

Breast cancer metastasis to the nasopharynx: A case report

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Abstract. Breast cancer is a leading cause of cancer-related mortality in women, with metastasis posing a significant clinical challenge. However, spread to the nasopharynx and nasal cavity is exceptionally rare. The current study presents the case of a 53-year-old woman diagnosed with invasive ductal carcinoma of the right breast, which later metastasized to the nasopharynx. Despite undergoing modified radical mastectomy, chemotherapy and endocrine therapy, the patient developed symptoms indicative of distant metastasis. The present study reviews the diagnostic and therapeutic approaches for such rare occurrences, offering insights into effective management. The study analyzes this case alongside previously reported instances with the aim of enhancing awareness and facilitating early detection and intervention.

Introduction

Breast cancer remains a leading cause of cancer-related mortality in women, with a high incidence of metastasis. In total, 20-30% of patients with early stage breast cancer develop metastatic disease, and metastatic breast cancer accounts for the majority of breast cancer-related deaths. However, metastases of the nasopharynx and nasal cavity are exceedingly rare, representing <1% of all metastatic breast cancer cases (1). Primary tumors most frequently metastasizing to the nasopharynx originate from the lung, liver, kidney, breast and colon. Among these, lung cancer has the highest incidence rate of nasopharyngeal metastasis, with it being reported in 30-40% of cases. Liver cancer follows next, with an incidence of 10-15%, while kidney cancer has an incidence rate of 5-10% of cases. Colorectal cancer has a relatively low incidence rate, ranging from 2-5%. Breast cancer is the least frequent, with an incidence rate of <1% of all nasopharyngeal metastases (2-6). The current study presents a case of breast cancer metastasizing

to the nasopharynx, alongside a literature review, to explore diagnostic and therapeutic approaches, and provide valuable clinical insights.

Case report

In February 2013, a 53-year-old female patient detected a progressively enlarging right breast mass (4.0x5.0 cm) accompanied by distending pain, pruritus, skin ulceration and reddish nipple discharge. In May 2013, the patient was admitted to Affiliated Hospital of Shandong Second Medical University (Weifang, China). A breast ultrasound suggested malignancy, leading to an immediate modified radical mastectomy (Fig. 1). Postoperative histopathology confirmed invasive ductal carcinoma with axillary lymph node metastasis (4/15 lymph nodes affected). Immunohistochemistry (IHC) results were positive for estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2), with a Ki-67 proliferation index at 30% (Fig. 2). All IHC staining procedures (Data S1) followed standardized protocols at the Department of Pathology, Weifang People's Hospital (Weifang, China). The Tumor-Node-Metastasis stage was classified as T2N2M0 (stage IIIA) according to the 8th edition of the American Joint Committee on Cancer Staging Manual (7). The patient underwent four cycles of gemcitabine plus docetaxel chemotherapy, followed by tamoxifen therapy.

In October 2015, the patient developed pleural and bone metastases. IHC (Data S1) revealed HER2 overexpression. Declining intravenous anti-HER2 therapy, the patient opted for oral lapatinib with capecitabine after providing informed consent. The patient experienced sequential metastases to the brain, liver and soft tissue of the hip. Brain metastases were treated with GammaKnife radiosurgery, while liver metastases underwent local tumor-reducing therapy combining microwave ablation with radioactive seed implantation. The treatment regimen was promptly adjusted in response to disease progression. Despite treatment, metastatic progression continued. Regular follow-ups allowed timely treatment adjustments.

