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Case Report

Middle Ear Metastases as the Initial Presentation of Breast Cancer Progression

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Abstract

Breast cancer (BC) is the most prevalent malignancy in women, and most of their deaths from BC are caused by metastases. The bone, liver, lungs, and skin are the most frequently involved organs in metastases. We report a rare case of middle ear metastasis from BC in a 67-year-old woman. The patient had a curative modified radical mastectomy for her right BC 24 years ago and was treated with letrozole as a first-line therapy for the recurrent disease since 2016. After more than 5.5 years of treatment, computed tomography revealed otitis media with mastoiditis, and a granular tumor was found in the attic space and mesotympanum during the operation with the initial symptom of decreased left ear hearing. The mass was incompletely removed, and a biopsy eventually confirmed metastatic BC. There are very few case reports in the literature. Our case highlights the importance of surgical biopsy in differentiating middle ear neoplastic lesions.

Keywords: Breast cancer, hormone receptor positive, middle ear, rare metastasis

Introduction

The most common cause of breast cancer (BC)-related death is distant metastasis, with bone, lungs, and liver being the most common metastatic sites.[1] When recurrence is suspected, advanced imaging must be performed; however, periodic intensive follow-up with chest roentgenography and bone scan appears to have no effect on long-term prognosis.[2,3] As patients with BC live longer due to more effective treatment, it may become possible to identify an increasing number of uncommon metastatic sites. Metastases to the middle ear from BC are uncommon, and there are few reports of them. Cancer metastases rarely affect the middle ear, and those affected are frequently asymptomatic for extended periods. When symptoms of metastatic middle ear disease manifest, they may be misdiagnosed as mastoiditis or otitis media.[4] Recent reviews by Micco *et al*. on rare sites of BC metastasis revealed

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only two case reports of ear metastases, one of which is the middle ear.[5] After more than 5 years of hormone therapy, we report a rare case of newly developed middle ear metastases in a patient with metastatic BC.

Case Report

A 67-year-old woman with hypertension was evaluated in the otolaryngology department for hearing loss in her left ear. Otoscopy revealed that the left tympanic membrane was hyperemic and swollen. Pure-tone audiometry revealed hearing loss in the left ear with a threshold of 51.3 decibels and an air–bone gap of 25 decibels.

Before this event, the patient underwent a right modified radical mastectomy for invasive ductal carcinoma 24 years ago. She was diagnosed with pathological stage IIB disease with axillary lymph node metastasis based on the final pathology report. The immunohistochemistry analysis revealed the presence of estrogen receptors (ER) and progesterone receptors (PR), but not human epidermal growth factor receptor 2 (HER2). The combined histologic grade of the tumor was 2, and there was the presence of lymphovascular invasion. The bone scan and chest X-ray revealed no evidence of disease metastasis. And therefore, she received complete adjuvant chemotherapy and 5 years of adjuvant endocrine therapy with tamoxifen 18 years after the initial diagnosis; an annual chest radiograph revealed new nodules in the left lung. The biopsied lung tumor revealed recurrent BC with positive ER and PR. In addition, a bone scan revealed multiple bone metastases. She received treatment with letrozole. The disease had been under control for over 5 years before a relapse in the left middle ear. Computed tomography of the brain revealed opacities in the left middle ear and mastoid cavity, indicating otitis media with mastoiditis. Endoscopic surgery revealed a granular tumor in the attic space and mesotympanum. The pathological report confirmed the presence of metastatic adenocarcinoma with a BC origin. Tumor cells were positive for ER, E-cadherin, and GATA-3, but negative for PR and HER2 [Figure 1]. The patient is now receiving an oral selective ER degrader as the next line of treatment. After 15 months of observation, her disease remains stable [Figure 2].

