CASE REPORT

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# Chemotherapy in the ICU – Challenge of Risk versus Benefit

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## Abstract

***Suitability of chemotherapy in advanced cancers depends on various patient-related factors, disease-specific factors and lab parameters. It is quite unlikely that a breast cancer patient with progressive disease after failure of multiple lines of treatment with complications arising from previous chemotherapy can be revived in the intensive care with further chemotherapy. This case report describes a patient of chemorefractory breast cancer with huge tumour burden who received 4-lines of chemotherapy followed by severe complications leading to admission in the ICU. However, timely clinical judgement followed by judicious administration of 5th line chemotherapy with high element of risk, while the patient was in the ICU, helped her to recover and come out of intensive care.***

***Keywords: Chemotherapy, advanced breast cancer, intensive care, selection.***

## Introduction

The selection of an appropiate patient is extremely important while contemplating chemotherapy for any advanced cancer which has progressed on several lines of chemotherapy[1]. Where the intention of treatment is only palliative[2] and not curative, chemotherapy is normally administered only after checking performance status, associated comorbidities, haematological and biochemical parameters especially renal and hepatic functions, estimated survival of patients (being preferably beyond six months) and most importantly chemosensitivity[3] of the disease, for example breast cancer[4]. If the timing of chemotherapy, drug and dose selection and subject selection are erroneous, patients might end up with fatality in the ICU.

## Case report

A 49-year-old married lady, first presented in November 2015 with a gradually increasing ulcerative lesion in the centre of right breast along with a progressive painless lump in her right axilla for a duration of 6 months. She also noticed a second lump of shorter duration appearing in the right side of neck. Clinical examination revealed a 5 x 4 cm ulcer in the centre of breast along with large right axillary and supraclavicular lymph nodes. Receptor studies done by immunohistochemistry (IHC) revealed oestrogen receptor positive and Her2neu receptor positive breast cancer[5]. Metastatic work-up revealed bilateral lung metastases (Fig. 1) and increased radiotracer uptake in bones. Haematological parameters, biochemical parameters and baseline echocardiography were within normal limits. Multidisciplinary tumour board decided in favour of life prolonging chemotherapy, as cure was unlikely.

Combination chemotherapy (CT) consisting of docetaxel (microtubule inhibitor)[6] and anti Her2Neu antibody trastuzumab[7] at 3 weekly intervals with growth factor support was initiated in November 2015. Though the interim assessment after 6 cycles demonstrated partial tumour response, 3 additional cycles did not. There was an increase in size of primary breast lesion and right axillary lymphadenopathy.

From October 2016 patient was switched to 2nd-line chemotherapy with Vinorelbine[8] (another microtubule inhibitor) along with continuation of trastuzumab at 3 weekly intervals. After 4 cycles, response was unsatisfactory as the ugly looking ulcer started to bleed with foul smelling discharge. However, there was reduction in the size of right supraclavicular lymph node. Toilet mastectomy to improve QOL (Quality of Life) with chemoport insertion was performed in February 2017. This time the repeat receptor status revealed ER negative but Her2Neu positive disease. Following this, patient received 2 more cycles of the same chemotherapy. PET CT scan performed in June 2017 showed disease progression in bilateral cervical lymph nodes and lungs thus warranting change of CT protocol.

3rd-line chemotherapy consisting of an oral antimetabolite Capecitabine[9] (2 gm/day in divided doses) along with oral tyrosine kinase inhibitor targeting Her2Neu pathway - lapatinib[10] (250 mg x 4 tabs/day) was started. She received total 3 cycles of this combination from July to September 2017 but the disease progressed and patient developed severe respiratory distress due to bilateral pleural effusion with hilar lymphadenopathy. Haemorrhagic fluid was drained for symptomatic relief. Repeat echocardiography

