

An unusual case of metastatic male breast cancer to the nasopharynx – review of literature

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Abstract: Metastatic breast carcinoma has been described to the various areas in the head and neck region. However, these metastases are rarely found in nasopharynx. Herein we are presenting the first case of male breast carcinoma with the longest survival secondary to distant metastases in right maxillary sinus and extending to the nasopharynx with extensive skeletal & lung metastases. Here we present a case of 65-year-old male with past medical history of right breast carcinoma, presented clinically with symptoms of recurrent sinusitis. Physical examination revealed a mass in the nasopharynx, which subsequently proved to be hormonal receptor positive high-grade adenocarcinoma secondary to metastasis of primary breast cancer on biopsy. The patient received three cycles of palliative chemotherapy based on Doxorubicin with Paclitaxel weekly. In spite of that, he developed pulmonary, liver and bone metastases. Later, treatment regimen was changed to Gemcitabine, Paclitaxel and injectable Zolendronate with calcium and vitamin D supplementation. Still he didn't show any improvement and later, he developed febrile neutropenia. Then, he refused further chemotherapy and died after 12 months of receiving the best hospice care. Breast cancer is one of the most common cancers in terms of incidence and mortality; breast cancer deserves extensive studies and research in different aspects. Breast cancer metastasizing to nasopharynx would be the last diagnosis that comes to mind for a male patient presenting with clinical features suggestive of recurrent sinusitis infection. As recurrent sinusitis is a very common ailment affecting human kind and is mostly due to benign causes. Metastasis, although rare, should be included in the differential diagnosis of nasopharyngeal lesion since it may clinically mimic a benign neoplasm or primary carcinoma. Based on our clinical experience and review of literature, although it is a very rare possibility in a patient with sinusitis, still we advise not to overlook any symptoms suggestive of the etiology of recurrent sinusitis.

Keywords: Breast carcinoma; metastasis; nasopharynx

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Introduction

Advancement in the medical science facilitated early detection and better adjuvant systemic chemotherapy for the breast cancer following which the mortality rates from breast cancer have been decreasing steadily in most Western countries since the early 1990s. However, it is still the leading cause of cancer death in women in both

developing (269,000 deaths, 12.7% of total) and developed (189,000 deaths, 15.5% of total) regions. Approximately 5% to 10% of breast cancers are metastatic at diagnosis; of these, approximately one-fifth survives for 5 years. Depending on the prognostic factors, up to 30% of node-negative and up to 70% of node-positive breast cancers relapse. The prevalence of metastatic disease is high because many women live with this disease for several years.

Metastasis is the most poorly understood aspect of breast cancer. Metastatic spread to nasal cavity, nasopharynx and hypopharynx is extremely rare, and if it occurs, the primary site of malignancy is usually a renal cell carcinoma (1,2). Breast cancer metastases to the nasopharynx are extremely rare, and the case would be incredibly rare if it happened to occur in a male patient as in this case. However metastases from any tumor, not only from the breast, are rare in the nasopharynx (3). We performed English literature search using PubMed and CrossRef on 10th May 2015, which yielded more than 1,340 results of published material on PubMed. The MeSH terms used were “metastatic breast cancer”, “nasopharyngeal metastasis” and “recurrent sinusitis”. We have critically analyzed and included most of the important case series, reports and previous reviews from 1970 to May 2015 in our present review.

Literature analysis reported two cases, in which, breast tumor metastasized to the nasopharynx, and another two cases with metastasis to the nasal cavity (4,5). Here we present a very rare case report, where a male patient had nasopharyngeal metastases originally suspected to be a primary malignancy, and underlines how the final diagnosis clearly required a meticulous clinicopathological analysis. A review of the literature appears to indicate that, once breast carcinoma metastasizes to the sinonasal region, it may be related to an extremely poor prognosis. Finally, the use of a broad spectrum and appropriate panel of immunohistochemical markers may play a key role in this specific scenario. In this review, we discuss the clinical presentation, investigations and management options for breast cancer metastasizing to sinonasal region as well as other tumors metastasizing to the nasopharynx.