In April 2023, a CT scan of the patient showed no evidence of a nasopharyngeal mass (Fig. 3A). In June 2023, the patient presented with nasal congestion and rhinorrhea. A computed tomography (CT) scan detected a nasopharyngeal soft-tissue mass (Fig. 3B). Biopsy findings revealed fragmented mucosal tissue with scattered atypical cells (Fig. 4A). The IHC results were as follows: ER(-), PR(-), HER2(3+), guanine-adenine-th

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ymine-adenine-binding protein 3 [GATA3(+)], cytokeratin 7 [CK7(+)], CK5/6(focal +) and p40 (sparse +) (Fig. 4; Table SI; Data S1). Considering the medical history, histopathology and IHC profile, the diagnosis confirmed metastatic breast cancer. Later that same month, treatment was initiated promptly, with four cycles of albumin-bound paclitaxel and trastuzumab, resulting in a partial tumor response in August 2023 (Fig. 1C). However, drug resistance developed, leading to rapid disease progression by December 2023 (Fig. 1D and E). By January 2024, after 7 months, the patient was transferred to a local hospital, where treatment modifications failed to lead to an improved condition. Despite optimal hospice care, the patient ultimately passed away at the local hospital. The patient timeline is presented in Fig. 5. Detailed treatment protocols are presented in Table I.

Discussion

Metastasis of breast cancer to the nasopharynx is exceptionally rare, with only a few documented cases (8-11) (Table II). Unlike more common metastatic sites such as the bones, lungs, liver and brain, nasopharyngeal involvement poses unique diagnostic and therapeutic challenges. The clinical presentation varies widely and depends on multiple factors, including the primary tumor stage, tumor aggressiveness, pathological type, immunohistochemical profile and extent of invasion. The first reported case of breast cancer metastasizing to the nasopharynx was described by Saab *et al* (1) and initially presented with cervical lymphadenopathy. The present patient experienced nasal congestion and rhinorrhea, likely due to tumor-induced growth obstruction of the nasal cavity. Moreover, metastasis to this site can remain asymptomatic for an extended period, as observed in a case reported by Başpınar *et al* (12) in 2006. Other typical clinical manifestations include hoarseness, dyspnea, facial cellulitis, headache, periorbital mass, diplopia, ptosis, facial palsy, abducent nerve palsy, exophthalmos, vision impairment, headache and anosmia. The interval between breast cancer diagnosis and the onset of nasopharyngeal metastases can vary widely, ranging from 10 months to 10 years (Table II).

Due to the rarity of nasopharyngeal metastatic tumors and their frequent submucosal location, CT and magnetic resonance imaging fail to provide distinct diagnostic features. Positron emission tomography-CT remains the most effective imaging modality for evaluating systemic metastases, detecting disease recurrence, assessing tumor burden and identifying distant lesions (13). However, its high cost and the potential for false-positive results due to inflammatory conditions complicate the diagnosis. The clinical manifestations of metastatic nasopharyngeal tumors closely resemble those of non-specific nasal inflammation and upper respiratory tract infections, frequently presenting with facial pain, epistaxis, nasal congestion and rhinorrhea. When differentiation proves challenging, an empirical anti-infective treatment may be attempted. If symptoms persist, primary or secondary nasopharyngeal tumors must be strongly suspected. Given their high expression in breast tissue, IHC markers such as gross cystic disease fluid protein 15 and GATA3 are crucial in distinguishing breast cancer metastases (14). There is limited evidence suggesting that increased CK expression in

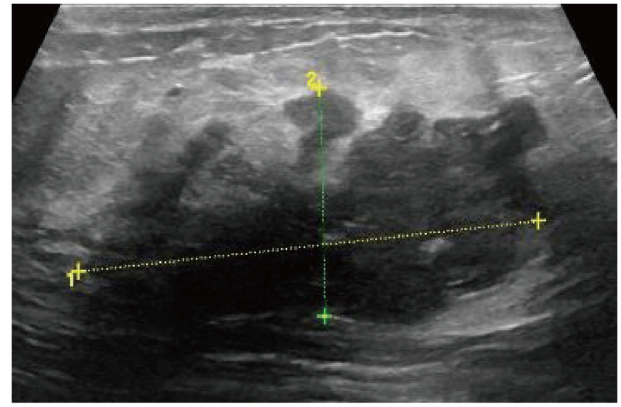


Figure 1. Breast ultrasound revealed a mass.