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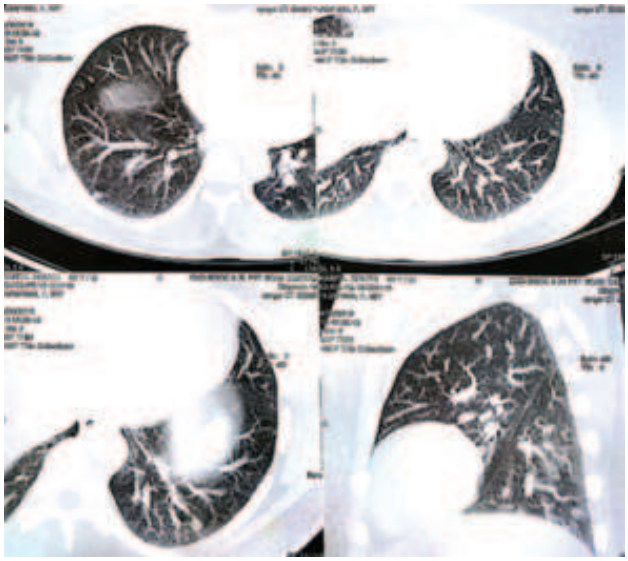

***Fig. 1:*** *Metastatic pulmonary nodules (baseline image).*

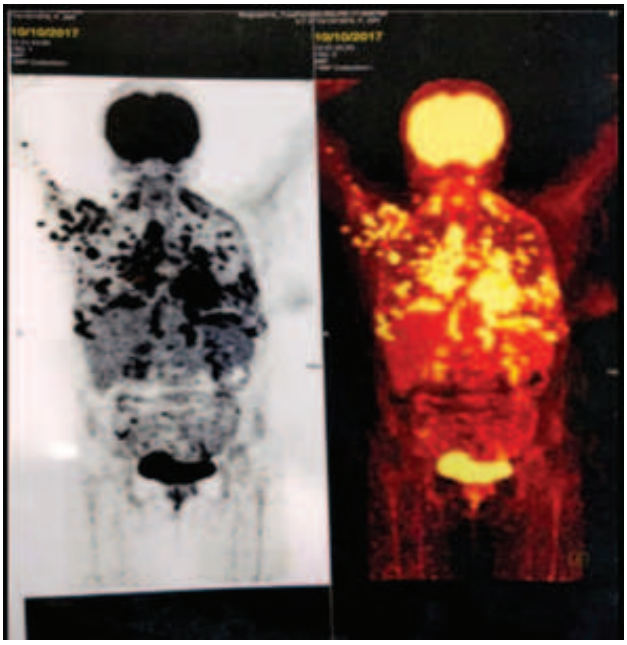

***Fig. 2:*** *Extensive visceral metastases as noted in the PET CT dated on 10/10/2017.*

was unremarkable. Once breathlessness diminished and her performance status improved, she was put on 4th-line drugs – doxorubicin (anthracycline) and cyclophosphamide[11]. However, the response was disappointing and she had to be transferred to the ICU in a grave condition due to severe respiratory distress.

PET CT scan (Figs. 2, 3) revealed extensive lung metastases with nodal involvement along with massive bilateral pleural effusion (legend 4).The prime concern for a clinician at that moment was to stabilise the patient. Her cardiac function had deteriorated due to previous cardiotoxic chemotherapy (anthracycline and trastuzumab). Unilateral chest drain was inserted and USG guided pleurocentesis was performed on the other side. As she symptomatically improved, the biggest challenge was to reassess the feasibility of continuing further chemotherapy in such a critically ill patient inside the ICU against all odds. Moreover, restricted future chemotherapy options and various clinical/ medicolegal issues added to the complexity of decision making process.

