

## Case Report

### A Rare Case of Breast Carcinoma Metastases to the Tongue - A Case Report and Review of the Literature

Benjamin Che-Cheng Yu<sup>1</sup>, Yu-Ching Wei<sup>2,3</sup>, Li-Ju Huang<sup>4</sup> and Li-Kun Ko<sup>1,5\*</sup>

<sup>1</sup>Division of Breast Oncology and Surgery, Department of Surgery, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan

<sup>2</sup>Department of Pathology, School of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

<sup>3</sup>Department of Pathology, Kaohsiung Medical University Gangshan Hospital, Kaohsiung, Taiwan

<sup>4</sup>Department of Medical Research and Development, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung, Taiwan

<sup>5</sup>Doctoral Program of Clinical and Experimental Medicine, College of Medicine, National Sun Yat-sen University, Kaohsiung, Taiwan

#### Abstract

**Background:** Metastasis of breast cancer to the tongue is extremely rare, with scarce cases documented. While common metastatic sites include bones, lungs, liver, and brain, gastrointestinal tract, especially tongue, is seldom reported. This case is notable as it is the first documented Taiwanese patient and includes comprehensive immunohistochemistry (IHC) analysis and germline BRCA testing, which further underscores TNBC disease course and potential clinical significance.

**Case Presentation:** A 52-year-old Taiwanese woman initially presented with a right breast mass, diagnosed via biopsy as grade 2 invasive ductal carcinoma, TNBC subtype (ER-/PR+/HER2-) with high Ki-67. Staging was T2N2, and her treatment regimen included neoadjuvant chemotherapy followed by modified radical mastectomy, which revealed residual disease. Postoperative imaging identified brain metastases, and concurrently, the patient noted a new mass on her tongue. A biopsy confirmed the tongue lesion as metastatic

breast carcinoma with triple negative and additional negative results for PD-L1 and BRCA mutations. The patient received one cycle of adjuvant chemotherapy but ultimately passed away two months later due to progressive CNS involvement.

**Conclusion:** This case highlights the clinical implications of rare metastasis to the oral cavity, specifically the tongue, in breast cancer patients. The unusual presentation underscores the necessity of comprehensive evaluation in advanced breast cancer cases presenting with atypical lesions. Additionally, it reinforces the importance of considering less common metastatic sites in patients with TNBC, which may signal further disease progression and necessitate specialized palliative strategies.

**Keywords:** Case Report; Germ-Line Mutation; Mouth Neoplasm; Triple Negative Breast Neoplasms

#### Patient Ethnicity

- The patient deceased and was known living alone without children, their parent or legal guardian, no further participation or distribution consents could be achieved.
- The derived study is approved by institutional review board

#### Introduction

Globally, breast cancer is the most prevalent form of malignancy among women, accounting for 23.8% of all newly diagnosed cancers in 2022 [1]. A similar situation is also observed in Taiwan. In 2021, over a quarter of newly diagnosed cancers in women were breast cancer, and among these cases, approximately 8% were de novo metastatic breast cancer [2]. Usual sites of distant metastasis include bone, lung, liver, and brain [3], but involvement of the tongue is very rare. Metastatic breast cancer to the tongue was first reported in 1943 [4], and only a few cases have been documented in the literature. Here we describe a 53-year-old female patient having a metastatic lesion on her tongue mobile part, which is secondary to breast carcinoma. This case represents the first documented instance of a Taiwanese patient with breast cancer metastasizing to the tongue. It is also the first known case where germline BRCA testing was conducted.

#### Case Report

A 52-year-old female presented with a right breast mass. Histopathology revealed a grade 2 invasive ductal carcinoma. Clinical staging was T2N2. The immunohistochemistry (IHC) staining showed estrogen receptor (ER) negative, progesterone receptor (PR) positive (20%), human epidermal growth factor receptor 2 (HER2) negative (0), and a high proliferation Ki-67 labeling index of 70% (Figure 1). The breast tissue was tested with SP142 assay (Ventana) with PD-L1 expressing tumor infiltrating immune cells less than 1%.

The patient received neoadjuvant chemotherapy with four cycles of liposomal doxorubicin combined with cyclophosphamide, followed by three cycles of bevacizumab, docetaxel, and carboplatin. Subsequent to chemotherapy, she underwent a right modified radical mastectomy (MRM), but a 65mm residual tumor was found. Of the ten lymph nodes examined, three were found to be involved.

