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Parotid Gland: An Unusual Site for Breast Cancer Metastasis: A Case Report and Review of Literature

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ABSTRACT

Background: Breast cancer, which is the most common site-specific cancer in women, usually metastasizes to lung, liver, bone, and brain, although other sites can be involved less frequently. Parotid gland invasion by breast cancer, first reported in 1950, is extremely rare with very few reports worldwide.

Case presentation: A 54-year-old woman with stage IIIA breast cancer presented with a right parotid mass and signs of facial nerve palsy 3 months after treatment completion, which was finally diagnosed as metastatic involvement of parotid gland.

Conclusion: Breast cancer metastasis to parotid gland is extremely rare but can happen metachronously or synchronously even years after the primary disease. Therefore, this diagnosis should be kept in mind in any patient with a history of breast cancer presenting with a periauricular mass. Despite proposed treatments, including surgery, radiation, and chemotherapy, patients have a poor prognosis with a reported 5-year survival rate of 10%. However, palliative management should be recommended to all patients with parotid metastasis.

Introduction

Breast cancer is the most common site-specific cancer in women. It is the first and second leading cause of cancer-related death in developing and developed countries, respectively.¹ Breast cancer is also the most frequently diagnosed cancer among Iranian women, accounting for 24.6% of all cancers, and it is reported the fifth leading cause of cancer death in Iranian females.² Nowadays, owing to comprehensive screening programs and remarkable improvements in treatment modalities, an increasing number of patients are diagnosed at earlier stages of the disease and few distant metastasis; as 5-year survival for stage I, II, III, and IV breast cancer patients are 100% and 93%, 72%, and 22%

respectively.³ However, patients at any stage of the disease can develop distant metastasis in her lifetime. The most prevalent sites of breast cancer metastasis are bone, lung, liver, and brain.⁴ Breast cancer metastasis to the parotid gland, first reported in 1950, is extremely rare, with only 21 cases reported between 1982 and 2017.⁴⁻¹⁰

Here we report the case of a 54-year-old woman with stage IIIA breast cancer who presented with right parotid mass and signs of facial nerve palsy 3 months after treatment completion, which was finally diagnosed as metastatic involvement of parotid gland.

Case presentation

A 54-year-old woman with a family history of breast cancer (aunt with breast cancer diagnosed at age 41) presented with a lump on the right breast at the 6 o'clock position. Diagnostic workup indicated invasive ductal carcinoma of the right breast with axillary lymph node involvement. IHC examination revealed an ER+/PR+/HER2- tumor with an average Ki-67 labeling index of 25%. She underwent breast-

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conserving surgery and axillary lymph node dissection. Pathologic examination reported invasive and in situ ductal carcinoma, grade 1. Maximum tumor size was 3.5 cm and lymphovascular invasion was present. All surgical margins were tumor-free. Of 20 excised lymph nodes, 7 were involved. In systemic workup, a 4-mm subpleural nodule in the posterior segment of the right lower lobe was reported, and follow-up CT was recommended. Abdominopelvic CT scan revealed no pathologic lesion. In the obtained bone scan, increased uptake in T7 vertebral body—which was highly suspicious for solitary osteometastasis—was observed. Magnetic resonance imaging of the spine showed small abnormalities in bone marrow signal of T7 vertebral body, which could be an atypical hemangioma. The patient received 8 sessions of adjuvant chemotherapy and 30 sessions of adjuvant radiotherapy. About 3 months after treatment completion and 11 months from the first diagnosis, she presented with a right periauricular mass, incomplete right eye closure, and mouth deviation, indicating right peripheral facial

nerve palsy. In ultrasound examination, a 16×12 -mm round lesion in the tail of the right parotid gland was detected. A fine-needle aspiration (FNA) biopsy of the mass was done, and pathologic examination reported a lesion which was highly suspicious for malignancy (Figure 1). For more evaluation, cervical CT scan was requested, which revealed a right masticator space mass measuring $23 \times 17 \times 21$ mm, suggestive of minor salivary gland tumor or trigeminal schwannoma. In PET-CT scan, hypermetabolic tumoral lesion in the right masticator space (periauricular region), hypermetabolic bone metastasis in T7, T8, and left sacral area, and suspicious metabolically inactive pulmonary nodules were reported (Figures 2 and 3). Core needle biopsy of the parotid lesion confirmed invasive ductal carcinoma metastasis (Figure 4). IHC examination was positive for ER, PR, and HER2 and negative for CK5/6 and P63. The case was presented to the ear, nose, and throat tumor board and breast cancer multidisciplinary team, and palliative chemoradiation with Herceptin administration was recommended.

