

Augmenting Effect of Hyperthermia in Neoadjuvant Chemotherapy for Advanced Breast Cancer – A Case Report

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Abstract:- Background: Locally advanced breast cancer encompasses a heterogeneous collection of breast neoplasms, constituting approximately 10 to 20% of newly diagnosed breast cancer cases annually. The patient often presents with an ulcerative lesion in the breast with foul-smelling or bloody discharge associated with supra clavicular lymphadenopathy and axillary lymphadenopathy. **Case report:** In this study, we reported a case of a 48-year-old female with complaints of an ulcerated lesion with severe pain over the right breast and foul-smelling serosanguinous discharge from the ulcer. Later, it was diagnosed as a case of carcinoma of the right breast stage cT4bN1Mx. The patient was given neoadjuvant chemotherapy and three sessions of hyperthermia per week for 22 sessions. **Results:** The tumor responded well to neoadjuvant chemotherapy and hyperthermia, converting the inoperable tumor into an operable tumor. **Conclusion:** Combined neoadjuvant chemotherapy and hyperthermia significantly reduce the size of locally advanced breast cancer by converting it into an operable one, and there was a reduction in pain over the ulcer, improving the patient's quality of life.

Keywords:- Breast Cancer, Chemosensitizer, Chemotherapy, Hyperthermia, Neoplasm.

I. INTRODUCTION

Locally advanced breast cancer (LABC) is a subset characterized by the most advanced breast tumors without distant metastasis (Sharma et al. 2022). They need to identify LABC as a separate group of breast cancers that arose because of the highly associated rate of locoregional and systemic failure, despite the best efforts of surgeons to remove the locoregional spread of the tumor in its entirety. It was recognized that multimodality treatment such as surgery, chemotherapy, and radiotherapy in combination with hormonal and targeted therapy could significantly improve outcomes in these patients. The study observed the additive

effect of hyperthermia, when given along with neoadjuvant chemotherapy in locally advanced breast cancer, in converting an inoperable breast cancer to an operable one. Hyperthermia is a type of cancer treatment given along with primary cancer therapy, such as chemotherapy, radiotherapy, and hormone therapy (Bornstein et al. 1993). HPT uses an external heat source to increase tissue temperature, kill cancer cells, or impede their growth. It is a medical modality for cancer treatment using the biological effect of artificially induced heat.

Even though the intrinsic effects of elevated body temperature in cancer tissues are poorly understood, increasing the temperature of the body has been recognized as a popular therapeutic method for tumorous lesions since ancient times. HPT raises the temperature of cancer cells, leading to the denaturation and unfolding of proteins, disrupting protein structure, thereby interfering with their normal function and causing cellular dysfunction and, ultimately, cell death. The increased temperature can also cause breaks in DNA strands, cross-linking of DNA molecules, and formation of DNA adducts, interfering with DNA replication and transcription, leading to cell cycle arrest and apoptosis (Iliakis et al. 1990). Interestingly, heat shock proteins are upregulated in response to hyperthermia and act as chaperones to help refold denatured proteins, stabilize cellular structures, and prevent protein aggregation. However, sustained or severe hyperthermia can overwhelm the heat shock response, leading to protein degradation and cell death. Recently accumulated evidence has shown that hyperthermia amplifies the immune response in the body against cancer while decreasing the immune suppression and immune escape of cancer. Increased temperature can promote the release of danger-associated molecular patterns (DAMPs) from dying cells, which act as signals to activate immune cells (Wan Mohd Zawawi et al. 2021). Hyperthermia can also enhance the presentation of tumor antigens and increase the cytotoxic activity of immune cells, leading to the elimination of cancer cells. It also inhibits the

repair of damaged cancer cells after chemotherapy or radiotherapy. Both local hyperthermia, as well as regional hyperthermia, is given to improve the efficiency. Hyperthermia causes cell death by activating all apoptotic pathways. It enhances intratumoral hypoxia and inhibits sublethal damage repair in the tumor.

II. CASE REPORT

A 48-year-old female non-hypertensive and euglycemic patient with ECOG performance status 1 presented with an ulcerated lesion in the right breast adjacent to the nipple with foul-smelling serosanguinous discharge and pain over the tumor site.

Local examination showed a lump in the upper outer quadrant of the right breast adjacent to the nipple measuring 10 x 8 cm with ulceration over the lump (Grade 2, partial thickness skin loss involving epidermis and dermis) measuring 4x3 cm. There was foul-smelling discharge from the ulcer. The pain score was 9/10 on the visual analogue scale.

A. Investigation

Histopathological examination of Breast lump biopsy reported as infiltrating ductal carcinoma. CECT chest showed a lump in the right breast, upper outer quadrant measuring 10 x 8 cm involving the skin, and multiple sub centimetric right axillary lymph nodes present (Fig.1).