\*Corresponding author: Li-Kun Ko, Division of Breast Oncology and Surgery, Department of Surgery, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, Tel: +886 976956260; E-mail: fur102tw@gmail.com

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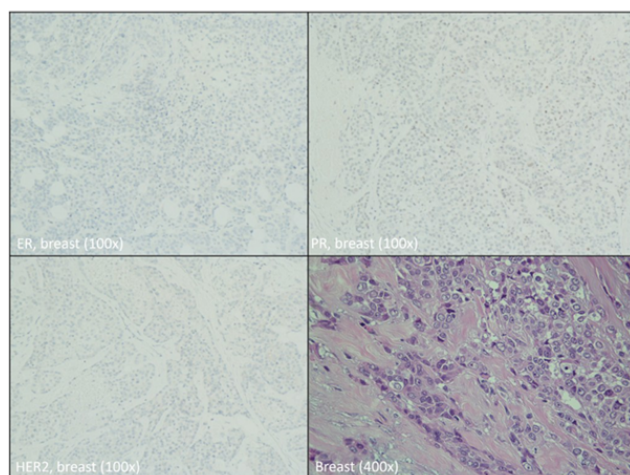
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Microscopically, the breast tumor was composed of neoplastic epithelial cells forming sheets or nests in fibrotic stroma with areas of necrosis. The IHC studies for biomarkers revealed Triple Negative Breast Cancer (TNBC). She also received adjuvant radiotherapy followed by oral chemotherapy with capecitabine postoperatively.

Four months later, she presented to the neurosurgery department with associated symptoms, and brain computed tomography (CT) imaging revealed multiple brain metastasis. Concurrently, the patient reported a protruding mass on her tongue tip, with biopsy confirmed malignancy. The tongue tumor revealed a similar histologic picture to that of the breast tumor. In addition, the IHC study of GATA3 stain was positive, indicative of metastatic carcinoma of breast origin. As for the following biomarker staining, the immunostains of ER, PR and HER2 revealed negative (Figure 2). Tongue metastatic lesion was tested with 22C3 (Agilent/Dako) with adequate tumor cell presence (at least 100 viable tumor cells) and combined positive score (CPS) 0 was measured.

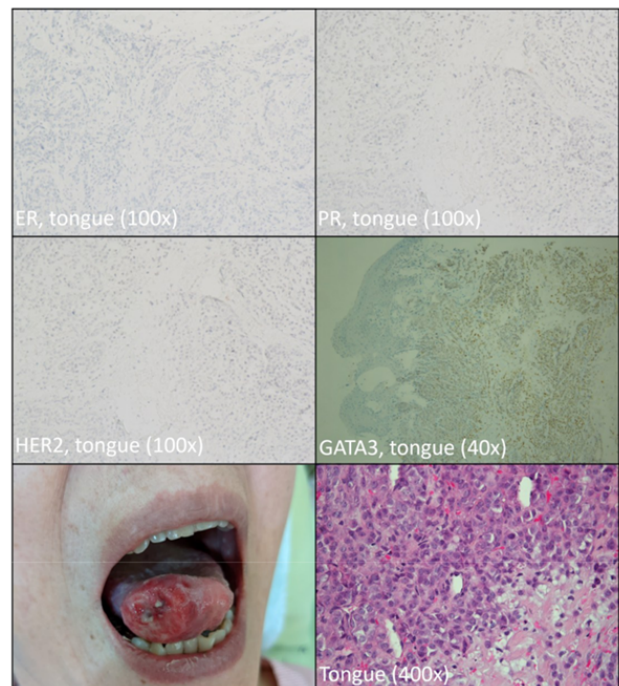
Germline BRCA 1/2 variant mutations were not detected in her genetic testing. A systemic chemotherapy regimen consisting of bevacizumab and eribulin was proposed. However, after careful consideration, the patient opted for palliative care, and she received only one cycle of chemotherapy before discontinuing active treatment. The patient died two months later with deteriorated CNS involvement and dyspnea.



**Figure 1:** Microscopically, breast tumors are composed of neoplastic epithelial cells forming sheets or nests in fibrotic stroma with areas of necrosis. The additional IHC for biomarkers reveal a triple-negative breast cancer.

## Discussion and Conclusion

In Taiwan, breast cancer is the most prevalent cancer among women, with its incidence rate steadily increasing, reaching 15,448 cases per 100,000 persons in 2021 [2]. Breast cancer is classified based on IHC, with ER+ and/or PR+ accounting for 60 to 80%, HER2 overexpression for 20 to 40 %, and TNBC for 15% [5]. Different subtypes of breast cancer indicate different 5-year survival curves and TNBC, with which being characterized by lack of ER (0%), PR(0%), and HER2 (0+) expression, tends to have the worst clinical outcomes amongst all kinds of breast cancer, with 5-year relative survival percentage of 78.0% from TNBC, lower than those with ER+ and/or PR+ with HER2- with 95.1% and ER+ and/or PR+ with HER2+ with 85.7% [6,7].



**Figure 2:** The tongue tumor reveals a similar histologic picture to that of the breast tumor. In addition, the immunohistochemical study of GATA3 stain is positive, indicative of metastatic carcinoma of breast origin. As for the following biomarker staining, the immunostains of ER, PR and HER2 also reveal negative findings. Tongue tip with metastatic breast lesion was noticed.

