

Hyperthermia Augments Neoadjuvant Chemotherapy on Breast Carcinoma – A Case Report

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Abstract:- Background: Carcinoma breast is the dominant cancer in urban females in India due to hormonal imbalance. The patient usually presents with symptoms of a painless lump in the breast axillary lymphadenopathy, skin discoloration over the breast, nipple discharge, and altered breast contour. **Case report:** In this study, we report a case of a 70-year-old female with complaints of a lump in the right breast and right axillary node, who was diagnosed with right breast cancer stage 3. The patient was given six cycles of neoadjuvant chemotherapy, followed by hormone therapy and hyperthermia using a remission one-degree machine. **Results:** The breast and axillary node tumor responded well to the treatment, and there was only minimal residual activity in the post-treatment positron emission tomography CT scan. **Conclusions:** Hyperthermia treatment provides additive benefits along with chemotherapy and hormone therapy for carcinoma breast patients.

Keywords:- Breast Carcinoma, Cancer, Hyperthermia, Neoadjuvant Chemotherapy, Tumor.

I. INTRODUCTION

Breast cancer is the most common cancer among women worldwide (Rojas and Stuckey, 2016). Despite the advances in treatment, some women still develop recurrent or metastatic diseases associated with poor prognoses (Loibl et al., 2021; Redig and McAllister, 2013). Breast cancer arises in the lining epithelium of the ducts or lobules in the breast's glandular tissue. Initially, the cancerous growth is confined to the duct or lobule, and over time, the cancerous growth may progress and invade the surrounding breast tissue, then spread to the nearby lymph nodes or the other organs in the body. Breast cancer treatment will be effective when the disease is identified early and usually treated with a multimodality approach, such as surgical removal, chemotherapy, hormone therapy, targeted therapy, and radiation therapy. Hyperthermia has been proposed as a treatment option for these patients, as it has been shown to improve the efficacy of chemotherapy, radiation therapy, and immunotherapy (Issels et al., 2010). Hyperthermia is a therapeutic approach that involves raising the temperature in a specific area to a level that destroys cancer cells while sparing normal tissue (Issels et al., 2010). Hyperthermia has been investigated as a potential treatment option for breast

cancer, alone or in combination with other treatments. Hyperthermia has been shown to induce several biological changes in cancer cells, including increased cell death, inhibition of DNA repair mechanisms, and enhanced immune response (Jolesch et al., 2012). These changes can sensitize cancer cells to other chemotherapeutic drugs and reduce the risk of recurrence or metastasis. While hyperthermia has shown promise in preclinical and clinical studies, its efficacy as a standalone treatment for breast cancer is still being evaluated (Skitzki et al., 2009). This study observed the additive effect of hyperthermia and chemotherapy in carcinoma breast patients. Hyperthermia is one procedure that can be combined with other modalities of (except surgery) oncological approaches to treatment.

II. CASE REPORT

A 70-year-old female patient with no comorbid condition complained of swelling in the right breast for 4 months. She also complained of alteration in the skin texture over the swelling and some changes in the shape of the nipple. She further added that swelling in the right armpit disturbed her day-to-day activities.

On examination, she was found to have a lump in the right breast, upper outer quadrant measuring 2 x 2 cm, associated with nipple inversion without any ulceration or discharge. The right axillary lymphadenopathy measuring 5 x 5 was observed with a hard and fixed node. Skin over the swelling was not pinchable.

III. INVESTIGATIONS

Trucut biopsy and histopathological examination reported infiltrating ductal carcinoma - Grade 2 (moderately differentiated). Immunohistochemistry confirmed Estrogen receptor (ER)-positive, Progesterone receptor (PR)-positive and Her2 neu-Negative (Fig. 1).

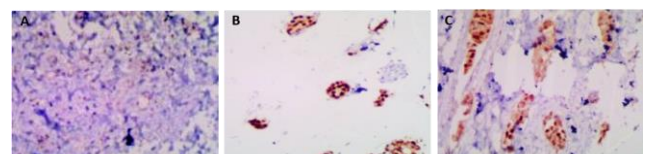


Fig 1. Immunohistochemistry images of the right breast biopsy specimen showed positive for Estrogen (A) and Progesterone (B) receptors and negative for Her2/ neu C).

IV. DIAGNOSIS

The patient was diagnosed with a case of carcinoma in the right breast stage 3 (cT3N2Mx)

V. TREATMENT

The patient was treated with 6 cycles of neoadjuvant chemotherapy (Inj. Cyclophosphamide 600 mg + Inj. Adriamycin 60 mg + Inj. 5 Fluorouracil 750 mg). The time interval between each cycle of chemotherapy was 21 days. The patient was planned for subjecting to a right modified radical mastectomy. However, the patient was not willing for surgery even after intensive counseling, and the negative sequelae of not undergoing surgery has been explained. Hence the patient was treated with hormone therapy and hyperthermia.