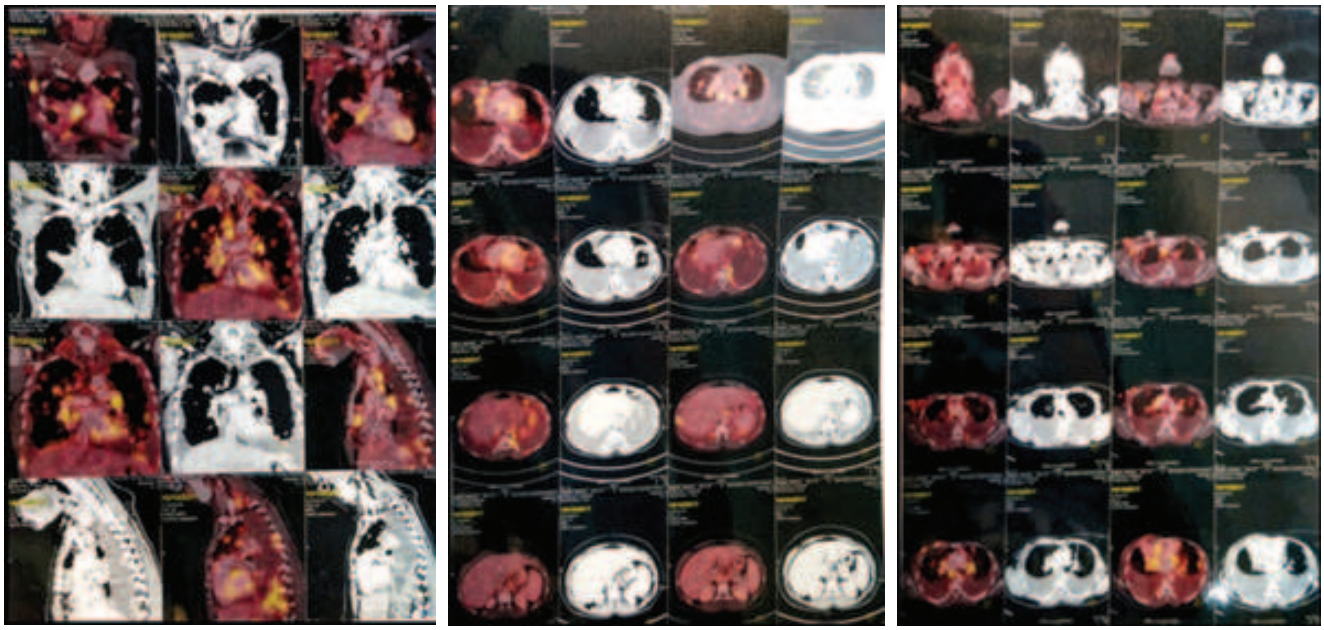

***Fig. 3:*** *Series of PET CT images showing massive lung metastases with nodal involvement as dated on 10.10.2018.*

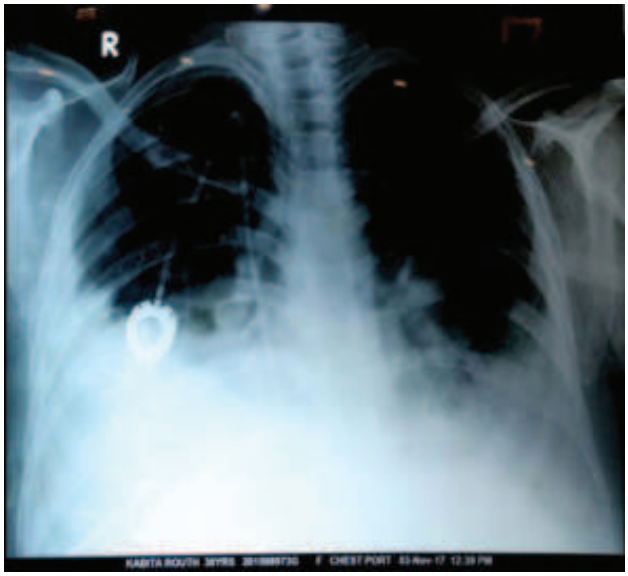


***Fig. 4:*** *Chest X-ray dated on 3.11.2017 showing massive bilateral pleural effusion because of which she developed breathlessness. ICD was inserted in ICU and repeated pleural tapping were also done to provide her symptomatic relief.*

