

Case Report

A Case Report of Triple Negative, Mixed Invasive Ductal and Lobular Carcinoma of the Male Breast: Uncommon Subtype in a Rare Tumour with Long survival

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ABSTRACT

Male breast cancer (MBC) is infrequent, representing about 1% of all breast cancer. Over 90% of MBC are Invasive Ductal Carcinoma and about 1% are Invasive Lobular Carcinoma. A mixture of these two types known as Mixed Invasive Ductal and Lobular carcinoma is quite uncommon as only 3 cases have been reported in literature. MBC are 14% HER-2 over expression, 90% estrogen and 85% Progesterone receptor positive. These three receptors are absent in Triple Negative Breast Cancer which is a very rare tumour subtype in men. We present an obese 52-year-old man who was diagnosed with stage IIA, Triple Negative, Mixed Invasive Ductal and Lobular carcinoma of the right breast in 2015. He had the complete range of treatment with modified radical mastectomy, 6 cycles of first line chemotherapy and external beam radiotherapy. Two years later, he developed pulmonary metastasis which is common with TNBC and had second line chemotherapy using Docetaxel and Xeloda®. He was diagnosed with brain metastasis during his 4th year follow-up and had whole brain radiotherapy with excellent response. Despite the aggressiveness of this tumour our patient is still alive in 2020, five years after presentation emphasizing the need for close follow up, multidisciplinary approach to care and a need to develop innovative funding for cancer patients.

Keywords: Male breast cancer, Mixed Invasive Ductal and Lobular carcinoma, Triple Negative Breast Cancer

INTRODUCTION

Carcinoma of the male breast is rare and represents about 1% of all breast cancers.¹ Mutation in BRCA2 gene is an important risk factor for MBC, others are hormonal imbalance due to obesity, testicular disorders, liver damage and infertility.^{2,3} Over 90% of MBC are Invasive Ductal Carcinoma and 1% are Invasive Lobular

Carcinoma, a hybrid of both histology is extremely rare.^{2,4,5} Triple Negative MBC is very rare as 90-95% of breast cancer cases in men are hormone receptor positive.^{6,7} A mixture of these two types known as Mixed Invasive Ductal and Lobular carcinoma is quite uncommon as only 3 cases have been reported in

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literature.^{5,6} MBC are 14% HER-2 over expression, 90% estrogen and 85% Progesterone receptor positive.^{5,7,8,9,10} These three receptors are absent in Triple Negative Breast Cancer which is a very rare tumour subtype in men.

The treatment and prognosis of MBC are mostly extrapolated from FBC studies due to limited studies in MBC. The treatment of TNBC involves surgery, chemotherapy and radiotherapy for local disease.⁹ While for advanced cases, Atezolizumab with Nab-Paclitaxel is the standard of care.¹¹ In patients with mixed invasive ductal and lobular TNBC, prognosis was found to be poor compared with patients who had other subtypes of breast cancer.^{12,13}

Herein, we describe a 52-year-old obese man with Triple Negative, Mixed invasive Ductal and Lobular Carcinoma of the right breast. Despite full complement of treatment, he subsequently developed metastases to the lungs, brain and pelvic bone during the course of the disease.

CASE REPORT

Mr. NP, a 52-year-old father of three children, referred to our oncology clinic in 2015 with a one-year history of progressively increasing painless right breast lump. He had no risk factor for breast cancer except for obesity (BMI: 39.74kg/m²). A modified radical mastectomy was done for him at the referring hospital, and histology report of mastectomy tissue revealed Mixed Invasive Ductal and Lobular Carcinoma. (figures 1(a) and 1(b))

At our center, a detailed clinical assessment was done, findings were that of a healthy-looking middle-aged man with Karnofsky performance score of 100%, clean surgical scar on the right chest wall, no palpable axillary nor supraclavicular lymph nodes bilaterally, and clinically stage IIA (T2N0M0). Tissue blocks from mastectomy specimen were sent to our pathology laboratory for immunohistochemistry. Result showed an estrogen receptor (ER), progesterone receptor (PR), and HER-2 negative tumour. (figures 2(a), 2(b) and 2(c)) Other investigations, such as full blood count, renal function test, liver function test, chest X-ray, abdominopelvic ultrasound scan, ECHO scan, RVS and Urinalysis were all normal.

