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Case Report

A remarkable response to palliative treatment in metastatic breast cancer: A case report and comprehensive literature review ☆☆☆★

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ABSTRACT

The case report describes a patient with stage IV breast cancer which metastasized to the lungs. The patient's initial computed tomography (CT) scan revealed a malignant lesion in the upper outer quadrant of the left breast and multiple pulmonary nodules, suggesting pulmonary metastasis. After starting palliative chemotherapy with intravenous paclitaxel

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and subcutaneous injections of Herceptin, a follow-up CT scan 3 months after the initiation of treatment showed the disappearance of metastasis, and her cancer regressed to stage II breast cancer that could be surgically resected. This case report highlights the importance of timely and appropriate palliative treatment measures, which can lead to unexpected outcomes, such as the regression of metastatic lesions and the possibility of curative treatment in such advanced cancer.

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Introduction

Breast cancer is considered the most common malignancy in the United States [1]. The incidence of breast cancer increases by 0.4% per year according to the literature. However, there is a 1.6% decline in the death rate annually [2]. Three major subtypes of breast cancer exist based on either the presence or absence of molecular biomarkers for estrogen, progesterone, and human growth factor-2 (ERBB2) receptors. These include hormone receptor-positive/ERBB2-negative (70% of cases), ERBB2-positive (15%-20%), and triple-negative in which the tumor lacks all 3 standard molecular biomarkers (15%) [3].

Advanced breast cancer can potentially lead to death, and this usually occurs when metastases have already spread to the lymph nodes and then to distant organs, compromising their function. It has a poor prognosis due to the presence of the Master Regulator of Cell Cycle Entry and Proliferative Metabolism (MYC) oncogenes in most cases [4]. These genes, which are identified in estrogen receptor (ER) positive breast cancer, are associated with a high load of mutations and increased infiltration of pro- and anticancerous immune cells, leading to aggressive local and distant tissue response [5].

Another indicator of poor prognosis in breast cancer is obesity. There is a poor outcome for both pre- and postmenopausal obese women with breast cancer, with an increased risk estimate of 1.82 in obese postmenopausal women [6]. Potential mechanisms that link obesity to breast cancer outcomes include higher levels of insulin and leptin, which lead to increased proliferation and reduced apoptosis [7].

Eradication of the tumor and preventing recurrence are the goal treatment for patients who do not have metastasis in their initial presentation. More than 90% of breast cancers are not yet metastatic at the time of initial diagnosis [3]. Breast cancer treatment options include surgery, chemotherapy, radiation therapy, and targeted therapy. Surgery is the first line of treatment, removing the cancerous tumor and surrounding tissue while sparing as much of the healthy breast tissue as possible. Chemotherapy is often recommended after surgery to kill any remaining cancer cells. Radiation therapy uses high-energy rays to kill cancer cells. Targeted therapy uses drugs that target specific gene mutations or protein receptors in cancer cells. It is used in patients with HER2-positive breast cancer, which tends to grow more quickly and aggressively than other types. Combination therapy, which involves using 2 or more treatments in combination, may also be recommended. Treatment guidelines have been developed to help doctors make decisions based on the lat-

est research and evidence. Termination of each type of treatment is made on a case-by-case basis in consultation with the patient.

Therapeutic options for breast cancer patients with metastasis include systemic drugs, surgical resection, and postoperative radiation after surgery. Metastatic breast cancer is treated depending on the subtypes; however, the treatment goal is mainly palliative as the majority of patients have a poor prognosis [3]. Breast cancer screening is expected to detect the early stage of potentially life-threatening breast cancer, which can lead to a reduction in the mortality rate [4]. Here, we present a case of advanced breast carcinoma that responded to initial treatment and regressed to surgically treated breast cancer.

Case presentation

We present a case of a 51-year-old female who presented at the outpatient oncology department with the chief complaint of a gradually growing lump in her left breast for the past 4 months before her initial presentation.

Upon further history taking, the patient mentioned that she had a lump in her right breast which was removed 6 years ago. The rest of her past medical history is unremarkable and she has never had mammography done before. On examining the left breast, the solitary lump was palpable, painless, irregular, hard, slightly mobile though fixed to the underlying skin, about 5 × 5 cm in size, and the 2 o'clock position. No color changes, edema, nipple discharge or retraction, or dimpling of the overlying skin were noted. Her vital signs and the rest of the systemic examination were unremarkable.