As observed in real world experience and literature, the most common site of distant metastasis in breast cancer is the bone. Studies have consistently shown that bone metastases occur in approximately 65-75% of breast cancer patients with metastatic disease. Other common sites include the lungs, liver, and brain [8]. Gastrointestinal tract metastasis from breast cancer predominantly arise from the lobular subtype, which exhibits a distinct propensity, with organ including the stomach (60%), esophagus (12%), colon (11%), small intestine (8%), rectum (7%), oropharynx (1%) [9,10].

The oral cavity is an extremely rare site for distant metastases, comprising only about 0.1% to 1% of all oral malignancies [11,12]. Soft tissue involvement most commonly affects the gingiva, tongue, lips, and buccal and palatal mucosa, with primary tumors typically arising from the lung, breast, kidney, and colon [13]. In another review of 6,881 autopsies involving various malignant diseases, identifying 12 cases of tongue metastasis and malignant melanoma was the most common primary tumor associated with tongue metastasis, accounting for 4.31% of cases [14]. In a study of 685 autopsies of breast cancer patients, only two cases (0.29%) exhibited metastasis to the tongue [15]. PubMed search strategy, using MeSH terms (“Breast Neoplasms” AND “Tongue Neoplasms/secondary”) yielded thirty-six articles, six case reports and one meta-analysis were under reviewed [4,16-21].

Reviewing articles regarding the tongue metastasis from breast carcinoma (Table 1), the prognosis of case reports with tongue metastasis from breast cancer is doom. The most under controlled case post chemotherapy and survived for at least 2 years, the remained cases’

survival length was found to have less than half of the year. As the oral soft tissue metastasis, one thirds had no other distant metastasis and could live up to 15 months [21].

Due to the patient’s negative PD-L1 expression, the use of pembrolizumab, a PD-1 inhibitor, was not anticipated to prolong PFS [22]. Additionally, the absence of a germline BRCA pathogenic variant precluded the use of PARP inhibitors. Given the demonstrated efficacy of bevacizumab in enhancing PFS and ORR in metastatic breast cancer patients, a combination regimen of bevacizumab and eribulin was selected [23]. Nevertheless, after completing one cycle of chemotherapy, the patient opted for palliative care and deceased two months later owing to CNS symptoms deterioration.

Considering tongue metastasis from breast cancer rarity, additional evaluation is essential when tongue lesions are observed in patients with breast cancer, might indicate progression from the patient’s disease content, and lesion biopsy might help us to detect patient’s disease progression earlier to other distant metastasis.

Our report concerned a patient diagnosed with TNBC and tongue metastasis, who was noteworthy for being the first known individual to have germline BRCA genetic testing. As next generation sequencing (NGS) prosperous application, more NGS related bioinformation being provided could lead more precision therapy in the future.

Literature	Age	breast tumor size (cm)	nodal status	histology grade	IHC subtype	gBRCA 1/2	breast carcinoma treatment	metastasis timing	solitary distant metastasis	diagnosis	tongue metastasis treatment	prognosis
Fink & Garb, 1943	NA	N/A	N/A	N/A	N/A	N/A	N/A	24 months	no (multiple)	surgical excision	N/A	N/A
Kolson, 1966	69	2.54	-	Adeno-carcinoma	3	N/A	MMM only	36 months	no (pulmonary)	biopsy	16 Fr 2086 cGy	died 2 months later
Meher-Homji et al., 1967	NA	N/A	N/A	invasive carcinoma	N/A	N/A	MMM and concurrent chemotherapy	no (multiple)	surgical excision	chemotherapy (fluorouracil)		died 4 months after survival
Perchick & Kim, 1986	NA	N/A	+	IDC	N/A	N/A	MMM only	14 months	no (pulmonary)	biopsy	15 Fr 5250 cGy	at least 6 months survival
Neelakantan et al., 2008	24	3.8	+	IDC	2	ER low positive, PgR and HER2 negative	MMM and chemotherapy	10 months	no (pulmonary)	biopsy	chemotherapy (docetaxel)	died 24 months later
Billan et al., 2009	53	at least 5 cm	+	IDC	3	TNBC	MMM and radiotherapy	3 months	yes	biopsy	radiotherapy	died 2 weeks later no pneumonia and airway obstruction
Our case	52	6.5 cm	+	IDC	2	ER/HER2 -, not PgR +ve (20%), pathologic Ki-67 70%	MMM and chemotherapy	4 months	no (intracranial)	biopsy	palliative	died 2 months later

Table 1: Reviewing articles regarding the tongue metastasis from breast carcinoma.

Declarations

Ethical Approval and Consent to participate

- The patient deceased and was known living alone without children, their parent or legal guardian, no further participation or distribution consents could be achieved.
- The derived study is approved by institutional review board

Consent for publication

Not applicable.

Availability of supporting data

The datasets during and analyzed during the current study available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Not applicable

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