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# Bilateral Metachronous Male Breast Cancer in a Patient with Poland's Syndrome: A Case Study

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## ABSTRACT

**Background:** Although breast cancer in males is not as frequent as in women, yet men tend to develop even more severe and advanced stages of this condition. In the given study, a case of 67 years old male with bilateral breast cancer associated with a rare syndrome has been considered.

**Methods:** The present study is based on a case study. The patient underwent right axillary clearance, and 19 lymph nodes were negative for malignancy. He received 6 cycles of adjuvant chemotherapy. He was started on adjuvant tamoxifen. Due to the last presentation for radiotherapy, the participant was in this given the option of completing mastectomy versus close observation, in which he preferred the latter. The subsequent follow-up did not show any evidence of recurrence.

**Results:** On close observation, the patient's follow-up did not show any evidence of recurrence. Thus, after his five-year adjuvant therapy, tamoxifen was discontinued, and the patient opted to continue his follow-up outside the centre in a private clinic. However, in 2022, he presented with a right breast lump and bloody nipple discharge for 4 weeks duration. The clinical and radiological assessment confirmed cT1N0M0, invasive ductal carcinoma with 5% mucinous component, ER 90%, PR –ve, her2 zero. Ki67%was 10%. The CT scan chest showed features of pectorals major hypoplasia and absence of right pectoralis minor. In our case, the second primary occurred six years later. In both occasions, the disease was diagnosed at an early stage (T2N0M0 and T1N0M0). Whether the disease behaviour is directly related to Poland's syndrome or other genetic pathophysiological factors needs to be explored more in such cases.

**Conclusions:** Poland's syndrome can be a risk for male breast cancer as well. Therefore, the molecular characteristics of this syndrome should be explored further to enable the prediction of future carcinogenesis types associated with Poland's syndrome.

**Keywords:** Male Breast Cancer; Poland's Syndrome; Bilateral Metachronous Male Breast Cancer; Cancer Research

## BACKGROUND

Breast cancer in men is a rare disease, accounting for around 1% of all breast cancers.[1] Men tend to be diagnosed with breast cancer at an older age than women and with a more advanced stage of disease.[2] The mortality and incidence of recurrence are higher in Male Breast Cancer (MBC),) compared to Female Breast Cancer (FBC).[3,4] The incidence of male breast cancer has increased over the last few decades.[2,5]

Unlike females, BRCA 2 mutations are more common in male breast cancer than BRCA 1 mutations. Performed A retrospective study performed multi-gene panel testing ion 715 male breast cancer patients, BRCA2 was found in 11% and BRCA1 in 1.3 %. Other mutations detected were CHEK (4.1%), ATM (1.5%) and PALB2 (0.8-6.4%). In this study, *CHEK2* 1100delC carriers had a significantly lower average age of diagnosis (54 years).[6]

The pathophysiology of male breast cancer could be related to excessive estrogen levels in men. Clinical conditions like obesity, liver disease, and thyroid dysfunction are considered as risk factors. The incidence of breast cancer increases with age.[7] In the USA, the condition is more common in non-Hispanic blacks.[8] The prevalence of infectious liver diseases in Central and South Africa might have contributed to the higher incidence of male breast cancer in these regions.[5] Males with Klinefeltreer syndrome have approximately 50 fold increased risk of developing breast cancer compared to the average population.[9]

Most male breast cancers (90~80%) are hormone receptor-positive, 5-9% overexpress human epidermal growth factor receptor 2 (HER2), and 0.3% are triple-negative.[10,11]

The general principles of management remain the same as in women's breast cancer. In early male breast cancer that is hormone receptor positive, adjuvant tamoxifen is the treatment of choice. The duration of therapy is usually between 5 and 10 years. Studies indicate that aromatase inhibitors may be associated with poorer outcomes in men when compared with tamoxifen. [12-14]

## THE CASE

A 67-year-old male of East African origin, has no significant comorbidities, and presented with a left breast painless lump that progressed, according to him, over the last 2 years prior to the investigations. He had no history to suggest distant metastasis at that time. He had an excisional biopsy in a private hospital in April 2015: histopathology revealed invasive cribriform carcinoma, grade 1, size was 2.5 cm, and margins were negative, ER100%, PR100 %, Her 2 negative. When seen in the medical oncology clinic, he was asymptomatic, and his performance status was zero. A staging work up was done, which did not reveal any evidence of distant metastasis. At that point, he was referred to breast surgery for the management of the axilla.

## METHOD/TREATMENT

The patient underwent right axillary clearance, and 19 lymph nodes were negative for malignancy. He received 6 cycles of adjuvant chemotherapy. He was started on adjuvant tamoxifen. For unclear reasons, the patient presented very late to the radiation oncology clinic. He was given the option of completing mastectomy versus close

observation. However, the patient preferred the latter. The subsequent follow-up did not show any evidence of recurrence. After his five years of adjuvant therapy, tamoxifen was discontinued, and the patient opted to continue his follow-up outside the centre in a private clinic.