metastatic lesions may indicate a predilection for nasopharyngeal colonization, as CK serves as a key immunomarker for nasopharyngeal squamous cell carcinoma. The patients in the studies by Marchioni *et al* (15) and Copson *et al* (16), and the present patient, all exhibited increased CK/CK7 expression, further supporting the potential role of CK/CK7 in the metastatic process. However, this phenomenon's mechanisms require further investigation (Table III). A thorough histopathological assessment, IHC analysis and a high index of suspicion are essential for accurately diagnosing nasopharyngeal metastases. The IHC profiles may differ from those of the primary tumor, exhibiting partial or complete heterogeneity. In a case reported by Copson *et al* (16), the only IHC difference between the primary breast cancer tumor and its nasopharyngeal metastasis was the HER2 expression, with HER2 positivity observed in the nasopharyngeal metastasis but lacking in the primary tumor, while the expression of estrogen and progesterone receptors remained consistent in both tissues. Significant discrepancies in hormone receptor and HER2 status have been observed between primary breast cancer and secondary nasopharyngeal lesions. While it was previously believed that HER2 status remained consistent between primary and metastatic tumors, recent findings challenge this assumption (17). However, up to 25% of patients exhibit discrepancies in IHC results (17,18), with inconsistencies in ER and PR expression being more prevalent than those in HER2 (19). In the present patient, prolonged secretion of ER and PR may have contributed to the suppression of hormone receptor expression. The heterogeneity of HER2 refers to variations in expression or amplification across different tumor sites, time points or within the same patient. This phenomenon has been extensively documented in previous studies and has been observed in up to 34% of breast cancer cases (20-23). Undetected HER2-amplified subclones were hypothesized to exist in the original pathological samples. This may be due to the fact that in genetic or tumor heterogeneity, chemotherapy selectively targets most HER2-related primary tumor cells, potentially enriching HER2-overexpressing clones. Moreover, long-term antitumor therapy may induce alterations in the tumor microenvironment, further contributing to these changes (24).

Treatment strategies vary across studies due to the rarity of nasopharyngeal metastases from breast cancer. Therapeutic selection depends on multiple factors, including the tumor's