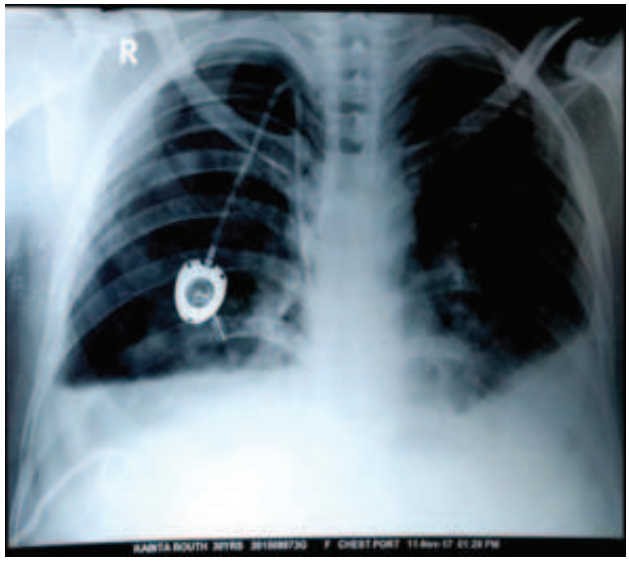


***Fig. 5:*** *Showing chest X-ray after she received 1st cycle chemotherapy with Eribulin Mesylate. Patient tolerated the first dose of chemo well and felt better. Subsequently she received further chemotherapy with the same protocol for 6 more cycles.*

Once her vitals stabilised, Performance Status (PS) improved, haematological and biochemical parameters settled, the medical team decided to initiate 5th-line chemotherapy inside the ICU. High risk consent was obtained from the patient and her guardian thereafter and a new chemotherapy agent – eribulin mesylate (a non taxane microtubule inhibitor) was administered.

This drug is active in breast cancer patients beyond anthracyclines and taxanes with a favourable cardiovascular and toxicity profile. Trastuzumab was avoided on account of existing cardiac dysfunction.

Patient tolerated the new drug eribulin, and had good symptomatic improvement of breathlessness. She was mobilised out from the Intensive care unit to general ward, and the pleural drain was removed. Response was noted in chest X-ray after fifth cycle (legend 5). Subsequently she went on to complete 6 cycles with the same protocol till April 2018. Disease response following 5th-line chemotherapy was actually better than all other previous schedules. Post-chemotherapy radiological images showed significant reduction in the lung metastases (Fig. 6) and pleural effusion (Fig. 7). Patient thus achieved sustainable benefit from chemotherapy with a significant improvement in performance status even when a very high risk patient was judiciously decided to be delivered CT in the ICU setting.

**Sequence of chemotherapy received by the patient during her lifetime**

| Line | Drugs | Frequency | No. of cycles | Results |
|---|---|---|---|---|
| First | Docetaxel and trastuzumab | Day 1 every 3 weeks | 8 | After 6 cycles patient showed good clinical response but after 9th cycle there was progression of the primary lesion and right axillary node |
| Second | Vinorelbine and trastuzumab | Day 1 and 8 Vinorelbine, Day 1 trastuzumab 3 weekly | 6 | After 4 cycles there was stable disease – foul discharge - palliative mastectomy – 2 more cycles and then disease progression was noticed |
| Third | Capecitabine and lapatinib | Oral capecitabine daily for 14 days followed by 7 days gap and restart, Oral lapatinib continuous daily | 3 | Disease progression after 3 cycles in the lungs in the form of bilateral pleural effusion and hilar lymphadenopathy. |
| Fourth | Doxorubicin and cyclophosphamide | Day 1, 3 weekly | 1 | Worsening of symptoms, progressive bilateral pleural effusion, heart failure |
| Fifth | Eribulin Monotherapy | Day 1 and 8, every 3 weeks | 6 | Partial response, reduction in pleural effusion and metastatic lesions |

