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CASE REPORT

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Application of optic neuro-ophthalmology imaging in latent meningeal metastases of lung cancer

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Abstract

Latent intracranial meningeal metastases (IMM) of lung cancer is difficult to determine, yet it is critical to do so given that it impacts the treatment agent. Studies on this disease are rare, thus necessitating further investigation. As a case study, we will explore the application of optic neuroimaging in IMM. A 62-year-old female patient was diagnosed with lung adenocarcinoma, which had progressed to osseous metastasis. During the course of chemotherapy, the patient had bilateral vision loss and paralysis of extraocular muscles. Ophthalmologists ruled out disease of the retina and suspected intracranial metastasis; however, brain-enhanced magnetic resonance angiography and magnetic resonance venography were normal. Given the patient's severe osteoarthropathy and poor physical condition, she refused to undergo a lumbar puncture examination. Optic neuro-ophthalmology imaging was ultimately used. Utilizing optical coherence tomography, we found that the basement membrane layer in the papilledema was protruding up towards the vitreous cavity. To assist in visualization, the optic nerve sheath was enhanced with optic magnetic resonance imaging. With these methods, the dural metastasis was identified, the treatment agent was changed for the patient, and she had a successful recovery. Thus, optic neuro-ophthalmology imaging should be recommended for patients who are in the latent course of dural metastasis, and it could also be used to evaluate therapeutic efficacy.

KEYWORDS

latent intracranial dural metastasis, lung cancer, optic nerve sheath, optic neuro-ophthalmology imaging, optical coherence tomography

INTRODUCTION

Intracranial meningeal metastases (IMM) is not frequent, but it is a complication of cancer metastasis often seen in lung and breast cancer.[1,2] Early diagnosis plays a pivotal role in guiding the treatment plan and prognosis. Image findings are useful for diagnosis, and gadolinium-enhanced brain magnetic resonance imaging (MRI) scans are mainly used.[3] The specific MRI findings are divided into diffuse dural enhancement and focal-type. Focal-type can be classified into convexity-case (CO), falx-case (F), and cerebellar tentorial-case (CT) depending on tumor localization. In F and CT, diagnosis may be delayed because it will be asymptomatic.[4] For asymptomatic patients with suspected IMM, repeated lumbar puncture (LP) is needed for diagnosis. However, there are some patients with contraindications of LP or for whom LP fails. A noninvasive, reproducible, and effective method for diagnosis is thus necessary.

Here we present an elderly patient with lung cancer combined with latent IMM. Although her brain imaging was normal, LP could not be conducted. Hence, optic neuro-ophthalmology imaging was used to identify the IMM. We review the process of diagnosis and systematically discuss the features of imaging used in IMM detection.

To our knowledge, this is the first study concerning the diagnosis of lung cancer with IMM through optic

neuro-ophthalmology imaging. These findings will be helpful for thoracic surgeons and oncologists to recognize that optic imaging is a better method for IMM diagnosis and clinical treatment.

CASE PRESENT

A tumor was identified in a 62-year-old female patient in the left chest wall 2 years ago. She occasionally coughed and felt chest tightness with accompanying weight loss. She had a history of thyroid nodules and osteoarthropathy. Chest computerized tomography revealed left upper lobe central lung cancer with obstructive atelectasis. There were multiple lymph nodes in the right hilar and mediastinum, in addition to a lot of small pulmonary nodules. Single-photon emission computed tomography analysis found multiple bone metastases. A biopsy was performed via bronchofibroscopy. Histopathological examination documented lung adenocarcinoma. The gene examination was made by RT-PCR and EGFR exon 19 del was found in this patient. Pemetrexed disodium (500 mg/m^2) with nedaplatin (100 mg/m^2) treatment were used for five cycles. Follow-up computerized tomography revealed that the mass had reduced in size. However, the general health of the patient became poor and she was only treated with pemetrexed disodium when she became unable to endure the standard chemotherapy.