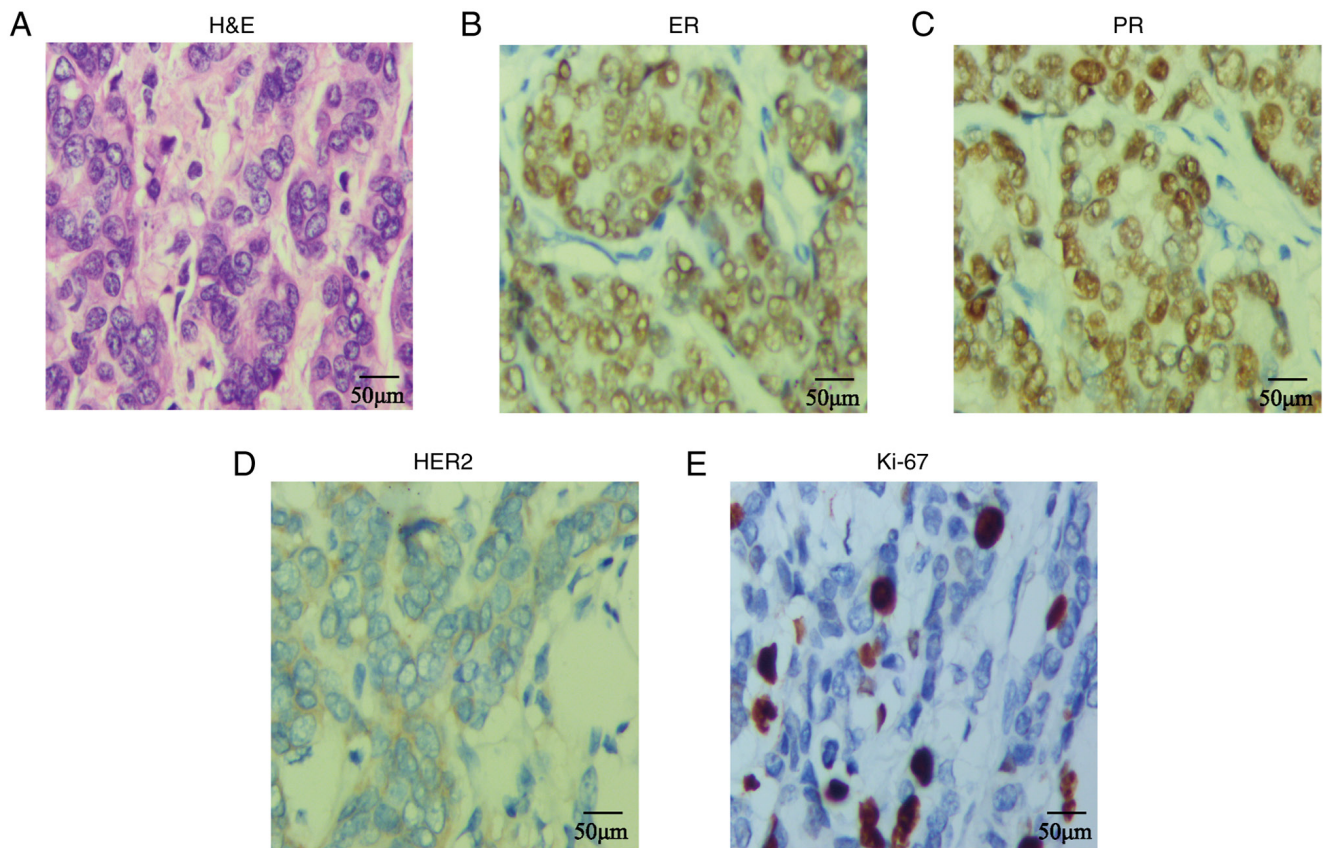


Figure 2. Histopathological (H&E staining; x400 magnification) and IHC (x400 magnification) images of the postoperative breast cancer specimen. (A) H&E staining revealed invasive breast carcinoma. Positive expression of (B) ER and (C) PR. Low expression of (D) HER2. (E) Ki-67 proliferation index at 30%. H&E, hematoxylin and eosin; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; Ki-67, proliferation index.

