ejpmr, 2020,7(9), 473-475

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Case Report

ISSN 2394-3211

EJPMR

NEOADJUVANT TREATMENT OF LOCALLY ADVANCED ER, PR AND HER-2 POSITIVE BREAST CANCER- A CASE REPORT

Anjaly P. Nair[1], Anjali Krishnan K.[1], Lakshmi R.[1]*, Siby Joseph[1], C. S. Madhu[2] and Sanjay Mukundan[2]

[1]Department of Pharmacy Practice, St. Joseph's College of Pharmacy, Cherthala, Kerala, India - 688524.
[2]Department of Oncology, Lourdes Hospital, Post Graduate Institute of Medical Science & Research, Pachalam, Kochi Kerala - 682012.

***Corresponding Author: Lakshmi R.**
Department of Pharmacy Practice, St. Joseph's College of Pharmacy, Cherthala, Kerala, India - 688524.

Article Received on 03/07/2020 **Article Revised on 23/07/2020** **Article Accepted on 13/08/2020**

ABSTRACT
Breast cancer expressing all three diagnostic markers (estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2)) is insufficiently characterized even though it is present currently in the patient population. Near 75% of all breast cancers (BC) express ER and/ PR, while only up to 20% of BC show an overexpression or amplification of HER2. Around 50% of all HER2-overexpressing BC show the coexistence of both ER and/ PR overexpression. Here we discuss a case of 51 years old female who was diagnosed with infiltrating duct carcinoma having receptor positivity only to ER and PR initially and on relapse was found to be triple positive and had a greater response to treatment with antiestrogen and anti HER 2 therapies.

KEYWORDS: Metachronous BC, Triple Positive, Breast Cancer, HER-2 Neu receptor, Endometrial hyperplasia.

INTRODUCTION
Breast cancer is the second most frequently diagnosed cancer worldwide and the leading cause of death among women. Once diagnosed with breast cancer the hormone receptor status should be determined.Breast cancer is confirmed by three immune histochemistry (IHC) tumor markers: estrogen receptor (ER), progesterone receptor (PR) and the human epidermal growth factor receptor-2 (HER-2).Triple positive breast cancer constitutes only about 10% of all BCs.[1-2] Here we present a case of 51 years old female patient who was initially positive for ER,PR and later on follow up found to be Triple positive.

Case description
A 51yrs old postmenopausal woman presented with 3.5× 3×1 cm mildly tender massin the right breast and axillary lymph node involvement. She gave a history of hypothyroidism and denied family history of cancer. She underwent right modified radical mastectomy and level III axillary clearance after investigation including metastatic work up.

Histopathology from the mastectomy specimen revealed infiltrating duct carcinoma grade III, nearest deep resection margin was at 1cm from the tumour. It also showed 33/44 positive axillary lymph nodes with 7/10 level III axillary lymph nodes having metastatic tumour of stage PT2N3Mx. Immuno histochemistry revealed estrogen receptor 66-100%, progesterone receptor 10-33% and HER2 Neu 0%.

Management and outcome
The patient had grade III breast cancer with stage PT2N3Mx and the tumour is of both hormone receptors positive(ER, PR – POSITIVE). The patient was given adjuvant chemotherapy with six cycles (3 cycles each of) Cyclophosphamide, Doxorubicin and Cyclophosphamide, Docetaxel. As per the immunohistochemistry report after the 6 cycles of chemotherapy, she underwent radiotherapy followed by Tab. Tamoxifen 20mg daily subsequently.

After three years of follow up, the patient had Tamoxifen induced endometrial hyperplasia diagnosed by Ultrasound study of whole abdomen and pelvis.

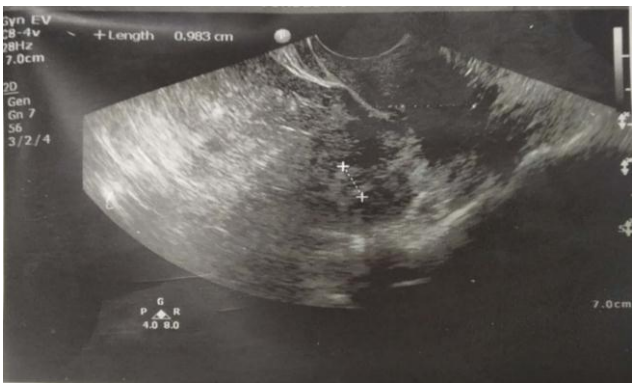

Fig 1: Ultrasound study of whole abdomen showing thickened endometrium up to 9.8mm.

