Case Report

Nasopharyngeal carcinoma metastasis to the breast

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ABSTRACT

Breast metastases from extra-mammary neoplasms are rare, accounting for <2% breast cancer cases. A 43-year-old female patient presented with a mass in her left breast and swelling in her left axillary region. A histopathological examination of the mass showed enlarged polygonal tumor cells with scant to moderate, eosinophilic to amphophilic cytoplasm and enlarged, hyperchromatic and pleomorphic nuclei with irregular nuclear membranes. An immunohistochemistry (IHC) examination was positive for pan cytokeratin and negative for CK7, CK20, S-100, LCA, HMB45, CD 20, desmin, myogenin, gross cystic disease fluid protein 15 (GCFDP-15), thyroid transcription factor (TTF-1) villin, estrogen receptor (ER), progesterone receptor (PR), and HER2, which led to the diagnosis of breast metastasis from nasopharyngeal carcinoma (NPC). The patient was deceased 3 months after the recommended medical intervention.

Keywords: nasopharyngeal carcinoma, metastasis, breast, Madinah, Saudi Arabia
a 2-month history of headache, epistaxis, nasal discharge, nasal blocking, unilateral hearing impairment, and bilateral neck swelling. Physical examination revealed bilateral neck nodes enlargement with the largest measuring 3.5 cm × 5 cm in the left cervical region. On nasopharyngoscopy, a mass in the nasopharynx was identified and biopsied. Histopathology findings of the biopsied mass reported as an undifferentiated nasopharyngeal carcinoma (NPC) (World Health Organization type III). Computed tomography (CT) and magnetic resonance imaging (MRI) of the head and neck showed a large heterogeneous mass at the left Fossa of Rosenmuller (FOR) with direct extension into the paranasal sinuses. Enlarged lymph nodes in the left supra-clavicular fossa is also noted which is in favor of metastatic lymphadenopathy. A complete metastatic work-up including CT of chest and abdomen, and bone scan was performed and revealed no significant abnormalities. She was thus diagnosed to have a NPC stage III (T3N3M0), according to the American Joint Committee on Cancer Staging. Three cycles of concurrent cisplatin (75 mg/m²) and radiation therapy (70 Gray) were administrated to the patient in March 2017 and were finally completed in May 2017.

**Clinical findings.** Upon completing her treatment, she was in clinical remission and was disease-free for 21 months until she presented again with a mass in her left breast and swelling in her left axillary region. The physical examination revealed a firm, rubbery, non-tender, and mobile lump involving the upper outer quadrant of the left breast. The skin and nipple-areola complex were unremarkable. The left axillary lymph nodes were matted, measuring 3 cm × 3.5 cm. No significant abnormalities were identified in the contralateral breast or axillary area.

**Diagnostic assessment.** Mediolateral and craniocaudal mammograms showed a spherical mass lesion in the left breast with ill-defined speculated margins, measuring 4 cm × 3.5 cm × 4.5 cm. A subsequent CT scan and MRI of the chest and abdomen revealed no signs of lung or liver metastases. Similarly, a bone scan revealed no bone metastases. An ultrasound-guided biopsy of the breast lesion and axillary lymph nodes was performed, and a histopathological examination from the breast and axillary lymph nodes showed cores of fibrous tissue infiltrated with cords and sheets of enlarged polygonal tumor cells with scant to moderate, eosinophilic to amphiphilic cytoplasm and enlarged, hyperchromatic and pleomorphic nuclei with irregular nuclear membranes (Figure 1). An IHC examination was positive for pan cytokeratin (phosphoenolpyruvate carboxykinase, monoclonal, MNF 116, 1:300, Dako, Carpinteria, California, USA) and negative for CK7, CK20, S-100, leukocyte common antigen (LCA), HMB45, cluster of differentiation (CD) 20, desmin, myogenin, gross cystic disease fluid protein 15 (GCFDP-15), thyroid transcription factor (TTF-1), villin, estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (Figure 1). As she was a known case of NPC, and based on the histopathology findings and IHC profile, the patient was diagnosed with metastatic NPC, undifferentiated type of the left breast and left axillary lymph nodes.

**Therapeutic intervention, follow-up, and outcomes**
She refused any further treatment and died 3 months after diagnosis (Figure 2). The case report was conducted ethically in accordance with the World

![Figure 1 - Microphotography showing poorly differentiated A) malignant cells (hematoxylin-eosin at magnification x 40) and B) positive staining of tumor cells for PCK (Avidin Biotin at magnification x 40) (arrows indicate malignant cells).](image-url)
Medical Association Declaration of Helsinki. Informed consent was not obtained from the patient due to no communication.

**Discussion.** The breast is an uncommon site for a metastatic tumor, with the incidence of metastatic breast tumors from other primaries having been reported in the range of 1.7-6.6% in an autopsy study, 1.2-2% in clinical reports, and 2.7% from fine needle aspiration cytology reports. However, many other studies have reported a rate of 0.5-6%. Moreover, breast metastases from NPC are extremely uncommon and usually occur as part of a disseminated disease. It has been observed that a metastatic breast lesion can be either the first evidence of recurrence or the first manifestation of a clinically occult malignancy. The first case of NPC metastasizing in the breast was reported in 1991; since then, only 12 cases of NPC metastasis in the breast have been described in the literature. A majority of these cases have reported it in the unilateral side, and only 3 case reports have reported it in bilateral breasts. Although metastatic NPC in the breast is seen mainly in female patients, 2 cases have been reported in males as well.