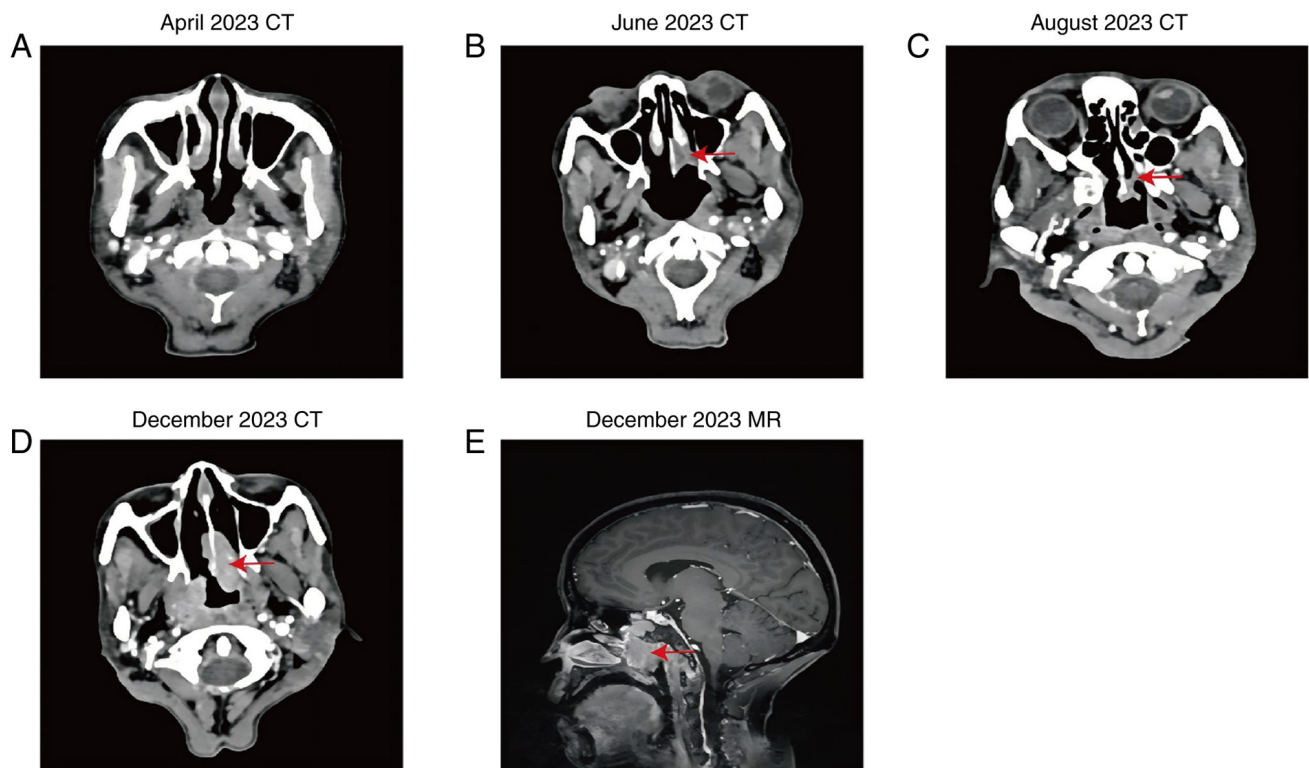


Figure 3. Imaging characteristics of breast cancer with nasopharyngeal metastasis at different stages. (A) Normal nasopharyngeal CT imaging. (B) Contrast-enhanced CT scan revealing a soft-tissue mass in the nasopharynx (arrow). (C) Partial regression of the mass (arrow) following treatment. (D) Progressive soft tissue thickening with heterogeneous enhancement (arrow). (E) MR imaging showing an enlarged nasopharyngeal mass with irregular density (arrow). CT, computed tomography; MR, magnetic resonance.

Table I. A more detailed treatment plan.

Month and year	Treatment
May 2013	Modified radical surgery for left breast cancer
May 2013	Postoperative adjuvant chemotherapy (4 cycles of GD, no details) followed by endocrine therapy (10 mg tamoxifen bid po)
October 2015	Recurrence: Pleural metastasis and bone metastases (1.25 mg lapatinib qd po/25 days and 1.5 g capecitabine bid po days 1-14/21 days)
March 2016	Brain metastases (Gamma knife treatment)
October 2016	Brain metastases, PD (Gamma knife treatment and 240 mg neratinib qd po)
December 2018	Lung metastases, PD (25 mg exemestane qd po + 3.75 mg leuprolide by subcutaneous injection/ q4w + 240 mg neratinib qd po)
August 2019	New lung metastases, PD (500 mg fulvestrant im/q4w + 3.75 mg leuprolide by subcutaneous injection/ q4w + 240 mg neratinib qd po)
December 2019	Liver metastases, PD (microwave ablation + radioactive seed implantation + capecitabine maintenance at 1.5 g bid po days 1-14/21 days)
November 2020	Mass of the hip, PD (trastuzumab: First time, 8 mg/kg, and after at 6 mg/kg iv drip + 240 mg liposomal paclitaxel day 1 iv drip)
January 2021	Vinorelbine: 30 mg day 1 and 40 mg day 8 iv drip + 1.5 g carboplatin bid days 1-14/21 days + 8 mg/kg inotumab iv drip + 400 mg pyrotinib qd po
October 2021	273 mg trastuzumab day 1 iv drip + 420 mg pertuzumab day 1 iv drip + 370 mg albumin paclitaxel day 1 iv drip
July 2022	400 mg pyrotinib qd po + 20 mg/kg cyclophosphamide q3-4w iv drip + 10 mg methotrexate q1w po
June 2023	Nasopharyngeal metastasis (4 cycles 100 mg albumin paclitaxel days 1, 8 and 15 q21d iv drip + 8 mg/kg trastuzumab day 1 iv drip)
December 2023	The nasopharyngeal metastasis was enlarged
January 2024	Patient succumbed

bid, twice daily; po, oral; qd, every day; q4w, every 4 weeks; im, intramuscular; iv, intravenous; GD, gemcitabine plus docetaxel; PD, progressive disease.