Her initial presentation and past history raised suspicion of malignancy and therefore, she was referred for several more tests. Mammography was first done which showed a partly circumscribed high-density mass lesion in the upper outer quadrant of the left breast with spiculated margins and adjacent architectural distortions as shown in Fig. 1. A correlative breast ultrasound was performed on the same day demonstrating an ill-defined large lobulated hypo-echoic mass lesion measuring approximately 32 × 45 × 46 mm with adjacent heterogeneous breast parenchyma. However, the ipsilateral axilla showed few benign-looking lymph nodes. The mammography and ultrasound of the right breast were significant for postsurgical changes and post lumpectomy scar at the upper outer quadrant, respectively, but were otherwise unremarkable as shown in Fig. 1.

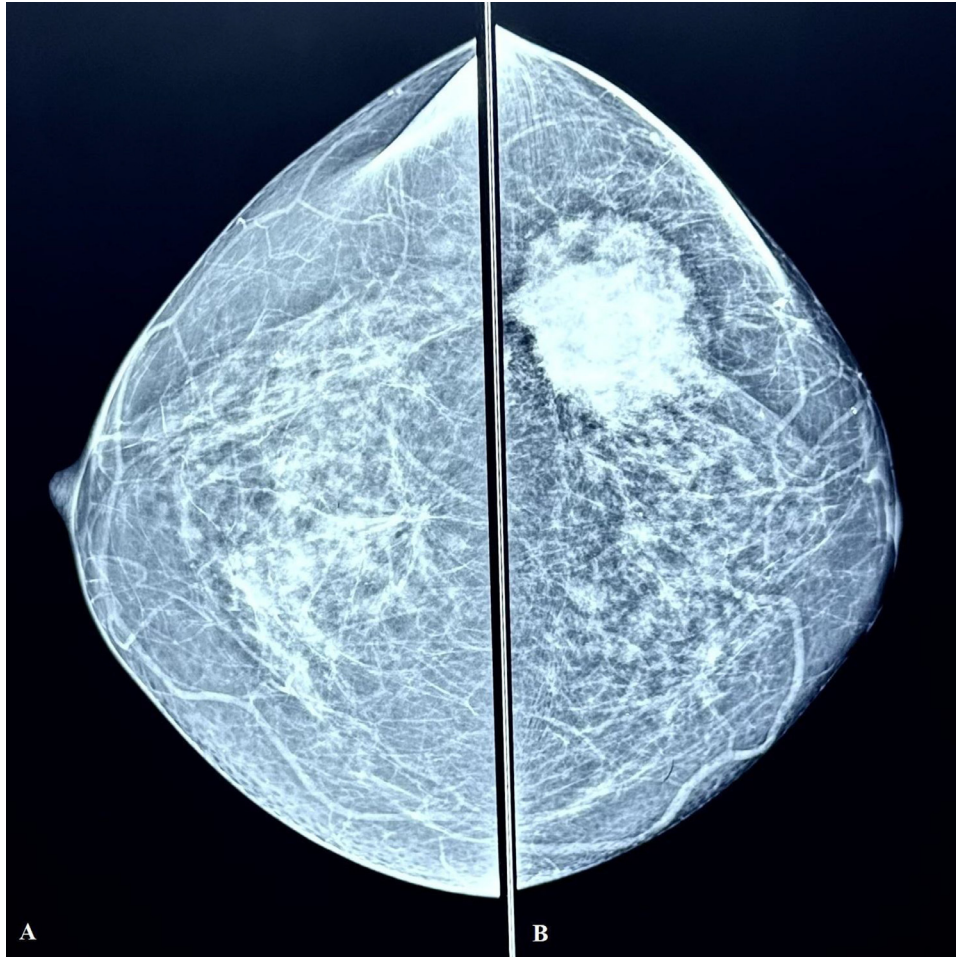


Fig. 1 – Mammography of the right (A) and left breasts showing a high-density mass lesion in the left upper outer quadrant (B).

Due to these findings, the patient was elected to undergo a tru-cut biopsy procedure which revealed an infiltrative tumor showing almost 50% duct formation with moderate pleomorphism and a mitotic rate of 6-10 mitoses/10 high-power fields as shown in Fig. 2. Furthermore, immunohistochemical staining of the specimen revealed it to be ER-positive in 15% of tumor cells, progesterone-receptors (PR) negative, and ERBB2 positive in 80% of tumor cells. Thus, the patient was diagnosed with grade II invasive ductal carcinoma. A complete blood count was also ordered and showed lymphocytosis and slightly elevated red cell distribution width, but otherwise unremarkable.