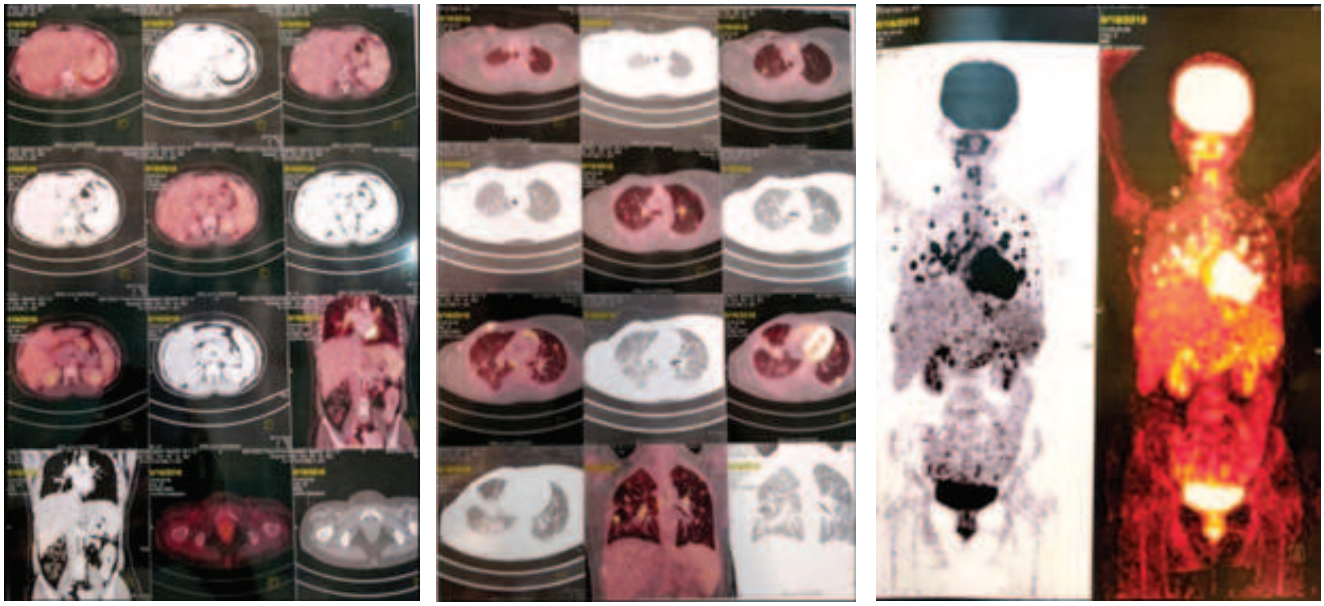

***Fig. 6:*** *Showing CT images of 18.5.2018 after total 6 cycles chemotherapy with Eribulin mesylate. Marked reduction in lung metastases as well as in visceral metastases is noted as compared to previous CT images as dated on 10.10.2017 (Figs. 1, 2). Thus providing her significant benefit from the chemotherapy.*