The mechanism by which NPC metastasizes to the axillary lymph nodes is not completely understood and can be explained by the following ways: i) retrograde lymphatic drainage due to obstruction; when the large supraclavicular lymph nodes block the lymphatic ducts, as in our patient, metastasis can spread retrograde to the axillary lymph nodes; ii) the destructive effect of radiotherapy during the first treatment, which cuts off blood supply to the tumor; this is unfavorable for tumor growth and causing it to relocate and occur far from the nasopharynx such as the axilla.

The previous literature has reported the age range of the breast metastases from NPC in the fifth and sixth decades of the patients’ lives; our patient was also in her fifth decade. Clinically, breast metastases from NPC are usually present as solitary, mobile, and well-circumscribed masses; however, Pai et al and Leach et al have reported multiple rubbery subcutaneous masses in their reports. In the present case, the tumor presented as a firm, rubbery, non-tender, and mobile mass. Following the primary NPC, the latency period from the initial diagnosis of NPC to the diagnosis of breast metastasis ranged between 6 and 42 months, with a median latency period of 27 months. It has been observed that a metastatic breast tumor could occur immediately after the first course of treatment or within 24 months of treatment completion. In our case, the patient developed breast metastasis after 21 months of initial treatment for NPC. A comparison of the present case report with previous cases of NPC metastasizing to the breast is summarized in Table 1.

Metastatic NPC can present a diagnostic challenge, which is mainly attributed to the rarity of this lesion. The distinction between metastatic NPC and primary breast tumors on clinical, histopathological, and radiological examination is challenging, as their characteristics are quite similar in the majority of cases. Metastatic NPC may mimic lymphoepithelioma like carcinoma, medullary carcinoma, or an infiltrating ductal or lobular carcinoma with inflammatory stroma. This is further complicated by the absence of ER, PR, and HER2 immunostaining, a phenotype unique to patients with triple negative breast cancer. Hence, histopathological, IHC, and radiological findings, along with the patient’s clinical history, must be considered in the
specialization of metastatic NPC from primary breast cancer. Therefore, the correct diagnosis is of critical significance, as the treatment modalities of these 2 types of tumor is variably different.\textsuperscript{13} An in situ hybridization using an EBV encoded RNA probe is the most sensitive and specific diagnostic tool available in the literature.\textsuperscript{14} Unfortunately, this technique is not available in our laboratory at present. However, we believe that the clinical history, histopathological findings, and IHC profile clearly confirm the diagnosis of NPC metastatic to the breast in our patient. The ideal treatment for metastatic NPC is chemotherapy and radiotherapy, and patients with solitary breast metastasis from NPC may gain long term survival, as observed by Xiao et al.\textsuperscript{3}

In conclusion, this case highlights the rarity of the NPC lesion and importance of clinical, histopathological, and IHC examination, along with the patients’ history, for appropriate diagnosis and treatment.

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\begin{table}
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\caption{Comparison of present case report with the previously reported cases of nasopharyngeal carcinoma (NPC) metastasizing to the breast.}
\begin{tabular}{llllllll}
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Author & Year & Age/ gender & Time to breast metastasis (months) & Site & Axillary lymph nodes & Other distant metastasis & Treatment & Survival \\
\hline
Driss et al\textsuperscript{8} & 2007 & 25/F & 42 & B/L & Present & Liver and bones & Palliative & N/R \\
Leach et al\textsuperscript{2} & 2013 & 49/F & 39 & Left breast & Present & Bone iliac lymph nodes & Chemo + radiation & N/R \\
Liang et al\textsuperscript{10} & 2014 & 49/M & 5 & Right breast & Present & Cervical lymphadenopathy & Chemo + radiation & Surviving till the reporting of the case \\
Li et al\textsuperscript{9} & 2015 & 56/F & 3 & Left breast & Present & Absent & Liver & Refused & 6 months \\
Xiao et al\textsuperscript{3} & 2015 & 46/M & 9 & Right breast & Absent & Absent & Chemo + mastectomy & >10 years \\
Vaishnav et al\textsuperscript{7} & 2015 & 28/F & 2 & B/L & Absent & Absent & Chemo & N/R \\
Pai et al\textsuperscript{11} & 2017 & 45/F & 52 & Right breast & Present & Supraclavicular and intraabdominal lymph nodes soft tissues & Chemo + radiation neck dissection & Surviving till the reporting of the case \\
Zhao et al\textsuperscript{9} & 2020 & 52/F & 12 & B/L & Present & Absent & Chemo & Surviving till the reporting of the case \\
Present case & 2020 & 43/F & 21 & Left breast & Present & Absent & Refused & 3 months \\
\hline
N/R: not reported B/L: bilateral
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