Her initial diagnosis raised further suspicion of metastatic disease and she was subsequently referred for further tests. A bone scan and whole-body computed tomography (CT) scan with contrast was later on performed. Her bone scan was negative for osteoblastic metastases, and her CT scan showed a lobulated enhancing left breast mass measuring 4.4×3.8 cm in the upper outer quadrant with ipsilateral axillary and retropectoral lymphadenopathy, along with multiple variable-sized pulmonary bilateral soft tissue nodules suggesting pulmonary metastasis as shown in Fig. 3.

Further evaluation with a positron emission tomography-computed tomography (PET-CT) scan revealed bilateral multiple fairly defined pulmonary nodules, likely metastatic, and ruled out any further metastasis in the adjacent lymph nodes and the rest of the body, indicating stage IV breast cancer (T3cN0cM1).

Upon establishing the diagnosis of advanced metastatic breast carcinoma, the patient was initiated on palliative chemotherapy with intravenous paclitaxel (175 mg/m^2) and herceptin (600 mg/m^2) subcutaneous injections once every 3 weeks. Following 4 cycles of treatment, a follow-up whole-body CT scan with contrast was done about 3 months after the initial presentation. While demonstrating a lobulated enhancing mass in the upper outer quadrant of the left breast, it unexpectedly revealed complete regression of the pulmonary metastatic nodules as shown in Fig. 4. The chemotherapy regimen was modified accordingly by temporarily substituting injections of cyclophosphamide (600 mg/m^2) and doxorubicin (60 mg/m^2) for 4 cycles, in place of herceptin and paclitaxel. Currently, 2 out of the 4 cycles have been completed. Following this if there is no metastatic disease, mastectomy has been advised followed by hormonal therapy.

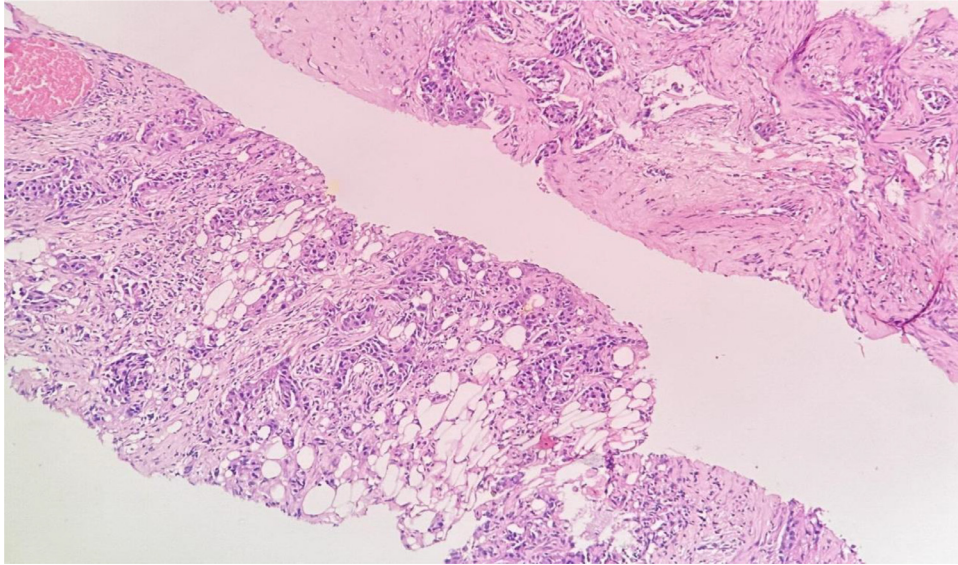


Fig. 2 – Breast mass biopsy showing an infiltrative tumor with abundant duct formation.