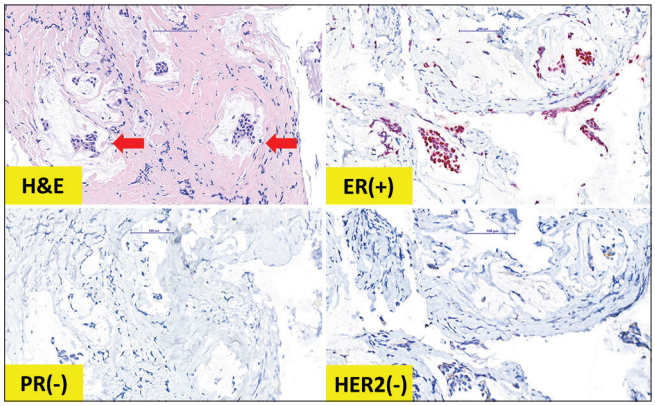

Figure 1: Hematoxylin and eosin staining of the middle ear shows metastatic adenocarcinoma cells (arrows), which are positive for estrogen receptor and negative for progesterone receptor and human epidermal growth factor receptor 2

Discussion

Primary middle ear cancer is extremely uncommon. Only 1–5 cases are diagnosed per million people each year.[6] The majority of primary middle ear tumors arise from the bone, nerve, and epithelial tissue. Paraganglioma, schwannoma, middle ear adenoma, and squamous cell carcinoma are the most prevalent histological subtypes (not in a specific order because of the variated incidence in literature).[7,8] As for the middle ear as a metastatic site, only a small number of studies had reported BC as the primary site. Pusiol *et al*. described a patient with BC metastasis to the middle ear approximately 20 years after quadrantectomy. The patient initially presented with an intratympanic mass and died due to the disseminated spread of her BC.[9] Marques *et al*. reported a patient with BC metastases in the internal auditory canal and cerebellopontine angle approximately 16 years after the primary tumor resection and adjuvant radiation.[10] Both of these cases presented initially with hearing loss and had disease recurrence many years after curative surgery.

In addition to the middle ear, external auditory canal (EAC) metastases of BC are also rarely reported. Sari *et al*. reported a case of BC with metastasis to the left EAC that manifested as a large, fleshy, and bleeding mass.[11] A high-resolution computed tomography of the temporal bone revealed that the EAC was completely occluded. An excisional biopsy confirmed the diagnosis of BC with EAC metastases. Cumberworth *et al*. additionally reported one case of late metastasis to the EAC.[12]

Since most middle ear tumors are benign, a malignant middle ear tumor can be mistaken for a cholesteatoma of the temporal bone. Once malignant etiology is suspected, surgical intervention is required because only a pathological evaluation can confirm the diagnosis.[8] In clinical practice, knowing the typical sites of metastases can facilitate earlier detection of symptoms associated with metastatic lesions. Despite the

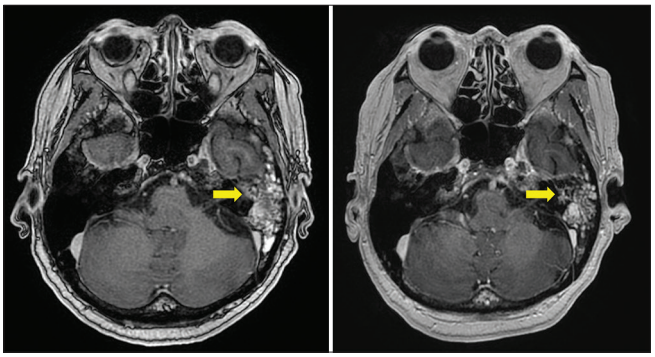

Figure 2: T1 axial views of the head with gadolinium magnetic resonance imaging show a stable status of the metastasis in the left middle ear (arrows) before (left) and after (right) treatment with an oral selective estrogen receptor degrader

fact that metastases can occur in unexpected locations, the diagnosis may be delayed due to uncommon symptoms. In our case, the cause of the patient's hearing loss was initially unknown. Regular examinations of her metastatic status revealed no evidence of disease progression in the breast, bones, or lungs. Her progressive disease was identified by a prompt evaluation of her middle ear, magnetic resonance imaging, and a surgical biopsy. Her multiple metastatic sites, including the left middle ear, are now under control as a result of the switch from letrozole to an oral selective ER degrader.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published, and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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