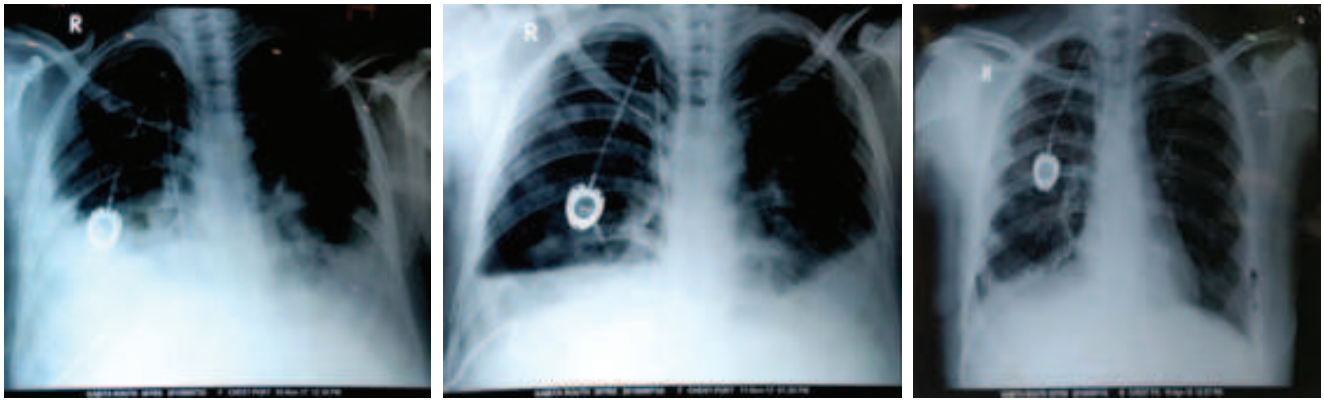

***Fig. 7:*** *Chest X-ray showing gradual improvement . She had massive bilateral pleural effusion as noted in the first image. Second image is after she had received 1st cycle chemotherapy with Eribulin, following which she received total 6 cycles of chemo with the same protocol. Last image as dated on 19.4.2018 shows the outstanding outcome with the chemotherapy. As it is evident from the images pleural effusion has subsided almost completely. Thus providing symptomatic relief to the patient.*

## Discussion

While patient was undergoing resuscitation in the intensive care unit, several issues surfaced– like huge tumour burden, worsening of the performance status, ongoing heart failure from past exposure to trastuzumab and anthracycline, lack of response even after 4-lines of chemotherapy, unpredictable survival and restricted future chemotherapy options.This case is an eye opener for oncologists as well as physicians. It shows that appropriate patient selection and suitable drug administration can revive a chemo-refractory breast cancer patient from the ICU and offer better survival along with a good quality of life.

## Conclusion

Administering chemotherapy in the ICU setup to critically ill patients suffering from refractory cancer with several complications and multiorgan failure is hugely challenging. On one hand it can lead to fatality from complications, on the other hand, like in this patient, judicious choice of drugs can actually salvage the patient with clear improvement in QoL.

## *References*

1. Holly G, Prigerson, Yuhua Bao, *et al*. Chemotherapy Use, Performance Status, and Quality of Life at the End of life . *JAMA*

*Oncol* 2015; 1 (6): 778-84.

2. National Consenses Project for Quality Palliative Care. 2008. Clinical Practice Guidelines for Quality Palliative Care. Accecsed at http://www.nationalconsensusproject.org.
3. Sommerova L *et al*. New Approaches For Chemosensitivity Testing In Malignant Diseases. *Klin Oncol* 2018; 31 (2): 117-24.
4. Cardoso F, Costa A, Norton L *et al*. ESO-ESMO 2nd international consensus guidelines for advanced breast cancer (ABC20 dagger). *Ann Oncol* 2014; 25 (10); 1871-88. doi:10.1093/annonc/mdu385
5. Web Med. Breast Cancer Health Centre: types of breast cancer: ER Positive, HER2 Positive, and Triple Negative. Accessed at http://www.webmd.com/breast-cancer/breast-cancer-types-er-positive-her2-positive.
6. Smith IC, Heys SD *et al*. Neoadjuvant chemotherapy in breast cancer: significantly enhanced response with docetaxel. *J Clin Oncolo* 2002; 20 (6): 1456-66.
7. Piccart-Gebhart MJ, Procter M *et al*. Trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer. *N Engl j Med* 2005; 353: 1659-72.
8. Degargin M *et al*. Vinorelbine (navalbine) as a salvage treatment for advanced breast cancer. *Ann Oncol* 1994; 5 (5): 423-6.
9. Wagastaff AJ *et al*. Capecitabine: A review of its pharmacology and therapeutic efficacy in the management of advanced breast cancer. *Drugs* 2003; 63 (2): 217-36.
10. Ryan Q, Ibrahim A. FDA drug approval summary:lapatinib in combination with capecitabine for previously treated metastatic breast cancer that over expresses HER-2. *The Oncologist* 2008; 13 (10): 1114-9.
11. Schmid P, Krocker J, Kreienberg R *et al*. Non pegylated liposomal doxorubicin and docetaxel in metastatic breast cancer:final results of a phase II trial. *Cancer Chemo Pharmacol* 2009l 64 (2): 401-6.