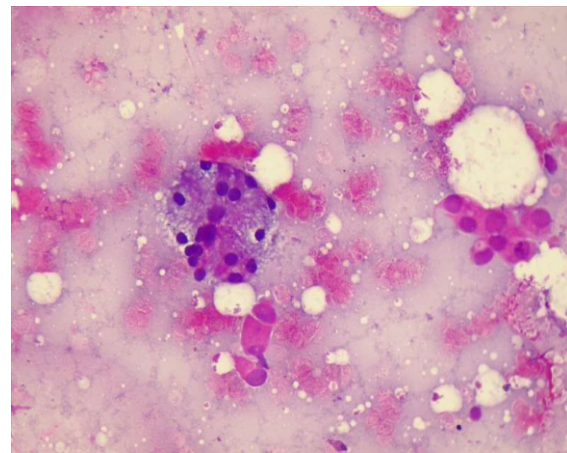
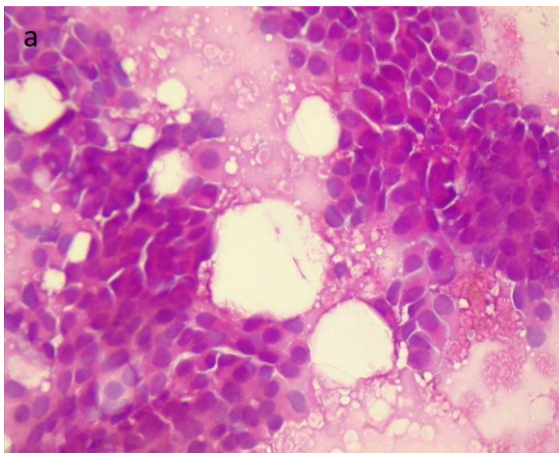


Figure 1. Fine needle aspirate of the right parotid mass with papanicolaou staining(a). Tumoral cells are depicted at the right and salivary gland cells at the left central part of the picture(b).

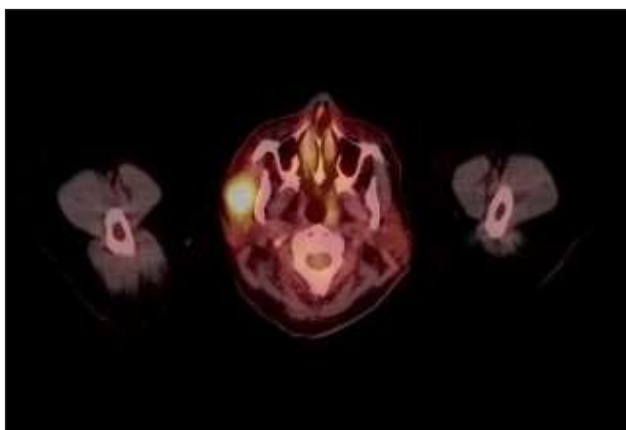


Figure 2. PET-CT scan reveals accumulation of SUV 9.36 in the right masticatory space in periauricular region

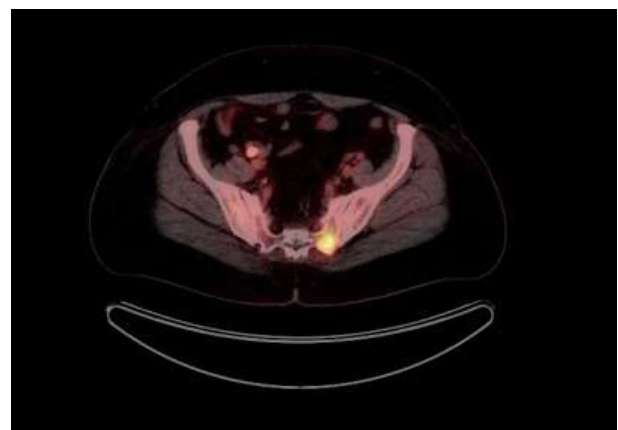


Figure 3. PET-CT scan reveals accumulation of SUV 6.79 in the left sacral ala.

