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Case Report

Symptoms of Isolated Optic Neuropathy in a Patient with Systemic, Brain, and Meningeal Metastases from Breast Cancer: A Case Report

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Keywords
Breast cancer · Metastasis · Optic neuropathy · Imaging · Case report

Abstract
Introduction: Ocular metastases from breast cancer, particularly involving the optic nerve, are rare and pose a diagnostic challenge. Typically, optic nerve metastases are believed to originate from nearby choroidal metastases or hematogenous spread through the posterior ciliary arteries. However, there have been some reports of metastases through leptomeningeal dissemination. The aim of this report was to describe a case of multiple brain metastases from breast cancer without subjective symptoms other than central scotoma, which was diagnosed with repeated magnetic resonance imaging (MRI). ***Case Presentation:*** A 62-year-old woman who had previously undergone a mastectomy for left breast cancer complained of left ocular pain during eye movement and left visual loss. Initial contrast-enhanced MRI showed no significant abnormalities, and idiopathic optic neuritis was suspected. Despite steroid pulse therapy, her visual function did not improve. After four and a half months, her visual acuity worsened, and repeat contrast-enhanced MRI showed brain metastases involving the optic nerve sheath. ***Conclusion:*** Despite the multiple brain metastases, ultimately the patient's only symptom was unilateral visual loss. These findings highlight the usefulness of repeated contrast-enhanced MRI for detecting brain metastases, especially in cases without other apparent neurological symptoms or initial imaging abnormalities.

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Introduction

The most common sites for distant metastases of breast cancer are bone, lung, skin, lymph nodes, liver, pleura, and central nervous system, whereas ocular metastasis is relatively rare, at 0.2%. More than 90% of ocular metastases are found in the choroid, but metastases in the optic nerve are very rare [1, 2]. However, a few cases of metastases in the optic nerve have been reported without specific findings on fundus examination and ocular imaging [3]. On the other hand, brain metastases of breast cancer often present with various neurological symptoms, although 22% were reported to be asymptomatic [4]. In this report, we describe a case of multiple metastases of breast cancer to the brain, including the optic nerve sheath, that showed only unilateral optic nerve symptoms without fundus or neuroimaging abnormalities that were detected only by repeated contrast-enhanced magnetic resonance imaging (MRI). The CARE Checklist has been completed by the authors for this case report and attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000536189).

Case Report

A 62-year-old woman visited an eye clinic with a 2-month history of vision loss in the left eye and left ocular pain during eye movement. She reported neither photophobia nor night blindness. The critical fusion frequency (CFF) was decreased in her left eye, and she was referred to our hospital for detailed examination. She had a history of left breast cancer for which she underwent a mastectomy 24 years earlier. She experienced chest wall recurrence of breast cancer 19 and 11 years earlier and received several chemotherapy and radiation therapy cycles. Two years earlier, multiple liver metastases were discovered, and at the time of her first visit to our department while she was still undergoing chemotherapy.

Her best corrected visual acuity (BCVA) at the first visit was 1.5 in the right eye and 0.5 in the left eye with a Landolt C chart. Intraocular pressure was 17.0 mm Hg in the right eye and 15.0 mm Hg in the left eye. CFF was 45 Hz in the right eye and 15 Hz in the left eye, and the left eye showed a relative afferent pupillary defect. Slit-lamp microscopy and fundus examination showed no swelling of the optic nerve head or other abnormalities (Fig. 1a, b). Goldmann perimetry (GP) showed a central scotoma in the left eye and a dense nasal scotoma in the periphery (Fig. 1c, d). Fluorescein angiography showed no abnormal findings in the left eye including the optic nerve head (Fig. 1e, f). Contrast-enhanced MRI of the brain including the orbital region was reported as normal (Fig. 1g, h). Blood examinations, including anti-aquaporin-4 antibodies, were negative for any evidence of neuromyelitis optica. Since there were no findings to suspect metastases of breast cancer to the optic nerve or intracranial space on contrast-enhanced MRI, no further examinations, including lumbar puncture, were performed. Based on the clinical findings, a therapeutic trial for idiopathic optic neuritis was started with steroid pulse therapy (prednisolone 1,000 mg/day for 3 days, 2 courses). Fifteen days after the initial visit, at the end of the second course of steroid pulse therapy, her left BCVA was 0.3, the left CFF was 5 Hz, and there was little improvement in the visual field defects on GP (Fig. 2a). Therefore, the effect of steroids was considered poor, and the patient was followed up every 1.5 months without treatment.