He received 6 cycles of adjuvant chemotherapy using the FEC regimen (5-Fluorouracil 600mg/m², Epirubicin 60mg/m², and Cyclophosphamide 600mg/m²). This was followed by external beam radiotherapy, which he received 50Gy in 25 fractions over 5

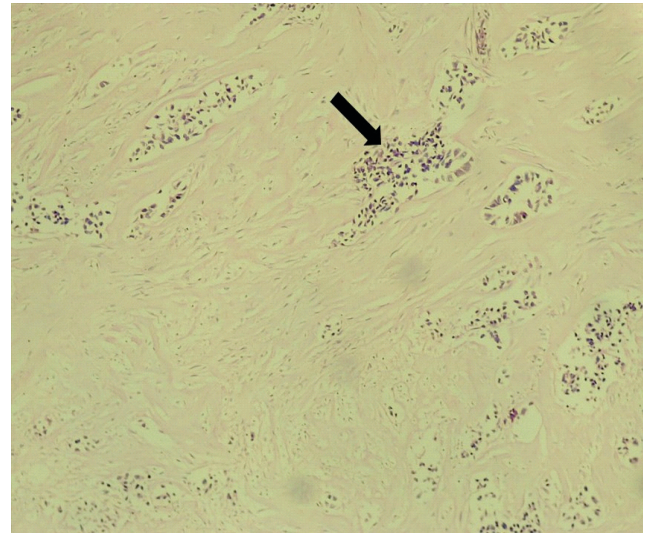


Figure 1(a)

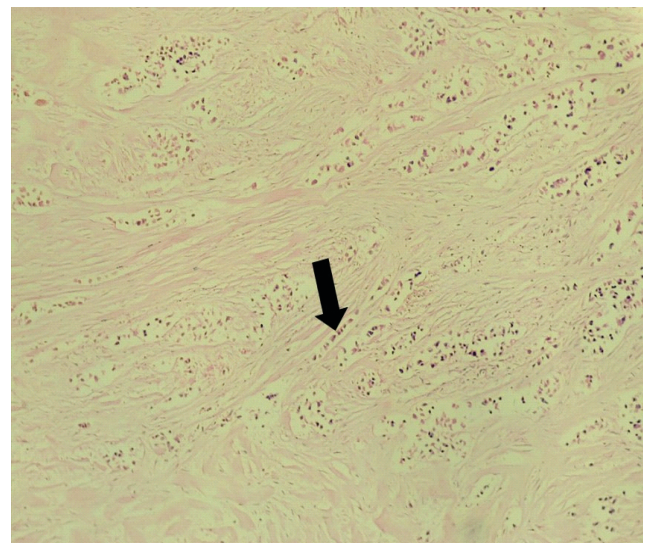


Figure 1(b)

Figure 1: photomicrographs of tissue specimen from right breast mass stained with H&E at medium magnification showing mixed invasive ductal and lobular carcinoma. **1(a)** invasive ductal carcinoma with hyperchromatic nuclei and abortive tubule formation. **1(b)** invasive lobular carcinomas with small dyscohesive cells in Indian file pattern.

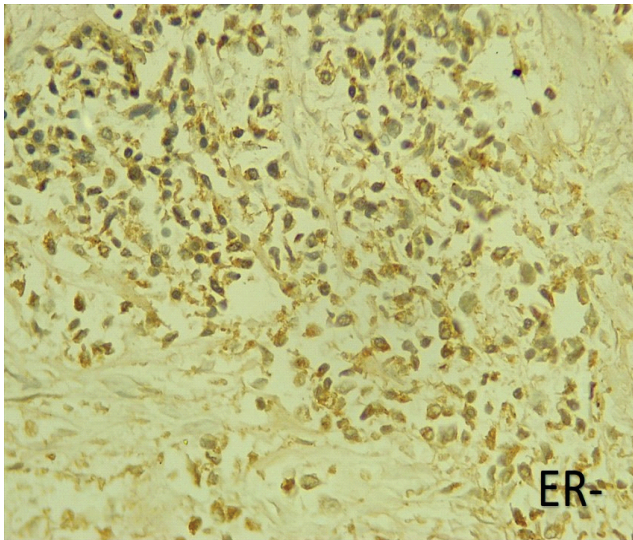


Figure 2(a)

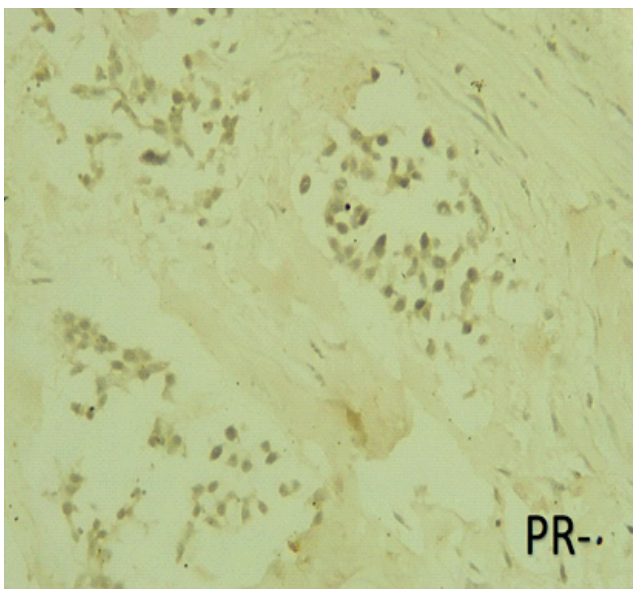


Figure 2(b)