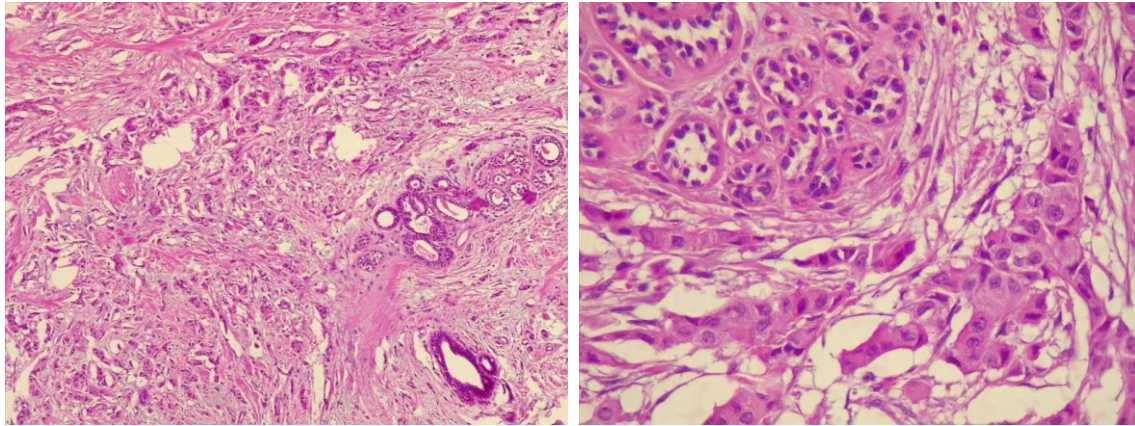


Figure 4. Core needle biopsy of the right parotid mass with H&E staining (10X and 40X) showing tumoral cells in the salivary gland.

Discussion

The most common sites for breast cancer metastases are bone, lung, liver, and brain.⁴ Breast cancer metastasis to the parotid gland is extremely rare, with the first one reported in 1950 by Abrams *et al.* in a review of autopsy studies of 167 cases of breast cancer, in which only 1 case of metastasis to the parotid gland was detected.⁴⁻¹⁰ From 1982 to 2017, only 21 cases were reported worldwide.⁴ Metastasis to other salivary glands, i.e., submandibular gland, is even rarer, with very few reports in the literature.^{11,12}

About 9% to 14% of parotid lesions are primary or metastatic malignant lesions.⁴ Head and neck malignancies (mostly squamous cell carcinomas) comprise most cases of metastatic lesions.^{4,6,8,13} Infraclavicular origins of metastatic involvement of parotid glands, including breast, kidney, lung, GI tract, and prostate, are rare (0.16%-0.4%).^{4,8} In one report by Franzen *et al.* on 644 consecutive parotidectomies between 1980 and 2012, 89 patients (14%) had malignant tumors, of which 39 were metastatic (6% of total); in 5 cases, the primary tumor was located below the clavicle (0.77% of total), only one of them being a breast carcinoma.¹⁴ Infraclavicular metastases of the parotid gland are thought to reach the parotids through the thoracic duct or Batson's paraspinal venous plexus.^{8,13} Different studies have proposed that breast cancer metastasizes to the parotid gland via a hematologic route, as the involvement of the right and left parotid has been reported in patients with carcinoma of right and left breast.^{4,6,8}

Metastatic involvement of the parotid gland in breast cancer patients has been reported at different ages (36 to 74 years) and various disease stages (II, III, IV), and may occur synchronously or metachronously, and alone or along with metastases to other sites—although the sole involvement of the parotid is less common).^{4-9,13,15-17} Metachronous involvement of the parotid gland has been reported to happen from 11 months to 21 years after the primary disease.^{4-9,13,16,17} Metastasis from different types of

breast cancer, including invasive ductal carcinoma, invasive lobular carcinoma, and even malignant phyllodes tumor, has been reported, although the most frequent type has been invasive ductal carcinoma.^{4,6-8,15}

Patients usually present with a periauricular mass, sometimes with signs of peripheral facial nerve palsy, which is seen in 30% to 40% of malignant parotid lesions.^{4,7,8} Imaging alone cannot differentiate between a primary malignant tumor of the parotid gland and a metastatic one; therefore, when a patient with a history of breast cancer presents with a periauricular mass, an FNA is usually done after proper imaging. FNA is considered to be an appropriate and accurate primary diagnostic intervention, with a diagnostic accuracy of 85% in distinguishing malignant from benign lesions and primary neoplasms of the parotid from metastatic ones.^{4,5,8} Rarely, FNA results may be misleading, as in a case of parotid metastasis from hepatocellular carcinoma reported by Yu *et al.*, where FNA did not show any specific cytopathologic features to allow an appropriate diagnosis.⁷