She had (TAH-Total Abdominal Hysterectomy with BSO-Bilateral Salpingo-Oopherectomy). On further evaluation patient complained of breathlessness and was evaluated with chest X-ray; whole body PET CT and FNAB. PET CT showed abnormally increased FDG uptake in the large conglomerate soft tissue mass -nodal mass involving right level IV cervical,bilateral upper and lower paratracheal, paraesophageal, carnial, subcarnial, bilateral hilar nodal stations extending into right thorax, engulfing and partially compressing right main bronchi distally and its dividing segmental bronchi proximally and extending infero medially up to the right diaphragm-Metabolically active. CT detected right moderate pleural effusion and PET CT suggestive of disease progression.

FNAB revealed metastatic adenocarcinoma and repeated immunohistochemistry after relapse showed tumor positivity for all the three receptors (ER, PR and HER).

During her relapse the HER2 was also found to be positive and then the treatment regimen changed from Tamoxifen to chemotherapy with Paclitaxel, Carboplatin and Trastuzumab(Three cycles). Later on the regimen was switched over to Trastuzumab and Capecitabine which was given for around 15 cycles and then 32 cycles of chemotherapy with Trastuzumab and Letrozole. A total of 50 courses of chemotherapy with Trastuzumab have been administered to the patient.

PET CT was repeated after two years and was found to have complete metabolic and near complete anatomic resolution of previously seen FDG avid discrete right level IV cervical, bilateral upper and lower paratracheal, paraesophageal and multiple mediastinal and bilateral hilar lymph nodes, metabolic resolution of previously FDG avid mild focal pleural thickening in right anterior costal pleura, right pleural effusion has resolved.

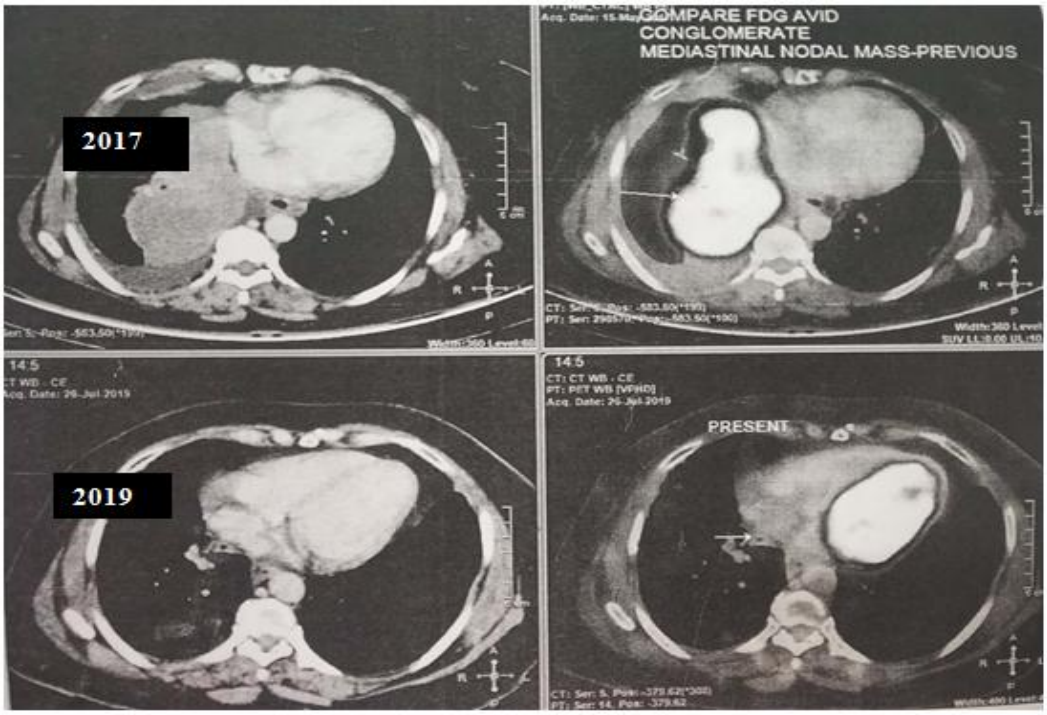

Fig 2: Comparison of initial PET CT after relapse and the current status.