Four and a half months after the initial visit, the patient had no subjective deterioration, but her left BCVA was reduced to 0.06, CFF was unmeasurable, and the GP showed an exacerbation of the central scotoma (Fig. 2b). Therefore, contrast-enhanced MRI was repeated and showed enhancement of the swollen left optic nerve and sheath, left occipital lobe, and left cerebellar hemisphere, which were considered to be metastatic breast cancer in the optic

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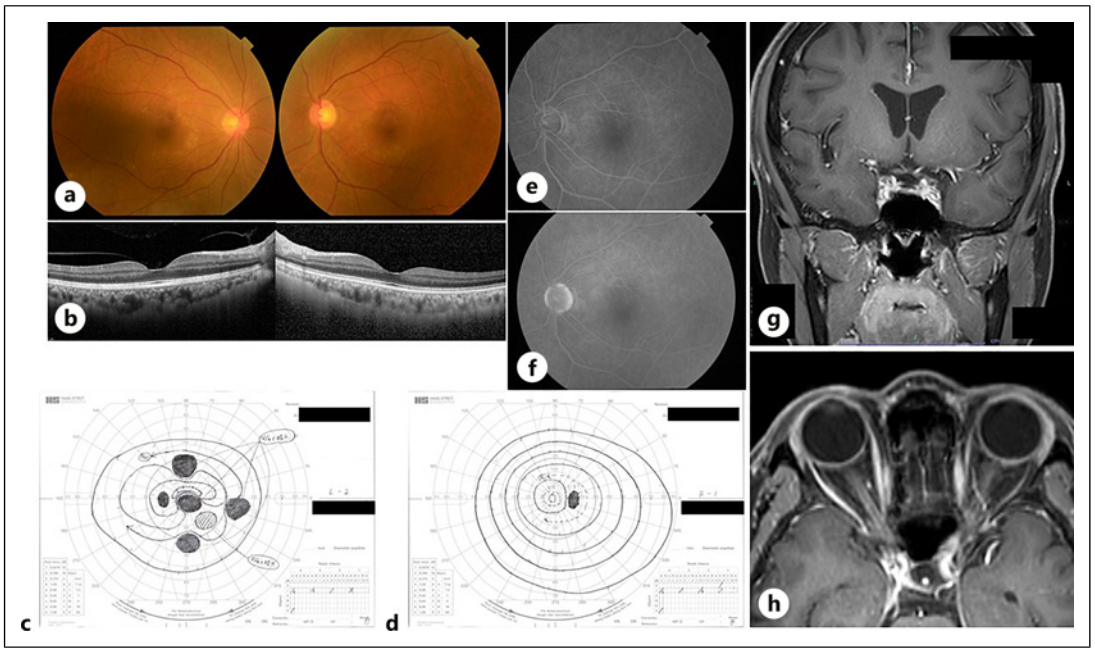

Fig. 1. Baseline findings. **a** The fundus photographs of both eyes show no abnormalities such as swelling and redness of the optic nerve papillae. **b** Optical coherence tomography shows no abnormalities in both macule. **c** GP at the first visit shows a central scotoma in the left eye and an absolute scotoma in the periphery. **d** The visual field of the right eye is normal. Fluorescein angiography of the left eye in the early (**e**) and late (**f**) phases shows no abnormal findings, including the optic nerve. On MRI of the brain including the orbital region at the initial visit, the coronal (**g**) and axial (**h**) images were reported as normal by the radiologist.

nerve sheath and brain (Fig. 3). In addition, computed tomography showed an increase in the liver metastases; she then underwent chemotherapy with radiation. Fifteen months after the initial visit, the left optic nerve head was pale, and her left BCVA remained poor at 0.04.