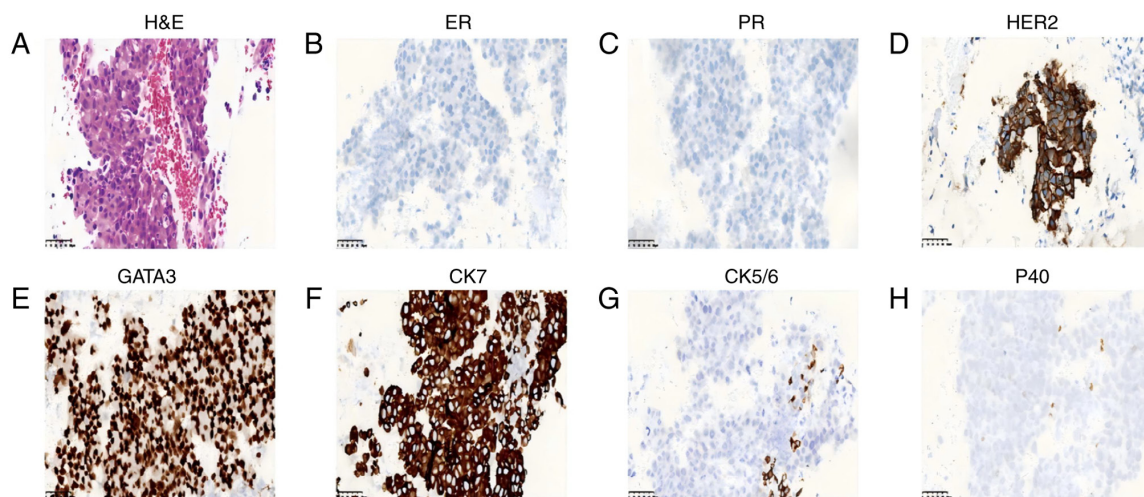


Figure 4. Histopathological (H&E staining; x400 magnification) and IHC (x400 magnification) images of the nasopharyngeal metastatic tumor. (A) H&E staining showing diffuse infiltration of neoplastic cells into the nasopharyngeal mucosa. Negative expression of (B) ER and (C) PR. Positive expression of (D) HER2, (E) GATA3 and (F) CK7. (G) Focal weak positivity for CK5/6. (H) Sparse positivity for p40. H&E, hematoxylin and eosin; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; GATA3, guanine-adenine-thymine-adenine-binding protein 3; CK, cytokeratin.

hormonal and HER2 status, the local invasion extent and other metastatic sites. The present study describes the patient treatment in detail, hoping to enlighten the general medical staff in

the treatment of such patients (Table I). To date, to the best of our knowledge, only one case was reported with isolated breast cancer metastasis to the nasopharynx, involved a 54-year-old

Table II. Cases of nasopharyngeal metastasis from breast cancer reported in the literature.