Common adverse effects noted includes neutropenia, mucositis, diarrhea, nausea and vomiting, neuropathy and fatigue. She also had small risk of symptomatic heart failure. Guidance on how to manage some of the most common adverse effects were provided and also she was prescribed with antiemetics (Inj. Ondansetron 3mg, Tab Apprepitant 125mg on D1 and 80mg on D2&D3)antidiarrheals (Tab Bisacodyl 5mg) and iron supplements(Tab Folic acid 5mg) inorder to prevent most common adverse events.

DISCUSSION

Women with a history of BC are more prone to develop MCBC than women who develop their first BC. ER/PR positive BC is less likely to develop MCBC when compared to ER/PR negative cases. HER-2 positivity refers to HER-2 gene overexpression in breast and is relatively uncommon, it increases the risk of developing contralateral BC. In patients with "triple positive" BCs, it is not clearly known whether ER/PR receptor or HER-2 receptor is a strong marker for carcinogenesis and whether any synergy exists between them.[2]

Approximately half of HER-2 neu positive breast cancers are hormone receptor (ER, PR) positive. In TPBC, HER-2 neu positive status brings a special challenge to the treatment pattern due to its aggressive nature. Intravenous Trastuzumab, an anti-HER-2 neu targeted therapy, has proven to be a powerful treatment option in clinical practice leading to improvement in survival and an increase in sensitivity to chemotherapeutic agents.[3] A therapeutic approach in these HER2 positive and HR

positive breast cancer patients is to combine targeted therapies to block both ER and HER-2 pathways, that is by combining Trastuzumab with either Letrozole/Anastrozole.[4]

Our case is unique in the sense that the primary tumor (ER and PR - positive) achieved a near complete pathologic response by introducing hormonal therapy, yet it had an aggressive course leading endometrial hyperplasia due to Tamoxifen administration. The development of endometrial malignancy may be promoted by the growth stimulating effect of the drug acting in conjugation with a genotoxic stimulus.[5] Later the patient was found to be triple positive(ER,PR,HER-2) which is now resolving with antiestrogen and anti HER-2 therapies. Given the rarity of triple positive breast cancer and the occurrence at different time points contribute to the need for further research in the area of triple positive metachronous BC.

CONCLUSION

The current study shows that multiple mechanisms are engaged which are expected to alter three cellular processes (HER2 and PI3K pathway signaling; transcriptional regulation). Here the patient's tumor biology provides hope that, as we assemble the molecular portraits of patients' disease variations during different time period, specific therapies can be rationally selected to precisely treat the patients with similar molecular patterns. By specific tailoring treatments to molecular dysregulations, the emergence of cancer as well as resistance mechanisms, effective, more tolerated, durable regimens can be given to manage the patient's condition.

ACKNOWLEDGEMENTS

The authors would like to thank the management of Lourdes hospital and St Joseph's College of Pharmacy for their support and encouragement.

Conflict of interest

The authors declare no conflict of interest.

REFERENCE

1. Schwab RB, Koehler M, Ali SM, Murray BW. Genomic profiling and treatment of HER2+, ER+, PgR+ "triple positive" breast cancer: a case report and literature review. CA Treatment & Rsrch Comm, 2016; 1(9): 27-31.
2. Chhatrala HS, Khuu J, Zuberi L. A Rare Case of Triple Positive Metachronous Breast Cancer. J Inves Med High Impact Case Reports, 2019; 7: 1-4.
3. Negi P, Kingsley PA, Jain K, Sachdeva J,Srivastava H, Marcus S et Al. Survival of Triple Negative versus Triple Positive Breast Cancers Comparison and Contrast. Asian Pac J CA Prev, 2016; 17(8): 3911-6.
4. Montemurro F, Di Cosimo S, Arpino G. Human epidermal growth factor receptor 2 (HER2)-positive and hormone receptor-positive breast cancer: new insights into molecular interactions and clinical implications. Annals of Onco, 2013; 24(11): 2715-24.
5. Ismail SM. Pathology of endometrium treated with tamoxifen. J clinical patho, 1994; 47(9): 827-33.