A month later, she developed a loss of vision in her right eye with an accompanying headache. Her vision acuity was down from 20/20 to <20/200. At the same time, the right eyeball had lateral rectus paralysis. Ophthalmological examination revealed papilledema of bilateral eyes. Given that most patients with papilloedema have elevated intracranial pressures, the ophthalmologist suggested excluding intracranial metastasis from consideration. Since the patient suffered from severe osteoarthropathy and poor physical condition, she refused LP examination. Brain enhanced magnetic resonance angiography and magnetic resonance venography were performed to exclude intracranial metastasis and intracranial venous sinus occlusion. While all of the examinations were normal, the patient's physical condition further deteriorated. The tumor marker, carcinoembryonic antigen (CEA), increased to 129 ng/ml. According the gene examination, we changed the pemetrexed disodium to gefitinib, and as a result the lesions improved and the tumor markers decreased.

Four months later, the vision in her bilateral eye started to deteriorate to a visual acuity of no light perception on the

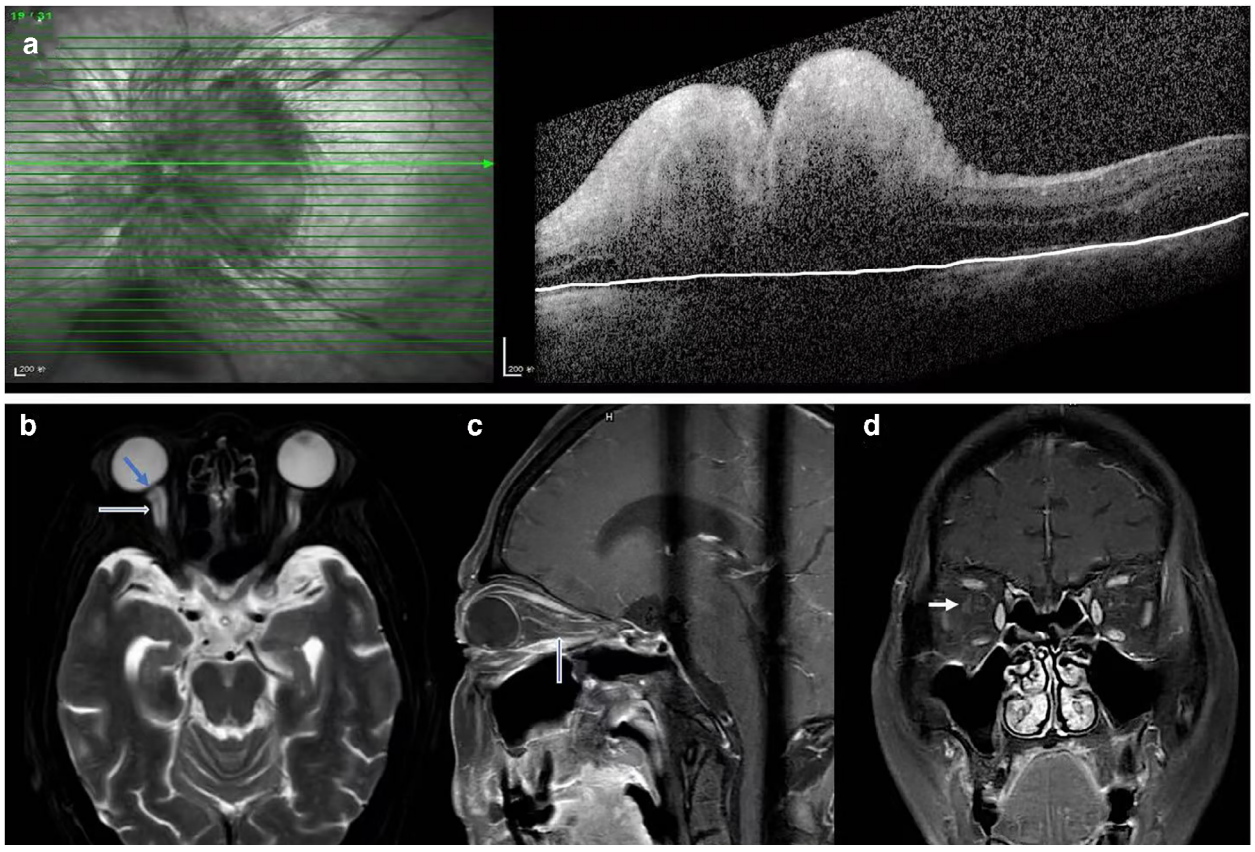

FIGURE 1 OCT and orbit MRI findings for the patient. (a) The basement membrane layer in the papilledema is protruding up towards the vitreous cavity from the OCT. (b) The axial T2 weighted MRI revealed that the optic nerve distortion is accompanied by atrophy and subarachnoid space dilatation. The optic papilla protrudes up to the vitreous (white arrow). (c) Axial gadolinium-enhanced TI orbit MRI revealed the enhancement of the optic nerve sheath (white arrow)