However, in May 2022, he presented with a right breast lump and bloody nipple discharge for 4 weeks duration. The clinical and radiological assessment confirmed cT1N0M0, invasive ductal carcinoma with 5% mucinous component, ER 90%, PR ve, her2zero. Ki67%was 10%. The CT scan chest showed features of pectorals major hypoplasia and absence of right pectoralis minor. This picture was suggestive of Poland's syndrome. He underwent right simple mastectomy and SLNB on r in addition to left completion mastectomy. Postoperative histopathology confirmed pT1cN0 (1.5 cm). There was no evidence of malignancy in the left breast after the completion mastectomy. The patient was referred to the genetic oncology clinic, where a breast multi-gene panel test was carried out. The coding exons of ATM, BRAD1, BRCA1&2, BRIP1, CDH1, CHEK2, MRE 11, NBN, PALB2, RAD51D, STK11 and P53 were tested. The results are summarised in Table 1.

## RESULTS

**Table 1:**

| Gene (Isoform) | Phenotype MIM number (Mode of inheritance) | Variant | Zygosity | MAF gnomAD [%] | Classification |
|---|---|---|---|---|---|
| ***BRCA2*** (NM_000059.3) | 114480 (AD) | c.3848T>C | het. | 0 | Variant of Uncertain Significance |
| | 613347 (AD) | p. (Val1283Ala) | | | |
| | 176807 (AD) | chr13:32912340 | | | |
| ***ATM*** (NM_000051.3) | 114480 (AD) | c.640T>C | het. | 0.00091 | Variant of Uncertain Significance |
| | | p. (Ser214Pro) | | | |
| | | chr11:108114823 | | | |

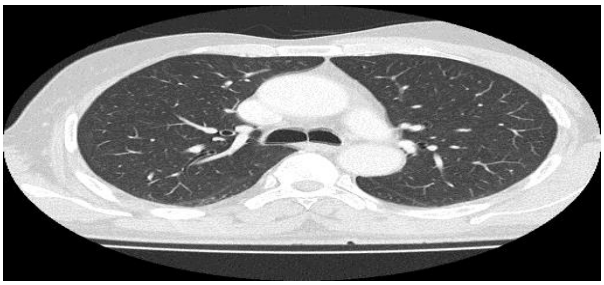

**Figure 1:** Evidence of Poland's Syndrome.

Ct scan chest has done pre-operating on the second primary (right breast), showing absent right pectoralis minor muscle and partial hypoplasia of the pectoralis major.

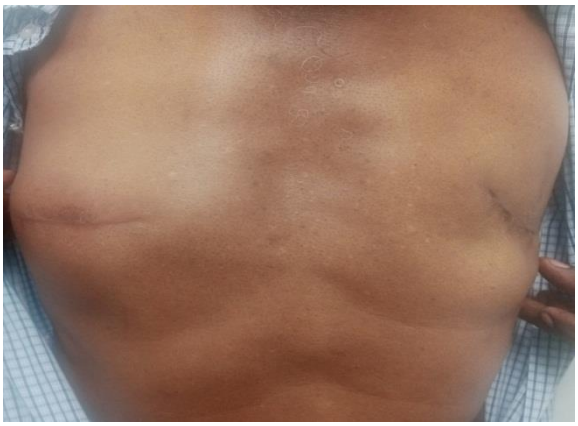

**Figure 2:** Evidence of Poland's Syndrome: mild pectus excavatum with hypoplia of male breast tissue, less prominent on the right side because of a postoperative seroma (recent mastectomy).

## DISCUSSION

Bilateral Male Breast Cancer (bMBC) is relatively rare.[15,16] The incidence of metachronous breast cancer is higher than that of synchronous male breast cancer. Synchronous bilateral breast cancer has been reported in a patient with Klinefelter syndrome.[17] In another case, the second primary breast cancer was detected five months later. The patient was in his sixties, and BRCA1/2 were negative.[18] A 67-year old male with a strong family of male breast cancer (brother) was diagnosed with synchronous breast cancer. Again BRCA1/2 was negative, However, there was no mention in this case.[19]

Although the features of Poland syndrome were mentioned before it was Alfred Poland, a medical student, who had precisely described the condition in 1841.[20] It was not until 1962 that Clarkson, a plastic surgeon, confirmed these anatomic malformations during an operation and named them Poland's syndrome.[21,22] It is a congenital disorder characterized by a hypoplastic sternocostal portion of the pectoralis major muscle. Also, it can be associated with hypoplasia of the breast and subcutaneous chest wall tissue. Various types of chest wall deformities have been described.[22-24] In a clinic series evaluating reconstructive surgery in patients with Poland's syndrome, the authors proposed three categories of this syndrome according to the degree of abnormalities (degree I, II and III).[24] Poland's syndrome is associated with several types of malignancy, like breast cancer, lymphomas[25,26] and leukaemia.[27]

There are several case reports in which female breast cancer has been associated with Poland syndrome.[22,23] However, during our literature search related to this article, we did not encounter any case of male breast cancer associated with Poland's syndrome.

In our case, the second primary occurred six years later. In both occasions, the disease was diagnosed at an early stage (T2N0M0 and T1N0M0). Whether the disease behaviour is directly related to Poland's syndrome or other genetic pathophysiological factors needs to be explored more in such cases.

The association between congenital disorders and malignancy is well known. Although mutations in tumour suppressor genes and proto-oncogenes can lead to both, however, the exact mechanisms are not well understood.[28] There are no studies looking into specific genetic mutations associated with Poland's syndrome.

## CONCLUSION

Poland's syndrome can be a risk for male breast cancer as well. The molecular characteristics of this syndrome should be explored more. This may allow the prediction of future carcinogenesis types associated with Poland's syndrome.

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