It is of note that metastatic involvement of parotid gland can be mistaken for primary salivary duct carcinoma of the parotid gland, and the similarities between these two entities, including immunoprofiles, makes the differentiation difficult.^{5,8} Despite similarities, there are some characteristics that can be valuable in making an accurate diagnosis. In metastatic ductal carcinoma, residual normal parotid acini can be seen between the neoplastic glands, while salivary duct carcinoma of the parotid gland is expansile, leaving no or very rare normal parotid gland elements between its neoplastic cells. In addition, metastasis from breast cancer lacks the pattern of intraductal cribriform carcinoma that is characteristic of primitive salivary duct carcinoma of the parotid gland.⁸ Some studies have reported IHC staining to have limitations in distinguishing between primary salivary duct carcinoma of the parotid gland and metastatic ductal carcinoma from breast cancer as



salivary duct carcinomas are positive for CK 7, GCDPF-15 (87%), AR (72%), HER2/neu (40%) and, rarely, positive for ER (1%) and PR (5%). However, others claim that IHC staining can provide valuable information—the absence of expression of estrogen and progesterone receptors favors the diagnosis of a primary ductal tumor of the parotid gland.^{5, 8} In addition, salivary duct carcinoma has been reported to almost invariably express androgen receptors. Comparing the hormone receptors profile of both the parotid tumor and the primary breast tumor can be helpful, although discrepancies in hormone receptor expression between primary breast tumor and metastatic ones have been described in up to 25% of cases.⁸

Treatment for parotid metastatic disease includes a combination of surgical removal of solitary tumors, chemotherapy, radiotherapy, endocrine therapy, and targeted therapy (as needed).^{4, 6} For single parotid metastasis, some advocate parotidectomy (total or superficial) with negative margins (preferably with preservation of facial nerve) and postoperative radiotherapy to obtain local tumor control and to exclude a primary parotid tumor.^{4, 8, 9} Some authors have postulated that parotidectomy with complete excision of the tumor can be a curative measure or an essential part of symptom control and should be considered in all but the most moribund patients.¹⁴ Yet, others have suggested ipsilateral neck dissection; however, as this entity is extremely rare, only limited data about the benefit of such procedures exist. Shi *et al.* advocate the use of an ipsilateral neck dissection when the parotid metastasis is from head and neck primaries as spread occurred predominantly via the lymphatic system, whereas, in the case of hematogenous spread from distant sites, neck dissection is thought to be unnecessary. Adjuvant radiotherapy for the parotid gland and neck is recommended by most authors for patients without nodal involvement; however, others favor the use of adjuvant chemotherapy, reserving the use of irradiation for cases where local control could not be achieved by surgery alone.⁸

In the case of multiple-site metastases, chemotherapy alone or in combination with radiation therapy has been administered. For HER2+ tumors, targeted therapy with Herceptin following adjuvant chemotherapy is reported to be associated with increase disease-free survival, although the effectiveness of adjuvant chemotherapy in stage IV breast cancer patients remains disputed.⁶

Despite the proposed treatments, patients with metastatic involvement of the parotid gland have poor prognosis, with the 5-year survival rate reported to be 10%.^{4,8} Although metachronous solitary parotid metastases with longer disease-free survival are considered as good prognostic factors, many authors believe that parotid surgery does not improve life expectancy and that the management of a parotid

metastasis is palliative regardless of the therapeutic modality used as the prognosis of such patients is poor.⁸ However, palliative management should be recommended to all patients with parotid metastasis.⁴

In conclusion, breast cancer metastasis to parotid gland is extremely rare. It has been reported to happen synchronously or metachronously, even years after the primary disease regardless of the stage of primary cancer and appropriate primary treatment. Therefore, this diagnosis should be kept in mind in any patient with a history of breast cancer presenting with a periauricular mass. Proposed treatments are parotidectomy and radiation therapy for local control and palliation of solitary lesions—and chemotherapy, hormone therapy, and targeted therapy, if indicated. Despite these treatments, however, patients with metastatic involvement of parotid have a poor prognosis, with reported 5-year survival rate being 10%. Many authors consider that parotid surgery does not improve survival and that the management of a parotid metastasis is palliative regardless of the therapeutic modality used, as the prognosis of such patients is dismal. However, palliative management should be recommended to all patients with parotid metastasis.

Ethical Consideration

The patient declared her consent for reporting her disease for this case report.

Conflict of Interest

None

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