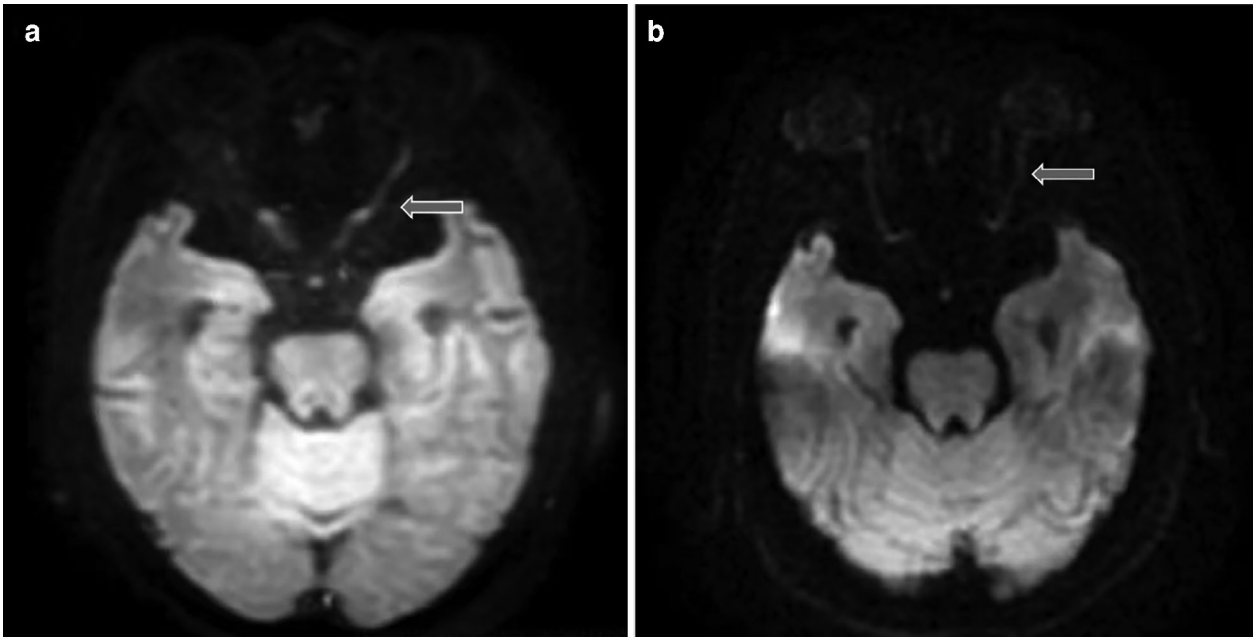

FIGURE 2 Magnetic resonance imaging (MRI) changes in the optic nerve before and after treatment. (a) Axial diffusion-weighted MRI found the diffusion limitation of the bilateral optic nerve with a high signal. (b) Axial diffusion-weighted MRI found that the diffusion limitation of the optic nerve was significantly improved after the treatment agent was changed. *Note:* The arrow indicates optic nerve

right and light perception on the left. Ophthalmological examination confirmed bilateral optic atrophy. Again, the patient refused the LP examination. Brain enhanced MRI continued to not detect any abnormalities. Two months later, the tumor marker CEA elevated slightly and bilateral visual acuity worsened to include no light perception. Because the patient refused LP, there was much difficulty determining whether the patient had high intracranial pressure, if there was intracranial metastasis and drug resistance, and the best treatment agent. A neuro-ophthalmologist advised performing optical coherence tomography (OCT) of the optic nerve head (ONH) with enhanced MRI of the optic nerve. The OCT revealed that the basement membrane layer in the papilledema was protruding up towards the vitreous cavity (Figure 1(a)). The MRI revealed that the optic nerve was distorted and atrophied, the subarachnoid space was dilated (Figure 1(b)), and the optic nerve sheath (ONS) was enhanced (Figure 1(c)). Based on clinical features, MRI findings, and tumor marker (CEA) findings, the patient was diagnosed with intracranial metastasis and intracranial hypertension.