weeks to the right chest wall, supraclavicular fossa, axilla, and parasternal area using the five-field technique. He tolerated treatment and was discharged home to be seen every three months in the follow-up clinic. Unfortunately, routine chest x-ray followed by a CT scan done two years later during his follow-up visit revealed multiple pulmonary metastatic nodules. Patient could not receive

targeted therapy with chemotherapy (Atezolizumab with Nab-paclitaxel) due to financial constraints. He received 6 cycles of second line chemotherapy using Docetaxel 75mg/m², and Xeloda 1250mg/m², then continued single agent Xeloda as maintenance. He had a total of 16 cycles of maintenance Xeloda which was well tolerated with complete resolution of lung metastasis on CT scan.

During a 4th year follow up visit, he presented with features suggestive of intracranial metastasis (blurred vision, slurred speech, right sided body weakness). A cranial MRI scan was done, and showed multiple intracerebral as well as cerebellar masses of varying sizes, the largest seen on the left occipital lobe (4.4 x 4.9cm) and left cerebellar hemisphere (4.0x 3.5cm). He was immediately referred to a center with functioning radiotherapy machine for whole brain radiation as our radiotherapy machine was faulty at that time. He had 30Gy in 10 fractions over two weeks and responded excellently, evidenced by resolution of presenting symptoms.

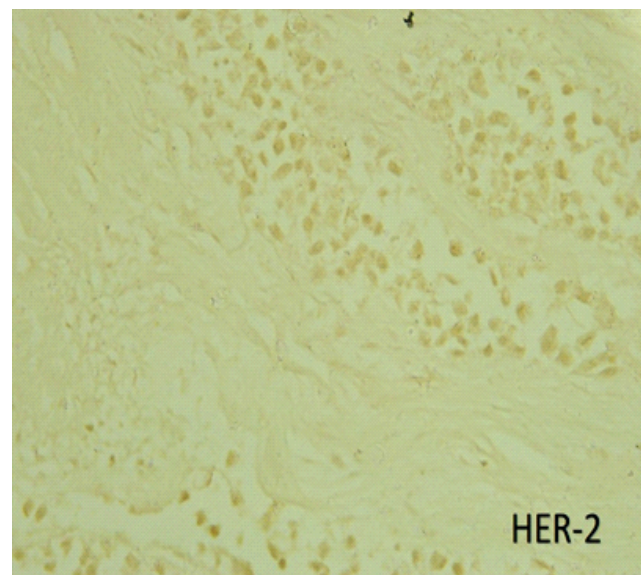


Figure 2(c)

Figure 2: Immunohistochemical staining at medium magnification showing triple negative breast cancer (a) negative stain for ER antibody (b) negative stain for PR antibody (c) negative stain for HER-2 antibody

He presented 4 months later for follow-up, with complaint of back pain. A lumbosacral and pelvic X-rays were done, which showed osteoblastic pelvic bone metastasis. He was referred for radiotherapy immediately, however, he is yet to commence treatment due to COVID-19 lock down in Nigeria as at 5th may 2020. He is being scheduled to commence bisphosphonate for the bone metastasis if the lockdown persists.

DISCUSSION

The case we have reported is a patient with male breast cancer(MBC) which is rare and accounts for about 1% of breast cancer cases.¹ The average age at diagnosis of MBC is approximately 67 years which is 5-10 years older than the mean age for females.⁴our patient was diagnosed 15 years younger than this average age for men.

This is not unusual as previous studies in our environment have earlier confirmed that cancer patients are 10 years younger than the mean age published in the literature.^{14,15}

The patient was obese as shown by his BMI (39.74kg/m²)which is a risk factor for MBC. Studies have suggested that obese men have over a 30% increase in circulating estrogen.³ Other risk factors include: genetic mutations such as BRCA 1 and 2, Klinefelter syndrome, estrogen intake, testicular damage, liver damage, infertility, benign breast conditions and radiation exposure to the chest.^{1,16} There is a positive family history in about 15-20% of male patients with breast cancer, but no history of such in our case.¹ Genetic studies have shown that BRCA 2 mutation is most linked to MBC, and accounts for 4-40% of cases.² We were not able to test for BRCA 1 and 2 mutation in our center because the test was not available at diagnosis.