Discussion

In this report, we have described a case of multiple metastases of breast cancer to the brain, including the optic nerve sheath, that presented with only unilateral optic nerve symptoms without any abnormalities on fundus examination or initial MRI. The metastases were subsequently diagnosed by repeated contrast-enhanced MRI that led to the discovery of increased liver metastasis by (body) CT, which in turn influenced the treatment strategy for breast cancer. The characteristic of this case was the presence of multiple brain metastases, despite the absence of neurological findings and symptoms other than a central scotoma. Most optic nerve metastases are considered to be direct metastases from choroidal metastases near the papilla or hematogenous metastases from the posterior ciliary artery [3, 5], but cases of meningeal dissemination have also been reported [6], and in general, multiple metastases in the cranium are presumed to be meningeal carcinomatosis. The present patient had no choroidal metastases, and contrast-enhanced MRI showed metastases in the occipital lobe and cerebellar hemisphere, as well as contrast effects on the optic nerve sheath, suggesting metastasis to the optic nerve sheath due to meningeal seeding.

The main symptoms associated with meningeal carcinomatosis include headache (83%), nausea and vomiting (72%), abnormal mental and physical behavior (42%), and other

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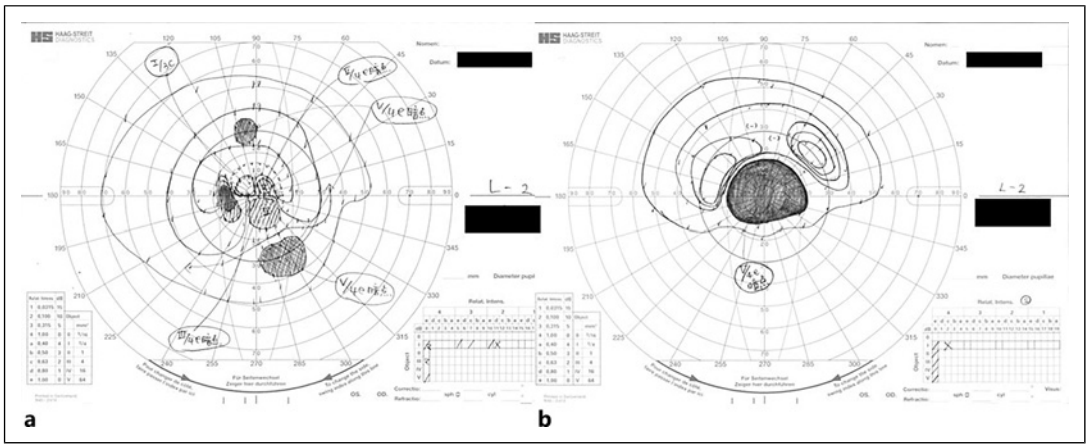

Fig. 2. GP. **a** Visual field impairment in the left eye as assessed by GP at the completion of steroid pulse treatment. **b** Worsening of the central scotoma in the left eye is observed on GP four and a half months after the initial visit.

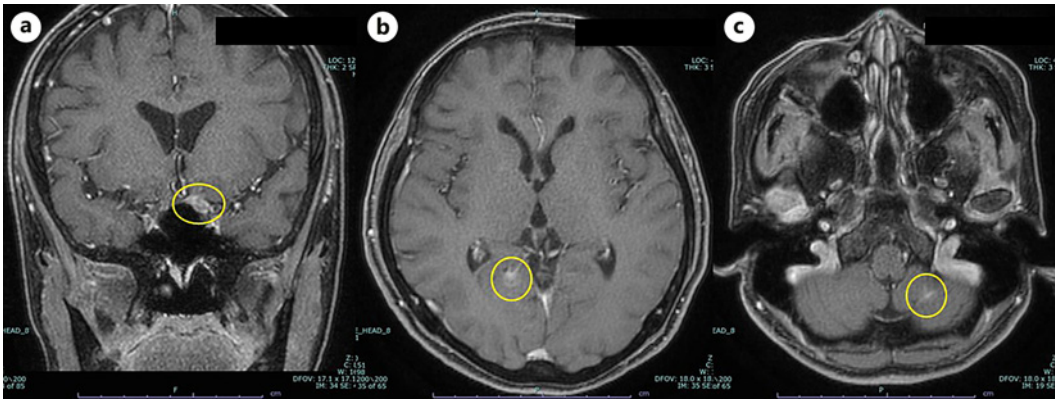

Fig. 3. Contrast-enhanced MRI of the brain, including the orbital region, four and a half months after the initial visit. **a** Coronal images through the optic nerve show swelling and the presence of meningeal enhancement of the left optic nerve. Ring-shaped enhanced lesions are identified in the right occipital lobe (**b**) and left cerebellar hemisphere (**c**).