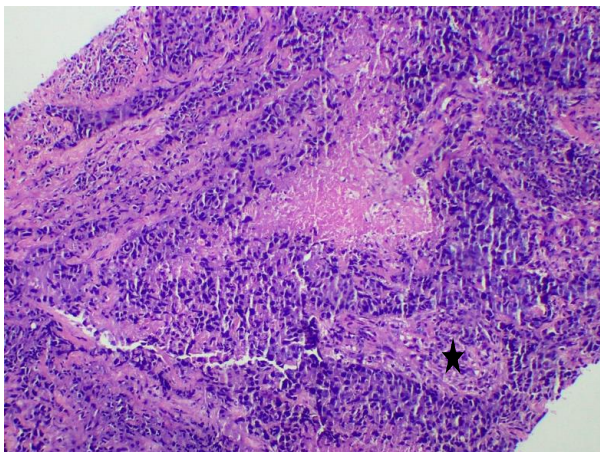


Fig 1: Histopathological examination of Breast lump biopsy reported as infiltrating ductal carcinoma. Asterisk represents ductal carcinoma.

B. Treatment

The patient was treated with neoadjuvant chemotherapy (Inj. Cyclophosphamide 1000 mg intravenous infusion every 21 days for 6 cycles) and 3 hyperthermia sessions per week to 22 sessions, as given in the following table.

Table 1: Hyperthermia and Neoadjuvant Chemotherapy for Breast Carcinoma

Hyperthermia Chart					
Age/ Gender: 48 years old female				Diagnosis: Carcinoma in the right breast	
Type of Rx: HPT + chemotherapy					
Session #	Duration (Minutes)		Radio Frequency (RF) Hz		Temperature achieved (°C)
	Regional (Abdomen)	Targeted (Right breast)	Regional (Abdomen)	Targeted (Right breast)	
SESSION (1-5)	40 MTS	20 MTS	40 RF	36 RF	39°C
SESSION (6-10)	40 MTS	20 MTS	38 RF	36 RF	39°C
SESSION (11-15)	40 MTS	20 MTS	38 RF	37 RF	40°C
SESSION (16-22)	40 MTS	20 MTS	38 RF	38 RF	40°C

III. RESULTS AND DISCUSSION

On session 1 of hyperthermia, local examination showed a lump in the right upper aspect of the breast measuring 10x8 cm, ulceration present over the tumor site (total thickness skin loss involving epidermis/dermis with serosanguinous discharge), with foul smelling discharge. The pain was assessed using a visual analogue scale (VAS) rated 9/10 (Figure 2a). In session 5, tumor size was reduced to 8 x 6 cm, ulceration healed to some extent, and foul-smelling discharge was reduced. The VAS pain score is 5/10 (Figure 2b).

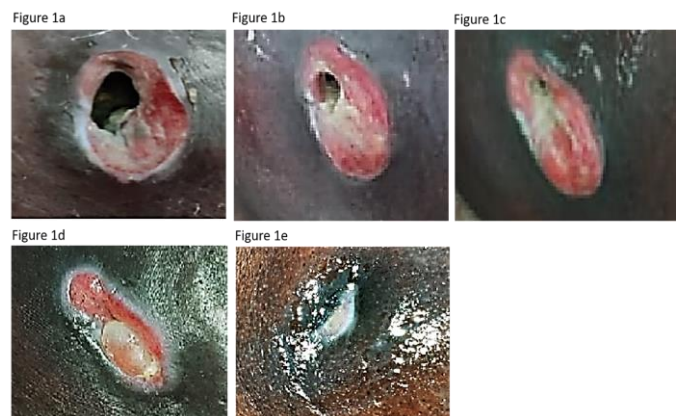


Fig 2: Augmenting effect of hyperthermia in neoadjuvant chemotherapy for advanced breast cancer.

In session 15, tumor size was reduced to 4x4 cm, ulceration healed, and no foul-smelling discharge. The VAS pain score was reduced to 2 out of 10 (Figure 2c). In session 22, local examination showed the tumor size reduced to 3x3 cm, ulceration healed, and discharge stopped. The patient has not reported any pain (Figures 2d and 2e). The patient tolerated the treatment well, with a better response to treatment, and planned for surgical management.

IV. CONCLUSION

In conclusion, the combination of neoadjuvant chemotherapy and hyperthermia demonstrated promising results in treating locally advanced breast cancer. The case report presented a 48-year-old female with an ulcerated lesion and inoperable tumor who underwent a treatment regimen of neoadjuvant chemotherapy and hyperthermia sessions. The tumor responded well to the combined therapy, resulting in a significant reduction in tumor size, healing of the ulceration, cessation of discharge, and a marked improvement in the patient's pain score. This successful

outcome led to the conversion of the inoperable tumor into an operable one, offering a potential opportunity for surgical management. The study highlights the potential of hyperthermia as an adjunct therapy to enhance the effectiveness of chemotherapy in locally advanced breast cancer. Through its biological effects on cancer cells, including increased cell death, inhibition of repair mechanisms, and immune system modulation, hyperthermia has shown the ability to improve treatment outcomes. By utilizing hyperthermia alongside neoadjuvant chemotherapy, the study demonstrated the synergistic effect of these modalities in reducing tumor size and improving the quality of life for the patient. While these findings are promising, further research is warranted to establish the efficacy and safety of combined neoadjuvant chemotherapy and hyperthermia in more extensive randomized controlled trials. Nevertheless, this case report provides valuable insights into the potential of hyperthermia as a chemosensitizer and its role in converting inoperable breast cancer into operable tumors, thus offering new avenues for managing locally advanced breast cancer.

Conflict of Interest

The authors have declared that no competing interests exist.

Author contributions

DSR and SG conceived and designed the analysis, and RV collected the data, DSR, SG, and MA contributed the data analysis; DSR wrote the paper.

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