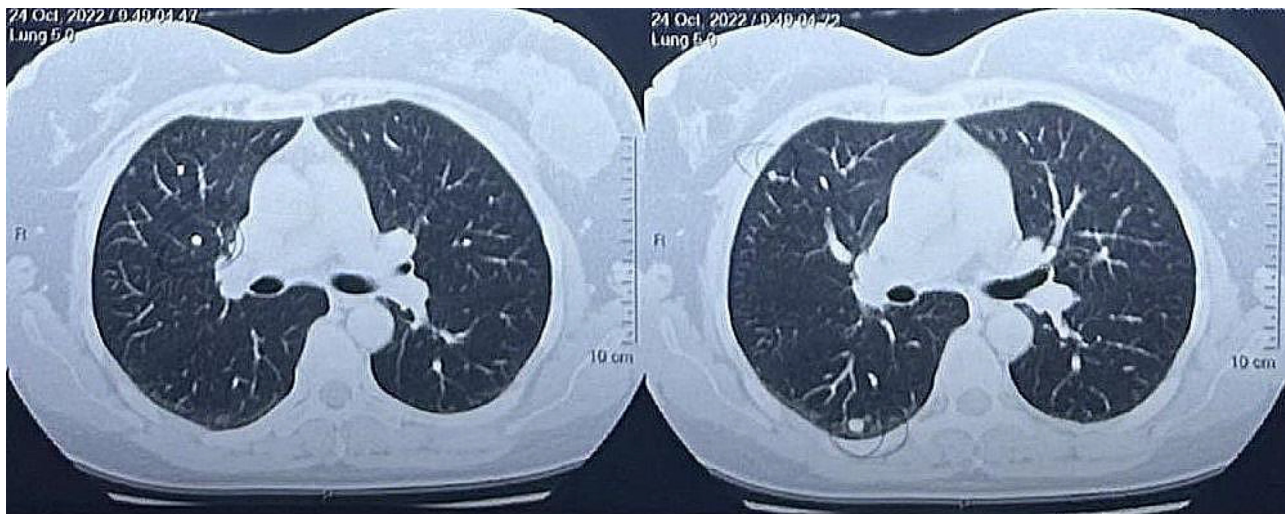


Fig. 3 – CT scan showing a left breast mass and pulmonary nodules.

Discussion

Breast cancer is considered the second leading cause of cancer death among women in the United States [8]. In the past 3 decades, its mortality rate has been decreasing steadily as a result of increasing public awareness and annual screening using mammography [9]. The median age for diagnosis is 62, and African American women have a higher risk of developing the disease at a younger age. Many risk factors have been well described in the literature, which includes genetic mutations, early menarche, nulliparity, obesity, and alcohol consumption [10]. The most common presenting symptom by far is a breast lump that is frequently noticeable by palpation. A

less common presenting symptom includes breast pain and skin changes commonly referred to as *peau d'orange* [11].

Mammography is the primary screening test for breast cancer in the United States and is usually offered to women beginning at the age of 40 [12]. Although clinical breast examination alone is not recommended as a screening method among average-risk women at any age as it can miss many asymptomatic cancerous lesions, it can still be utilized and relied on in low and middle-income countries where access to mammography is not feasible [13].

The most common classification used in breast cancer is the World Health Organization (WHO) classification which describes both benign and malignant neoplasms of different origins [14]. Grading breast cancer by examining a specimen of