Invasive Ductal Carcinoma of no special type is the commonest subtype of MBC accounting for about 90% of cases, other subtypes are Papillary and Medullary Carcinoma.² Lobular Carcinoma is quite rare representing only 1% of all MBC cases because lobules and acini are not commonly found in non-pathologic male breast tissue.⁴In our patient, there were features of both ductal and lobular differentiation, thus giving a Mixed Invasive Ductal and Lobular Carcinoma. However, E-cadherin and high molecular weight cytokeratin immunostaining was not available in our center at that time, this would have aided further categorization of this tumour

(positivity to E-cadherin and high molecular weight cytokeratin are features of ductal and lobular differentiation respectively).^{17,18} A review of the literature revealed only 3 cases of mixed ductal and lobular MBC have been reported.^{5,6}

Male breast cancer is mostly hormone receptor positive compared to female breast cancer, and several studies done showed that about 90% and 85% are ER and PR positive respectively.^{7,8,9,10} While HER-2 over expression is about 14% of MBC which is lower compared to HER-2 positivity in female breast cancer.⁵ There is absence of ER, PR and HER-2 receptors in our patient, this subtype is classified as Triple Negative Breast Cancer (TNBC) and it is extremely rare in MBC.¹⁹ The tendency of hormone receptor positivity in MBC may be an effect of the low level of circulating estrogen in the male system.¹⁰ This is similar to that observed in postmenopausal women, but not in our patient who was obese.^{3,20} Triple negative breast cancer (TNBC) implies the driving force for the initiation, progression and metastasis of the breast cancer is not caused by the ER, PR receptors and HER2 over expression. Research into tumour biology revealed that TNBC shows the presence of PD1 and PDL1 expression in the tumour. Similarly, TNBC showing the expression of PD1 and PDL1 expression were found to respond to anti PD1 and anti PDL1 immunotherapy drugs (Atezolizumab) in combination with Nab-Paclitaxel chemotherapy.¹¹ This patient could not afford this regimen despite its availability in the country due to financial constraints. The pattern of distant spread and therapy of MBC has basically been deduced from studies of FBC , because large clinical series of MBC are lacking.¹⁹ The sites of distant spread of breast cancer are the bone, lungs, liver and brain in decreasing order of occurrence.²¹ In contrast, patients with TNBC had increased propensity of distant metastasis, mostly to the lung , brain and distant nodes.^{12,19} This is similar to the pattern of metastases observed in our case. Metastasis to the brain is being seen also in highly treated patients even in the absence of local recurrence. This may be related with the inability of most chemotherapy drugs crossing the blood brain barrier, rendering the brain a sanctuary site for distant relapse.

The stage at diagnosis of MBC is crucial in its treatment, other factors are the hormone and HER-2 receptor status.² Treatment is generally by a multidisciplinary approach with surgery , this

may be followed by radiotherapy, chemotherapy, hormonal therapy (Tamoxifen) for hormone positive tumours and targeted therapy (Trastuzumab) for HER-2 positive tumours.⁹ In our case, he had modified radical mastectomy, chemotherapy, and radiotherapy, then second line chemotherapy and whole brain radiotherapy because of pulmonary and brain metastases respectively.

Radiotherapy is the choice of treatment for brain metastasis where lesions are multiple or inaccessible for surgery.²² Response are usually excellent especially if they are detected before symptoms and are not located in very critical part of the brain. We advise that in long survivals, highly treated breast cancer patients to have routine yearly evaluation of the brain so as to pick metastasis early and treat promptly.

Financial toxicity, the hardship arising from cost of cancer treatment, is a major factor in our environment as most patients pay out of pockets without any health insurance scheme to support them.²³ As a result, our patient was unable to source for funds and could not receive the gold standard treatment for triple negative breast cancer as shown by Impassion 130 landmark trial.¹¹ It is obvious that there is an urgent need for innovative funding for cancer treatment for all cancer patients with coverage of all modality of treatments and where this is not possible, there is need for special support for the indigent patients so as to obtain optimal care. This case report shows that even if immunotherapy could not be used for any reason, the use of available regimen of chemotherapy could substantially prolong survival and quality of life.

CONCLUSION

A rare case of an obese male with Triple Negative, Mixed Invasive Ductal and Lobular breast carcinoma, with distant spread to the lungs, brain and pelvic bone. Despite the aggressiveness of this tumour, our patient is still alive as at August, 2020, five years after presentation. This emphasizes the need for close follow up, multidisciplinary approach to care.

Recommendation

There is need to develop innovative funding by the government and private organizations for cancer patients. This will aid cancer patients to access the best standard of care available.

Conflicts of interest

The authors declare that they have no conflicts regarding this report.

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