symptoms such as dizziness, seizures, and increased intracranial pressure [7, 8]. The frequency of vestibulocochlear neuropathies has been reported to be 39%, but the frequency of cranial nerve symptoms increased as the disease progressed, eventually being present in 75% of patients with meningeal carcinomatosis [9]. However, our patient did not complain of any such symptoms other than unilateral vision loss, and she had no cerebellar symptoms despite the presence of metastatic lesions in the cerebellar hemispheres. Cho et al. [3] reported a case of a solitary optic nerve metastasis from breast cancer that initially presented with only unilateral visual loss mimicking idiopathic optic neuritis-like, with no specific findings on MRI, cerebrospinal fluid (CSF) cytology, or fundus findings. However, cases such as the present one, in which vision loss alone leads to the diagnosis of multiple brain metastases, are relatively rare. Furthermore, it has been reported that 30% of cases of meningeal carcinomatosis are completely unidentifiable on imaging studies [5], which can make diagnosis difficult. CSF cytology is considered useful for the definitive diagnosis of meningeal carcinomatosis, but

false-negatives are very common, and multiple lumbar punctures (LPs) are often required to identify tumor cells [10, 11]. In fact, the yield of the initial lumbar puncture is 44–67%, but this increases to 84–91% on the second lumbar puncture [12], and in patients who undergo three high-volume LPs, the sensitivity becomes greater than 90%, with a specificity exceeding 95% [13]. Lumbar puncture carries risks of complications such as brain herniation, spinal herniation, nerve damage, infections, and bleeding; however, the frequency of complications is relatively low [14]. Therefore, CSF cytology is highly valuable when there is suspicion of leptomeningeal dissemination in solid cancers.

A point of reflection in this case is that we did not perform additional tests when the limited effectiveness of steroids became apparent. Initially, we suspected optic nerve metastases from breast cancer, and MRI was performed. The radiologist reported that there were no abnormalities on MRI, despite the fact that abnormal signal enhancement was observed in the left optic nerve, as shown in Figure 1h. We classified the findings as artifacts based on the radiologist's opinion. In addition, as mentioned earlier, optic nerve metastases from breast cancer are primarily thought to occur as a result of choroidal metastases or hematogenous spread. This patient presented with only optic nerve symptoms, and because there were no other neurological symptoms, we did not consider performing invasive CSF analysis to explore the possibility of leptomeningeal dissemination. However, given that the patient was a known breast cancer patient and presented with evident optic nerve symptoms, leptomeningeal dissemination should have been considered. At the very least, after observing no response to steroids, we should have contemplated reevaluation with either contrast-enhanced MRI, serial LPs for CSF analysis, or both. Even though the imaging studies at the initial visit were reported as negative, retrospectively, we should have performed spinal fluid analysis at the initial presentation as the yield can be greater than 90% [13] given the context of suspected invasive optic neuropathy in a patient with a history of breast cancer. Despite the aforementioned points for reflection, in this case, the early detection of deteriorating ophthalmological findings by the frequent follow-up may have prompted the re-examination of imaging, ultimately aiding in the final diagnosis of metastatic optic neuropathy. Meningeal metastases from breast cancer are associated with a grim prognosis; however, there have been reports of extended survival and improved quality of life with systemic chemotherapy and craniospinal radiation therapy [15]. To enable more timely therapeutic interventions, it appears necessary to incorporate additional assessments at earlier stages of the clinical course.

We describe a patient with multiple brain metastases who presented initially with symptoms solely attributed to an optic neuropathy that mimicked optic neuritis clinically. However, the correct diagnosis was reached after a contrast-enhanced MRI was repeated. The possibility of a metastatic tumor should always be considered in the setting of optic neuropathy with poor steroid response in patients with a background of malignant disease. For better management of the underlying disease, repeated contrast-enhanced MRI, with or without serial CSF fluid analysis, may be useful despite the absence of findings to suggest meningeal dissemination.

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Statement of Ethics

This study was conducted in accordance with the Declaration of Helsinki. Written, informed consent was obtained from the patient for publication of this case report and accompanying images. Ethical approval is not required for this study in accordance with local or national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Akika Kyo managed the patient, reviewed her records, and drafted the manuscript. Manabu Yamamoto contributed to the conception and revision of the manuscript. Takeya Khono and Yusuke Haruna assisted in drafting the manuscript. Shigeru Honda actively revised and edited the manuscript. All authors have read and approved the final version of the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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