Considering that the osimertinib was better in treating the brain metastasis, we changed the treatment agent to 80 mg ositinib and 15 mg/kg bevacizumab. At a 2-year follow-up after treatment, the patient's condition was stable, her headache and extraocular muscle paralysis were significantly improved, and visual acuity was slightly increased. MRI found that the diffusion limitation of the optic nerve was significantly improved (Figure 2(a),(b)).

DISCUSSION

IMM is observed in various cancers, including lung and breast cancer, and its timely diagnosis is required for successful patient treatment. Selection of drugs with blood–brain barrier penetration and stable intracranial drug concentration is critical to prolong the survival period of patients. Latent meningeal metastasis of lung cancer is difficult to determine, and to date there have been few studies exploring a new method for diagnosis.

Gadolinium-enhanced brain MRI scans and LP are mainly used for the diagnosis of IMM. However, there are no features in latent IMM that can be detected with imaging. Evaluation of serum tumor marker levels is also used to assess the IMM development. A subgroup of lung and breast cancer patients with IM do not show elevated tumor marker levels.[5] Patients with brain metastases, especially meningeal metastases, may have increased cerebrospinal fluid (CSF) pressure, protein content, and biopsy cytology, which can be diagnosed with LP and CSF pressure detection. There are some patients with contraindications of LP, or for whom lumbar puncture fails. Thus, identifying novel indicators of IM is needed for these patients.

Intracranial hypertension (IH) can cause papilledema, and the OCT imaging of papilledema is different from that for other conditions. In normal controls, the retinal pigment epithelium (RPE)/brush member (BM) around the optic nerve is V-shaped and angled away from the vitreous as it approaches the neural canal opening. However, in patients

with papilledema due to IH, it has been shown on OCT to have an inverted U-shape towards the vitreous.[6] A limitation of utilizing peripapillary BM/RPE changes to guide clinical care is that these changes require intensive image processing, often with manual components. This is due to the difficulty in identifying the BM/RPE boundary beneath the swollen ONH.[7,8] Previously described orbital MRI imaging found protrusion of the optic neuritis (ON) head with IH, enhancement of the ON head, flattening of the posterior sclera, and increased peri-ON CSF.[9–11]

In this case, we also found enhancement of the ONS in MRI. It is a useful finding of an imaging feature for IMM. The optic nerve is the projection fiber of the white matter of the brain, which belongs to the central nervous system. The outer surface of the optic nerve is wrapped by the nerve sheath, which is extended by three layers of meninges. Thus, meningeal lesions affect the ONS.[12] Previous cases have indicated that the ONS and optic nerve are associated with carcinoma through paraneoplastic syndrome[13] and metastasis.[14,15] Metastasis of meningeal lesions also affects the ONS and optic nerve. Lung cancer is prone to intracranial metastasis, mainly blood metastasis, and the destruction of the blood–brain barrier is the main cause of metastasis. Lung cancer may metastasize to the orbit relatively early in the disease course, and the ONS could be involved.[16,17] While carcinoma metastasis to intracranial meningioma is rare, metastasis to intracranial meningioma could be caused by the ONS.[18] The orbit MRI revealed that the enhancement of the ONS mimicked optic nerve meningioma. Therefore, the enhancement of the ONS will appear in intracranial metastasis and meningeal metastasis. The lateral rectus paralysis in this case because the lateral rectus muscle is innervated by the abducent nerve and has the longest walking distance in the intracranial. When intracranial lesions occur, it is easier to involve the abducent nerve.

Since the enhancement of the ONS is a feature of IMM, optic neuro-ophthalmology imaging can be used for the diagnosis of IMM. Neuroimaging may be adequate to predict the benefit of tumor treatment. This technique should be recommended for patients in the latent stage of IMM.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

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