Case presentation

A 65-year-old man presented in Jan 2009, with palpable mass in his right breast. Fine needle aspiration cytology was done which was suggestive of malignancy, and a preoperative staging of T2aN1M0 was made. The patient underwent right modified radical mastectomy with an axillary lymph node dissection. The tumor was 3 cm in its largest diameter with 5 of 16 axillary nodes involved (pT2pN1M0) and the specimen was sent for histopathological analysis. The pathological diagnosis of invasive adenocarcinoma of breast was made (*Figure 1*). Immunohistochemical stains at that time indicated that tumor cells were positive for estrogen receptors (ER), progesterone receptors (PR) and negative for human epidermal growth factor receptor-

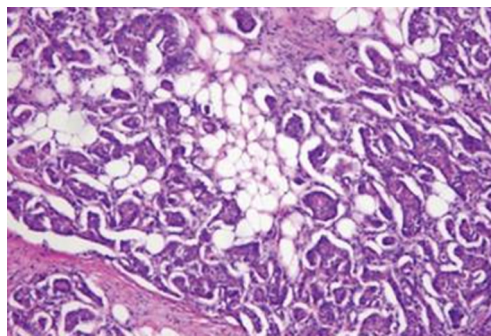


Figure 1 The tumor was histologically graded as invasive adenocarcinoma of breast (H&E, ×200).

type 2 (Her 2 neu). The pathological diagnosis of invasive adenocarcinoma of breast was made.

Postoperatively, the patient received six courses of chemotherapy based on FAC protocol, i.e., 5-FU 500 mg/m² IV on days 1 and 8 or days 1 and 4 plus doxorubicin 50 mg/m² IV on day 1 plus cyclophosphamide 500 mg/m² IV on day 1 every 3 weeks for six cycles. After completion of chemotherapy, he received adjuvant external beam radiotherapy 50 Gy in 25 daily fractions over 5 weeks to the chest wall, supraclavicular, infraclavicular regions and internal mammary region also additional small dose of radiation (16 Gy) to the area where the cancer was located.

Along with these, he also received hormonal agent tamoxifen 20 mg PO every day. Following completion of scheduled treatment, patient was doing well and was discharged in satisfactory condition.

Later in July 2010, he developed features of recurrent sinusitis as severe headache, postnasal drip, sinus fullness and dry chronic cough. Head and neck examination revealed a growth in the nasopharynx, which was confirmed by magnetic resonance imaging (MRI) of brain and paranasal sinuses. MRI revealed a soft tissue mass occupying the right maxilla and ethmoidal air spaces and extending to the right frontal sinus (*Figure 2*). Histopathological analysis of punch biopsy of mass showed large pleomorphic cells with hyperchromatic nuclei and scant glandular areas and solid epithelial sheets. The morphologic and cytologic features were similar to those of the primary breast carcinoma with Modified Bloom and Richardson Grade 3, score 8 & further molecular analysis showed that the tumor was ER, PR positive and Her 2 neu negative (*Figure 3*). Tuberculin testing was non reactive. High resolution computed tomography (HRCT) was negative for any lung metastasis. Bone scan with 99 mTc, was suggestive for no evidence

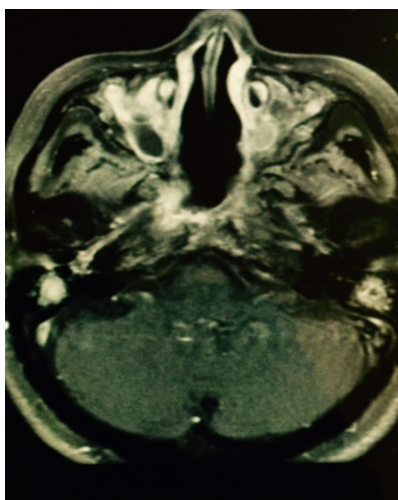


Figure 2 Magnetic resonance imaging showing a vegetant mass in the right maxillary sinus and adjacent areas.

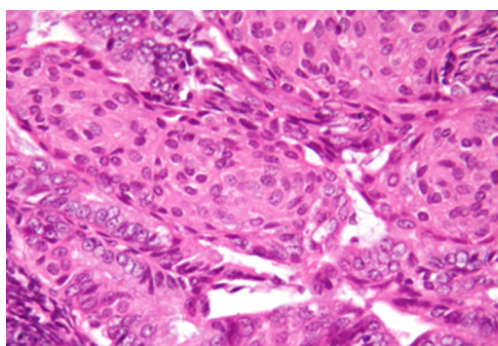


Figure 3 The histological analysis of right maxillary area reported as high grade invasive adenocarcinoma of breast (H&E, $\times 200$).

of metastasis. The patient was treated by three cycles of palliative chemotherapy based on doxorubicin and paclitaxel weekly and hormonal agent anastrozole. Further evaluation in 2011 showed a progressive disease with the appearance of pulmonary, liver and bone metastases on chest X-ray and ultrasonography abdomen, along with altered liver function test and bone scan suggestive of metastasis. After tumor board meeting, the treatment was changed to other protocol regimen, which was Gemcitabine with paclitaxel, exemestane and injectable bisphosphonate zoledronate with calcium and Vitamin D supplementation.