VI. HYPERTHERMIA TREATMENT

The patient was treated with hormone therapy (Tab. Letrozole 2.5 mg, once a day) based on immunohistochemistry reports (ER-Positive, PR-Positive, Her2/ neu-Negative as in Fig.1). A total of 22 sessions of hyperthermia were given at three sessions per week, as given in Table 1. Hyperthermia was given using a remission 1°C machine (Device Name: Remission 1°C hyperthermia, AdipoLABs Healthcare India Pvt. Ltd, Seoul, Republic of Korea) 3 days/ week along with hormone therapy as given in Table 1. Remission 1°C hyperthermia device, a therapeutic apparatus, generates high-frequency thermotherapy to the body tissue without stimulating sensory and motor nerves, causing no physical inconvenience or muscular contraction. Further, high-frequency electric energy is applied to the body with a Remission 1°C hyperthermia device that improves molecular movements by rotation, friction twist, or collision, generating frictional heat, thereby augmenting hormonal therapy.

VII. THE COURSE OF TREATMENT

During the first session, a mass in the right breast measured 2 x 2 cm. The size of the right axillary node measured 5 x 5 cm, as given in Figure 2a. The size of the breast carcinoma mass reduced, and the right axillary node measured 3 x 3 cm on the fifth session, as depicted in Figure 2b. At the end of the 10th session, the right axillary node size was reduced to 3 x 2 cm (Figure 2c). On the 20th session, the right axillary node measured 2 x 1cm (Figure 2d). PET-CT taken after completing 22 sessions of hyperthermia showed mild residual active disease.

Table 1: Neoadjuvant therapy for the breast carcinoma

Hyperthermia Chart					
Age / Gender: 70 years / Female			Diagnosis: Carcinoma of the right breast		
Type of Rx: Hyperthermia + chemotherapy					
Session #	Duration (Minutes)		Radio Frequency (RF) Hz		Temperature achieved (°C)
	Regional (abdomen)	Targeted (Rt. breast)	Regional (Abdomen)	Targeted (Rt. breast)	
Session (1-5)	40 MTS	20 MTS	40 RF	36 RF	38° C
Session (6-10)	40 MTS	20 MTS	38 RF	37 RF	39° C
Session (11-15)	40 MTS	20 MTS	38 RF	38 RF	40° C
Session (16-22)	40 MTS	20 MTS	38 RF	38 RF	41° C

VIII. RESULT

The patient's tumor responded well to neoadjuvant chemotherapy. Since the patient was not willing for surgery, she has been subjected to hormone therapy and hyperthermia. The disease had a better outcome with fruitful results. However, the cause of the excellent results could not be attributed to hyperthermia alone.



Figure 2: The photograph of a 70-year-old female with breast carcinoma. During the first session, a mass was present on the right upper anterior breast, measuring 2 x 2 cm (2a), and an axillary node about the size of 5 x 5 cm. After the 5th session of hyperthermia, mass was reduced on the right upper anterior breast, axillary node about the size of 3 x 3cm (2b). After the 10th session of hyperthermia, still, the mass was noticed on the right upper anterior breast, axillary node about the size 3 x 2 cm (2c). After the 20th session of hyperthermia, the mass was reduced significantly on the right upper anterior breast and the axillary node by about 3 x 1 cm (2d).

IX. CONCLUSION

In this case report, a 70-year-old female patient with stage 3 carcinoma of the right breast was treated with neoadjuvant chemotherapy, hormone therapy, and hyperthermia. The hyperthermia treatment was administered using a Remission 1°C machine and hormone therapy using letrozole. The treatment results showed a significant response in both the breast tumor and the axillary lymph nodes. The size of the breast tumor and the axillary lymph node decreased progressively with each hyperthermia session. A PET-CT scan revealed minimal residual activity in the breast and axillary region. The findings of this case report suggest that the addition of hyperthermia to the treatment regimen, consisting of neoadjuvant chemotherapy and hormone therapy, provided additive benefits in managing breast carcinoma. Hyperthermia, delivered using the remission 1°C machine, was well-tolerated by the patient and demonstrated efficacy in reducing tumor size. The observed response to hyperthermia can be attributed to its ability to induce several biological changes in cancer cells, including increased cell death, inhibition of DNA repair mechanisms, and enhanced immune response. These changes sensitize cancer cells to other therapeutic modalities, such as chemotherapy and hormone therapy, improving treatment outcomes. However,

it is essential to note that this case report represents a single patient, and further research is necessary to establish the generalizability and effectiveness of hyperthermia in breast cancer treatment. Randomized controlled trials involving larger patient cohorts are needed to validate these findings and assess hyperthermia's long-term outcomes and safety profile in combination with other therapies. The present case report highlights the potential benefits of hyperthermia as an adjunctive therapy for breast carcinoma. When combined with neoadjuvant chemotherapy and hormone therapy, hyperthermia showed favorable results regarding tumor response. Further research and clinical trials are warranted to elucidate the precise role of hyperthermia and its optimal integration into the treatment paradigm for breast cancer patients, ultimately improving outcomes for these individuals.

➤ *Conflict of Interest*

The authors have declared that no competing interests exist.

➤ *Authors Contributions*

GVB, DK, and SS conceived and designed the analysis; GVB collected the data; DK, GVB, SS, and MA contributed data or analysis tools; GVB performed the analysis; MA wrote the paper.

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