Advanced Breast Cancer with Cerb2 Over Expression - A case Report

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Abstract

A 53-year-old female presented with advanced carcinoma of the right breast with clinically positive right axillary lymph node. Triple assessment was done. FNAC confirmed ductal cancer, mammography showed soft tissue mass with micocalcification. Full systemic evaluation was done, and excluded any gross distant metastasis, at surgery, modified radical mastectomy with axillary clearance was done.

Histological the tumor was an invasive ductal carcinoma moderately differentiated ER/PR:-negative. Cerb2 shows > 90% strong membrane staining (3+ over expression) - Cerb2 (HER2) is transmembrane growth factor receptor, expressed in about 20% of invasive breast cancer & 80% of DCIS and associated with poor prognosis. It is one of a family of growth factor receptors and is product of erb-B2 gene. This receptor is present on the surface of breast cancer cell and is of 3 types HER1. Biological therapy is now targeting this receptor like humanized mouse antibody and herceptin (Transtuzumab).

Introduction

Breast cancer now is a major concern for the general surgeons and the oncologists, with new era of treatment started in the last 2 decades. Apart from surgery and its options chemotherapy, radiotherapy and hormonal therapy, we have now what we call the Biological therapy1-3.

Case Report(s)

A 53-year-old female presented to the Surgical Outpatient clinic with bilateral breast mass noticed by the patient herself for the past one month. No other symptoms. Past medical history showed previous CVA, hypothyroidism and hypertension on medication. On examination the patient was conscious, alert and oriented, mild facial puffiness, not dyspnic, no peripheral oedema.

On breast examination, the right breast showed diffuse swelling with peau d'orange appearance, no ulceration or scar, the nipple areola complex was within normal limits, a 10x10cm hard painless mobile mass felt occupying the upper and lower outer quadrant of the breast, a series of palpable axillary lymph node have been detected in the axillary tail up to level I and level II axillary lymph nodes.

The left breast was less diffusely enlarged neither ulceration, nor peau d'orange appearance were detected, but radial old healed scar in the lower outer quadrant with soft mobile mass occupying the medical lower portion of the breast and the nipple areola complex, normal left axilla.

No cervical mass was detected, chest examination revealed both lung fields normal. Heart sounds were within normal limits. Abdominal examination revealed no palpable mass, no fluid detected in the abdomen. Neurological examination was normal.

The patient was evaluated by the triple assessment, in which the ultrasound showed a complex mass in outer upper and lower quadrant of the right breast with multiple calcified foci, multiple axillary lymph nodes. The left breast showed a soft tissue mass of 6x7.5cm in diameter well circumscribed, no calcifications, clear left axilla.

Mammography showed wide spread micro calcification with irregular soft tissue mass in the right breast. FNAC was done revealing ductal carcinoma cells in the right breast, while showing non specific mixed inflammatory and mononuclear cells infiltrate no malignancy. Routine blood tests, metabolic panel had been done, revealing mild anemia (9.5mg/dl) with elevated THS 47mg/dl.

Metastatic workup was negative, including abdominal ultrasound, CT scan of the chest and the abdomen. In the view of clinical and laboratory findings the diagnosis of right breast cancer was made and with stage III, the case discussed with oncologist in Sudan.(Figure 1)

Fig 1: Gross appearance of the tumor

Treatment: The case was discussed with the family in the view of the clinical diagnosis, the patient and her family decided to have the operation done in our hospital.

- Medical consultation was done to stabilize her general condition. The dose of the thyroxin was...
increased for her up to 150 Mgm/day over three weeks. The TSH was 8 mg/dl, her vital parameters was within normal.

- The patient was prepared for Rt. modified radical mastectomy and axillary clearance and Lt. lumpectomy reduction mammoplasty at the same session. The patient was premedicated with administration of prophylactic antibiotics, pre operative LMW Heparin, under G A with placement of paravertebral block catheter.