In spite of this, he didn't show any improvement and later, he developed febrile neutropenia for which intravenous imipenem with gentamycin was also started. Patient's general condition deteriorated and his karnofsky

performance status was very poor. Later he refused for further chemotherapy in spite of all efforts and died at 12 months after receiving best supportive care.

Discussion

Breast cancer is the most common cancer among women in all countries, including developing countries, where one in eight women will be diagnosed with breast cancer at some point in their lifetime. The incidence was estimated by 232,670 new cases in 2014, which accounts for 14% of all new cancer cases in the USA this year. Breast cancer asseverates as the third most common cancer cause of cancer related mortality after lung and colorectal cancer, with 40,000 guesstimated deaths in 2014. Screening for breast cancer is an important role in decreasing the morbidity and mortality of the disease, given the much higher survival rate for earlier stage tumors versus more advanced disease. Five-year survival varies form 98.5% and 84.6% in localized and regional disease, respectively, to 25% in distant metastatic disease as outlined by the SEERS database (6).

The most established sites of the breast cancer metastases are bones (40-75%) followed by lung (5-15%) and pleura (5-15%) then liver (3-10%) and brain in less than 5% cases. Among various studies related to the autopsies performed over patients dying of metastatic breast cancer, the reported incidence of metastasis involving the most common organs were lung/pleura (59-80%), liver (65-56%), bones (44-71%), non axillary lymph nodes (40-55%), adrenal glands (31-49%), pleura (23-51%), pericardium (19-21%), brain (9-20%) and intestine (18%) (7).

The World Health Organization histological classification of tumors involving the upper respiratory tract and ear are outlined as (I) the nasal cavity and paranasal sinuses; (II) the nasopharynx; (III) the larynx, hypopharynx, and trachea; (IV) the external ear; and (V) the middle and inner ear. Unlike previous studies, we considered this classification in our literature review and after extensive analysis we found very few cases of distant metastasis to the nasopharynx, from the primary cancer (8).

Few notable ones are four cases from primary in the kidney, six cases with breast being the primary source, two cases from lung, one case from liver and one was Hodgkin lymphoma (*Table 1*). In the index case ER, PR positive invasive breast adenocarcinoma metastasizing to the nasopharynx was reported (15-17). Clinical presentation related to the occurrence of a metastatic tumor in the sinonasal tract are similar to non-specific symptoms seen

Table 1 Showing details of all reported cases of breast cancer metastasizing to nasopharynx

#	Year	Study	Presentation	Treatment	Outcome
1	1987	Saab <i>et al.</i> (9)	Symptomatic pulmonary mets & asymptomatic nasopharyngeal mass	Chemotherapy	Died
2	1993	Wanamaker <i>et al.</i> (10)	Case series (I) laryngeal metastasis; (II) facial cellulitis	–	Died
3	2004	Marchioni <i>et al.</i> (11)	Right periorbital mass, causing diplopia and ptosis	Palliative radiotherapy	Died (4 months)
4	2006	Başpınar Ş <i>et al.</i> (12)	Metastatic liver nodule with incidental mass in nasopharynx	–	Died (1 month)
5	2012	Davey <i>et al.</i> (13)	Horizontal diplopia and incomplete left abducens (VI) nerve palsy	Palliative radiotherapy + anastrozole	Died (4 months)
6	2013	Tewari <i>et al.</i> (14)	Visual symptoms, diplopia and abducens (VI) nerve palsy in right eye	Chemotherapy	NA
7	Index Case	Swati <i>et al.</i>	Recurrent headache, sinus fullness & chronic cough	Chemotherapy	Died (12 months)

in course of upper respiratory tract infections as facial pain, epistaxis, nasal obstruction and facial asymmetry represent the main manifestations and may remain silent for a long time. Conversely, in case of involvement of orbit they do present with diplopia, epiphora, blepharoptosis, decreased visual acuity and proptosis while headache might occur due to sinus fullness or meningeal involvement secondary to mets. Thus possibility of a primary or secondary maxillary tumor must be considered in case of ineffective sinus infection treatment (9-12).