First author, publication year	Age, years	Sex	Time interval ^a	Presentation	Other metastases	Treatment	Outcome	Survival time after discovery of nasopharyngeal (Refs.)
Saab <i>et al</i> , 1987	58	F	8 years	Enlarged cervical lymph node	Lungs, sella turcica and skull base	Radiotherapy and hormonal therapy	Died	15 months (1)
Wanamaker <i>et al</i> , 1993	i) 77; ii) 44	i) F; ii) F	i) 16 months; ii) 10 months	i) Hoarseness, progressive shortness of breath and dyspnea on exertion; ii) facial cellulitis	i) Bone; ii) contralateral breasts and lungs	i) Chemotherapy; ii) chemotherapy	i) Died; ii) died	i) 14 months; ii) 5 months (8)
Marchioni <i>et al</i> , 2004	78	F	6 years	Non-specific headache, a right periorbital mass, diplopia and ptosis	Lungs	Radiotherapy	Died	4 months (15)
Baspinar <i>et al</i> , 2006	56	F	2 years	A 0.5-cm mass in the nasopharynx but asymptomatic	Lungs, liver, spleen and left adrenal gland	Palliative chemotherapy	Died	1 months (12)
Liao <i>et al</i> , 2010	50	F	4 years	Nose bleeding and nasal congestion	-	Surgery	Alive	Disease-free for 37 months postoperatively (25)
Davey and Baer, 2012	75	F	2 years	Left facial weakness, diplopia, nasal obstruction and left abducens nerve palsy	Sphenoid and ethmoid sinuses	Radiotherapy	Died	- (9)
Tewari <i>et al</i> , 2013	62	F	3 years	Blurred vision in the right eye, proptosis, diplopia and abducent nerve palsy	Meninx, orbit and bone	Chemotherapy, bisphosphonate and radiotherapy	-	- (27)
Agrawal <i>et al</i> , 2015	65	M	18 months	Severe headache, postnasal drip, sinus fullness and dry chronic cough	Lungs, bone and liver	Palliative chemotherapy and hormonal therapy	Died	1 year (10)
Alaoui Slimani <i>et al</i> , 2016	65	F	3 years	Severe headache and bilateral blindness	Bone and lungs	Palliative chemotherapy	Died	- (11)
Copson <i>et al</i> , 2018	52	F	5 years	Nasal obstruction, anosmia, rhinorrhea and right facial paresthesia	Skull base, anterior cranial fossa, liver and lungs	Immunotherapy and palliative chemotherapy	-	- (16)
Sellami <i>et al</i> , 2025	52	F	2 years	Headache, unilateral hearing loss, otalgia	Bone	Palliative chemotherapy	Alive	- (26)
Present case, 2025	53	F	10 years	Nasal obstruction and rhinorrhea	Bone, brain, liver and hip	Targeted therapy, chemotherapy and hormonal therapy	Died	7 months

^aInterval between diagnosis of primary tumor and detection of nasopharyngeal metastasis.

Table III. Immunohistochemical profile of the primary breast lesion and its nasopharyngeal metastasis in the present case and previous literature.

First author, publication year	Primary tumor	Metastasis	(Refs.)
Saab <i>et al</i> , 1987	-	-	(1)
Wanamaker <i>et al</i> , 1993	-	-	(8)
Marchioni <i>et al</i> , 2004	ER(+), PR(+), HER2(-)	ER(+), PR(+), HER2(-), CK(3+), GCDFP-15(1+/2+), p53(3+)	(15)
Başpınar <i>et al</i> , 2006	-	-	(12)
Liao <i>et al</i> , 2010	ER(-), PR(-), HER2(2+)	ER(2+), PR(-), HER2(2+)	(25)
Davey and Baer, 2012	ER(+), PR(+), HER2(-)	ER(+), PR(+), HER2(-)	(9)
Tewari <i>et al</i> , 2013	ER(+), PR(+), HER2(-)	-	(27)
Agrawal <i>et al</i> , 2015	ER(+), PR(+), HER2(-)	ER(+), PR(+), HER2(-)	(10)
Alaoui Slimani <i>et al</i> , 2016	-	-	(11)
Copson <i>et al</i> , 2018	ER(-), PR(-), HER2(-)	CK 7(+), ER(-), PR(-), HER2(3+)	(16)
Sellami <i>et al</i> , 2025	ER(+), PR(+), HER2(-)	ER(+), PR(+), HER2(-), p63(-), GATA3(+)	(26)
Present case, 2025	ER(+), PR(+), HER2(+)	ER(-), PR(-), HER2(3+), GATA3(3+), CK7(3+), CK5/6(+), p40(+)	

ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; GATA3, guanine-adenine-thymine-adenine-binding protein 3; CK, cytokeratin; GCDFP-15, gross cystic disease fluid protein 15; p53, tumor protein p53.

