased 4 years and 4 months after her initial breast cancer diagnosis.

Discussion

LC is defined as leptomeningeal infiltration, including the pia mater, arachnoid, and subarachnoid space from a solid primary tumor [1]. In approximately 5%-10% of all solid tumors, LC has been reported to occur, mainly in adults with breast cancer, lung cancer, and malignant melanoma [2]. The incidence of LC in breast cancer has been documented to vary from 0.8% to 6.6% in clinical reports and 2.6%–16% in autopsy series [2]. However, a recent study demonstrated that LC prevalence was only 0.3% in a consecutive, unselected series of breast cancer cases [2].

To diagnose LC, CSF cytology and contrast-enhanced MRI are commonly used. However, sensitivity varies widely (45%–80% for cytology and 20%–91% for MRI), which renders the diagnosis challenging [2]. In the present case, CSF cytology was negative. Three consecutive contrast-enhanced MRI revealed no contrast enhancement in any of the lesions. The lack of enhancement in the lesions, despite their continuing growth, posed challenges in establishing the presence of metastases. Furthermore, the T1-weighted image demonstrated a linear lesion with high signal intensity along the cortex, leading to a suspicion of Trousseau's syndrome.

The lack of a contrast enhancement has 2 possible reasons: tumor expansion along the Virchow–Robin space and the effect of bevacizumab treatment.

In a patient with LC from lung cancer, multiple extensive lesions showed restricted diffusion but without contrast enhancement on Gd-MRI similar to the present case [4]. Pathological analysis showed tumor cell infiltration via the perivascular space and microinfarction due to intracapillary infiltration [4]. However, no probable evidence of destruction of vascular structures or tumor invasion within the brain parenchyma was observed. This absence of vascular disrup-

tion would not induce contrast media leakage from the vessels, leading to non-contrast enhancement of the lesions.

In the present case, nodular lesions that appeared as intraparenchymal metastases in the deep white matter were noted. In the previous case with LC from breast cancer, pathologic findings showed that the tumor cells also extended along the Virchow–Robin space and the disseminated lesions around the brainstem infiltrated and formed a nodular lesion within the parenchyma [5]. Similarly, in the present case, the nodular lesions would be disseminated lesions that spread along the perivascular spaces of medullary arteries, resulting in a lack of contrast enhancement.

Antiangiogenic agents, particularly those targeting the vascular endothelial growth factor, such as bevacizumab, can remarkably reduce contrast enhancement on Gd-MRI [6]. In our case, the impact of bevacizumab on contrast enhancement remains uncertain as we did not compare the contrast enhancement of the lesions before and after chemotherapy. However, bevacizumab could be responsible for the lack of enhancement, provided that the treatment had been administered from 8 months prior to the initial brain MRI.

T1-weighted images exhibited high signal intensity along the cortex, which resembled cortical laminar necrosis and prompted initial suspicion of cerebral infarction. In the biopsied specimen, a linear high signal intensity on T1-weighted images was included and it pathologically represented necrotic and edematous areas without evidence of calcification or hemorrhage. Histopathology further demonstrated that tumor cells occupied the perivascular space of the microvessels in the superficial layer, resulting in external compression (Figs. 2C and D). This finding could support the ischemic changes noted. However, other potential causes, such as the effects of coagulation necrosis due to bevacizumab treatment, could not be excluded.

Conclusion

It is noteworthy that contrast enhancement on Gd-MRI may be impaired in cases of tumor spread along the perivascular space secondary to LC or in patients treated with antiangiogenic agents. In such cases, biopsy should be considered if contrast enhancement is absent on repeated contrast-enhanced MRIs, and if the imaging course is atypical for metastasis.

Patient consent

Written informed consent was obtained for publication of this case report. We are retaining the agreement document with us for own record.

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