In this case the initial diagnosis of breast cancer was made through fine needle aspiration. Following the confirmation of the diagnosis, the appropriate management was initiated by surgery and evaluation of the regional lymph nodes showed a 3 cm tumor and five involved lymph nodes. As tumor was ER, PR positive breast cancer, we gave category one adjuvant chemotherapy, hormonal therapy along with postoperative radiation according to National Comprehensive Cancer Network (NCCN) guidelines which was done successfully (13,14,18-22) (*Figure 4*). Later, he presented with headache and nasal symptoms suggestive of recurrent sinusitis. On further evaluation, there was a mass in the nasopharynx on MRI and the confirmation of its nature was made by punch biopsy. The histopathological and hormonal receptor analysis confirmed that this mass appeared to be adenocarcinoma secondary to metastasis from primary breast cancer. The patient received an appropriate work up including

molecular analysis of the tumor, HRCT to determine any pulmonary involvement, bone scans and positive purified protein derivative (PPD) test which is a screening tool for tuberculosis (TB). The patient received doxorubicin with paclitaxel. In 2011, following the progression of the tumor and metastasis to bones, lungs and liver, the chemotherapy regimen was changed to another NCCN approved regimen, Gemcitabine and paclitaxel, along with injectable zoledronate, calcium and vitamin D supplementation in response to bone involvement. When the patient developed febrile neutropenia as a side effect to the cytotoxic therapy, he received Imipenem, a beta lactam, and gentamycin to cover gram-negative organisms. Although the mean survival of similar patients reported earlier was 1-4 months, but with the regimen given in the index patient we achieved a drastically increased survival of 12 months.

To our knowledge, this is the first reported case of nasopharyngeal tissue involvement in male patient with longest survival of 12 months secondary to metastatic breast cancer. The recent development of more effective chemotherapy regimens for treatment of breast cancer may make chemotherapy a more reliable option for treatment of life-threatening manifestations of this cancer. Although, there is no established guideline for the treatment such condition, anecdotal experiences suggest the role of few chemotherapeutic agents as platin based compounds, adriamycin and gemcitabine.

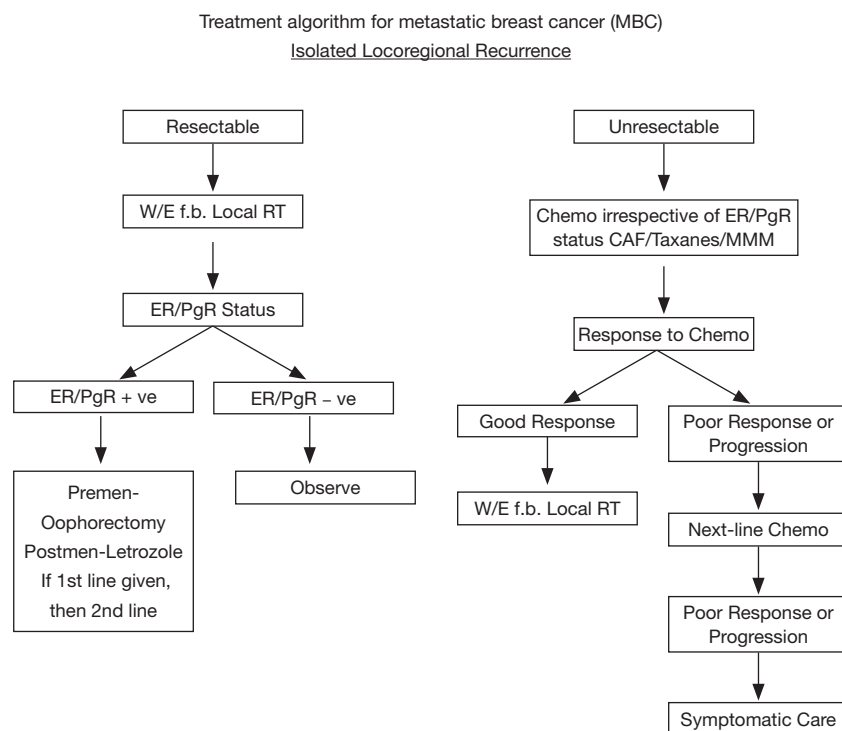


Figure 4 Treatment protocol for management of metastatic breast cancers.

Conclusions

The learning points we gained through this experience are:

- (I) Metastasis to nasopharynx from a distant primary is extremely rare;
- (II) A very high index of suspicion needed for the definitive diagnosis;
- (III) Immunohistochemical markers may be helpful in the correct diagnosis.

In absence of clear-cut treatment guidelines, we recommend further research in order to establish the development of newer chemotherapeutic regimen for such cases.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Consents: Written informed consent to publication was obtained from the patient.

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