- Rt. breast was dissected utilizing an elliptical incision involving the mass, the nipple-areola complex & was extended up to the axilla. Creating the upper and lower flaps utilizing the electrocautery, the tumor was fixed to the pectoral fascia and excised in block with the breast tissue, the axillary tail was followed to the axilla which was entered medially at the lateral edge of pectoralis major muscle, multiple large hard axillary lymph node was dissected from level I, II reaching the axillary vein and level III the introcostobrachial nerve was sacrificed as it was fixed to the excised lymph nodes, the long thoracic nerve and subscapular nerve are preserved.

- Hemostasis was insured using diathermy and ligation with 2/0 vicryl suture, the wound was drained by 2 large suction drains, subcutaneous tissue was approximated by 3/0 vicryl sutures, skin closed by 3/0 vicryl rapid subcuticularly.

- The left breast was painted and draped, reduction mammoplasty lumpectomy was done. The post operative period was uneventful except for mild C V A at the 15th day and patient recovered completely after one month.

The histopathological diagnosis was invasive ductal carcinoma moderately differentiated Grade II with axillary lymph node metastasis 4 out of 9 E R / P R - ve Cer B 2:-3+ overexpression

(Figure 2,3 & 4)

Fig 2: Axillary dissection with appearance of the axillary vein

Fig 3: The whole breast and the axillary tail after modified radial mastectomy

Fig 4: A complete healed wound

Discussion

The Biological therapy is targeting some molecular protein (HER2/neu protein)\(^1\).\(^4\).\(^5\).

HER2/neu protein is a transmembrane growth factor (member of tyrosine receptor family) and this over expression is amplification of the gene resulting in increase transcription in to mRNA and protein translation. This protein is of three types: H E R 1 (epidermal growth factor), e r b B 3 and e r b B 4.

Usually carcinomas that express this protein tend to be poorly differentiated and associated with shortened disease free and overall survival rate\(^2\).\(^4\).\(^5\).

- The expression profile reveals not only increased copies of H E R 2/neu in mRNA, but also increased transcription of other adjacent genes that are amplified within this segment of D N A.

These carcinomas do not express the genes that are characteristic of other subtypes of cancer in this array e.g. ER& basal keratin but do express e-cadherin\(^1\).\(^2\).\(^3\).\(^5\).\(^6\).

Breast cancers are routinely assayed for H E R 2/neu gene and protein using:-

1- F I S H (Fluorescent in Situ Hybridization)
2- I H C (Immunehistochemistry):- for the (erb 2 receptors)

F I S H: The evaluation of fluorescent in situ hybridization image evaluation study is a method used to determine H E R 2/ neu status of breast tissue sample. In this technique the fluorescent labeled genomic DNA probe containing the HER2/neu gene and its flaking sequence is allowed to hybridize to paraffin-embedded tumor cell DNA. A second DNA probe specific for the chromosome 17 centromere is used as a contrast.

FISH technique allows the analysis and quantification of specific abnormalities (gene amplification)\(^1\).\(^5\).\(^6\). DNA probes target the HER2/neu gene attach themselves to their target sequence, a process called hybridization. The probe carries special fluorescent markers that emit light, when the probes bind to HER2/neu genes\(^2\).\(^4\).\(^6\).

Conclusion

Trastuzumab is not directly cytotoxic, leading to HER2/neu-expressing breast cancer cells to accumulate in the G0/G1 phase when treated, so a variety of chemotherapeutic agents have been combined with trastuzumab to achieve cytotoxic effects. Clinical studies have confirmed that
trastuzumab in combination with paclitaxel or doxorubicin improves the survival in breast cancer patients with HER2/neu over expression in metastatic disease\textsuperscript{2,3}.

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Illustrations

Illustration 1

Figure 1: Gross Appearance of Tumor

Illustration 2

Figure 2: Axillary Dissection with appearance of the axillary vein
Illustration 3

Figure 3: The whole breast and the axillary tail after modified radial mastectomy

Illustration 4

Figure 4: A completely healed wound
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