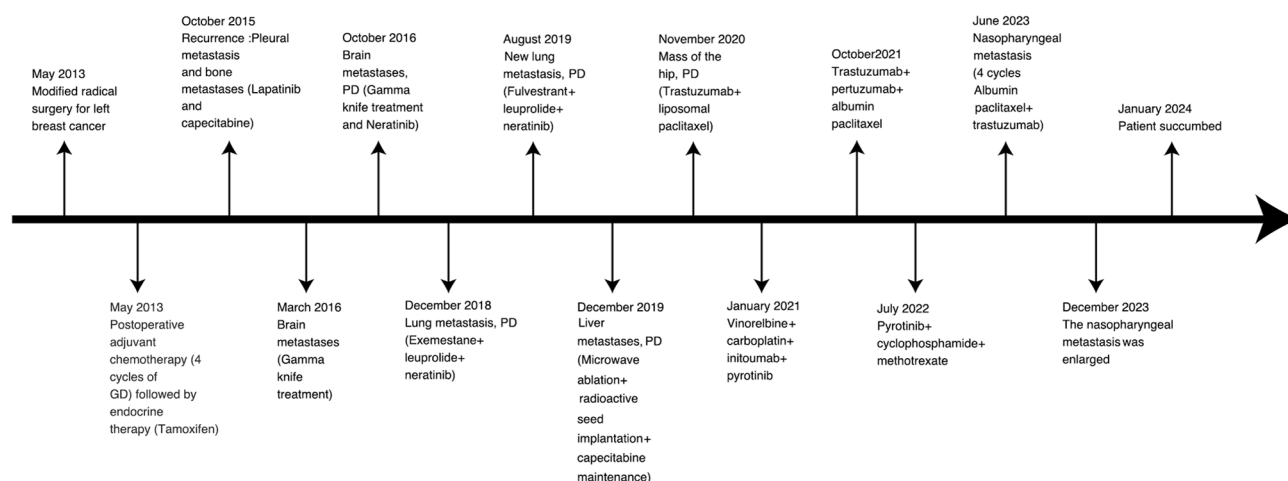


Figure 5. Timeline of treatment progression. GD, gemcitabine plus docetaxel; PD, progressive disease.

woman who underwent surgical resection (25). The patient remained disease-free for 37 months postoperatively, suggesting that surgical intervention may be a viable option for solitary nasopharyngeal metastases. However, most patients present with multiple metastases, limiting surgical feasibility. The present patient received four cycles of albumin-bound paclitaxel combined with trastuzumab, initially achieving a partial response. However, the nasopharyngeal tumor eventually developed drug resistance and progressed rapidly. As observed in previous cases, despite multimodal treatment, including chemotherapy, targeted therapy and radiotherapy, the prognosis remained poor. Given the limited number of reported cases, standardized treatment guidelines have yet to be established. The management is currently individualized, integrating targeted therapy, radiotherapy, chemotherapy,

immunotherapy and endocrine therapy, with multidisciplinary collaboration being essential for treatment planning (26). Early detection and intervention are critical for improving the patient prognosis (27).

In summary, the present case highlights the need to consider nasopharyngeal metastasis in patients with a history of breast cancer presenting with nasal or auditory symptoms. Prompt diagnosis and targeted therapy are essential for enhancing quality of life and prolonging survival. Further research is required to establish optimal management strategies for this rare metastatic presentation.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

YB conceptualized and designed the study, and drafted the manuscript. GY provided methodological guidance and revised the manuscript. CS obtained the medical imaging data. YN and XS conducted the analysis of the patient's clinical data. FH and GY were involved in the development of the patient's subsequent treatment strategy and participated in the medical decision-making process. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient to publish this case report and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

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