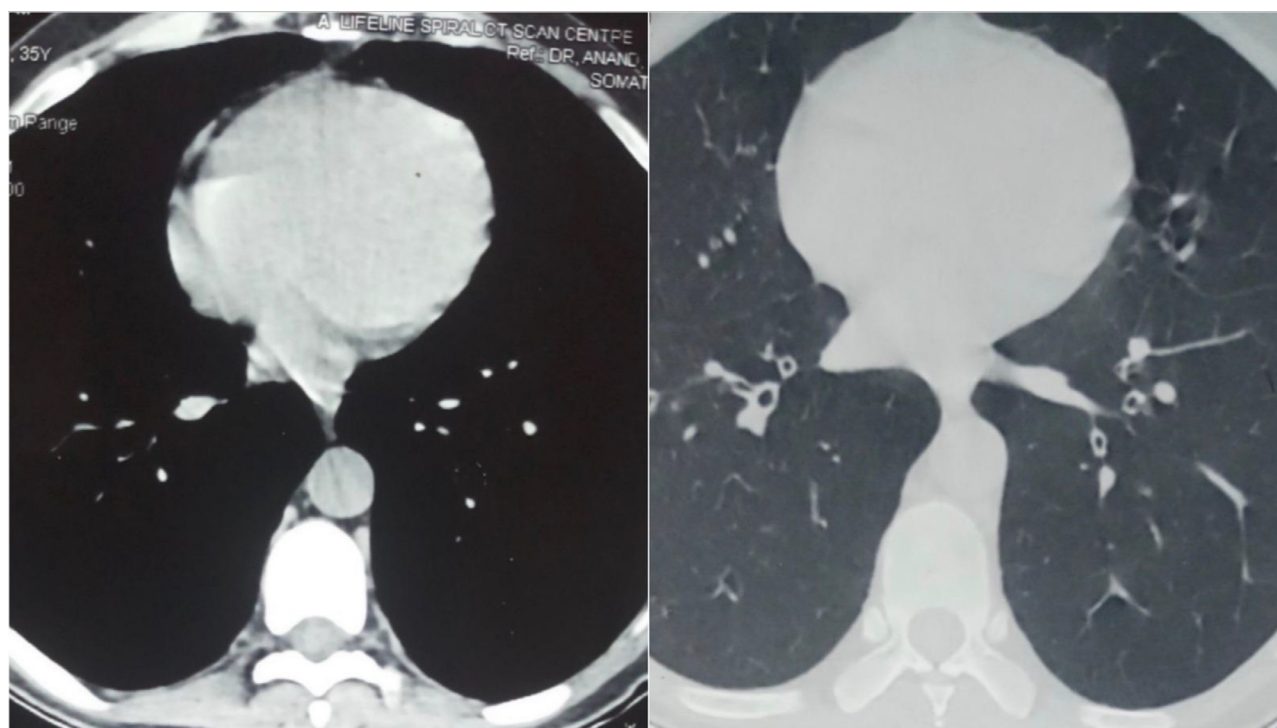


Fig. 4 – Follow-up CT scan showing complete resolution of pulmonary nodules.

tissue biopsy is used to determine the histological malignancy of breast cancer within the same WHO classification that can differ in its morphological features, by checking how much the cancerous cells look like normal ones [15]. Immunohistochemical and cytogenetic tests are crucial diagnostic markers that can help determine the proper treatment. Therefore, histologic examination via tissue biopsy remains the definitive diagnosis of breast cancer [16].

Staging breast cancer is also important in establishing the extent of the disease and relies primarily on the TNM system, which involves determining the size of the tumor, spread to nearby lymph nodes, distant metastasis, positive staining for ER and/or PR on tumor cells, ERBB2 status, and the grade of cancer [17]. Metastasis from primary breast cancer can involve any part of the body, but most frequently involves the bones followed by the lungs and brain. Therefore, investigative total-body imaging techniques are crucial in determining the stage of the disease, with the stage of cancer is inversely related to its prognosis [18].

The management of breast cancer depends primarily on the type and stage of cancer. Overall patients' health and their personal preferences should also be considered. Stage 0, which is ductal carcinoma in situ (DCIS), can be treated with breast-conserving surgery (BCS; sometimes called lumpectomy or partial mastectomy) and radiation, or by mastectomy. Studies have shown that there are no significant differences in the survival rate of mastectomy alone compared to BCS followed by radiation in patients with DCIS [19]. Chemotherapy can be added if DCIS is estrogen-positive. Stages (I, IIa, and IIb) are considered early invasive, while stages (IIIa, IIIb, and IIIc) are considered locally advanced. In these stages, treat-

ment involves different strategies and phases. A combination of surgery, radiotherapy, systemic chemotherapies, hormone therapies, and immunotherapies can be utilized. Targeted drugs are also essential in tumors expressing estrogen or progesterone receptors, or ERBB2 proteins [20].

Stage IV is considered an advanced breast cancer with metastasis, and is usually treatable but viewed as an incurable disease [21]. Systemic drugs are the mainstay treatment, and local surgery is usually less offered as a therapeutic option. Despite being considered an incurable disease, some cases of complete remission of advanced breast cancer under treatment have been reported in the literature [22]. Treatment for advanced breast cancer can often shrink the tumor or slow its growth, and halting the treatment would inevitably lead to relapse. Therefore, even if the tumor regresses and metastatic lesions fade away, treatment should not be stopped as it can prolong remission [23]. Our patient's advanced breast cancer has responded to initial treatment and unexpectedly regressed to stage II curable disease as witnessed on a follow-up CT scan.

Conclusion

Timely and appropriate assessment and treatment of advanced breast cancer, along with monitoring the response to treatment through radiographic imaging, can lead to life-changing outcomes, such as the disappearance of fatal metastases and the shrinking of cancer to a surgically curable mass. These favorable outcomes could potentially decrease

the patient's risk of developing comorbidities and increase their life expectancy.

Patient consent

Signed consent for a case report was obtained from the patient's legally authorized representative. The IRB approval was taken from CMH Lahore, Pakistan.

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