

*Case Report***Type-1 Neurofibromatosis with Male Breast Cancer- A Case Report**

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**ABSTRACT**

Neurofibromatosis type-1 is a neurocutaneous disorder having increased propensity of risk of developing different malignancies. Neurofibromatosis type-1 patients develop different malignancies like malignant peripheral nerve sheath tumor, gliomas and leukemias. Women with neurofibromatosis-1 are at increased risk of developing breast cancer and men also may be at risk, but established clinical studies correlating association of male breast cancer with neurofibromatosis are lacking and the results are extrapolated from the female breast cancer patients due to its rarity. The association of neurofibromatosis-1 with male breast cancer is a rare clinical entity, with only few cases have been reported in literature. Here is a case report of carcinoma male breast which developed in a sixty years old male patient with neurofibromatosis type-1. Patient had undergone modified radical mastectomy of right breast, then completed adjuvant chemotherapy and radiotherapy as he had invasive duct carcinoma of right breast. At present he is on regular follow up with no evidence of disease. This case is being reported herewith due to its rarity and for future documentation.

**Key words:** Breast cancer, male patient, type-1 neurofibromatosis.

**INTRODUCTION**

Carcinoma of male breast is a rare entity and accounts for less than 1% of all breast cancers. <sup>[1]</sup> NF-1 (neurofibromatosis-1) is one of the commonest neuroectodermal genetic disorders with autosomal dominant inheritance. It is caused by mutation in NF 1 gene which is considered a tumor suppressor gene. <sup>[2]</sup> Patients with neurofibromatosis have a higher propensity to develop benign and malignant tumors, particularly malignant peripheral nerve sheath tumor, optic gliomas, other gliomas and leukemias.

<sup>[3]</sup> The association of neurofibromatosis-1 with male breast cancer is a rare clinical entity, with only few cases have been reported in literature. Present study reports a case of carcinoma male breast in a patient with NF-1. This case is reported due to its rarity and for future documentation.

**CASE REPORT**

A 60 year old male patient presented with the complaints of multiple skin nodules, brown skin patches since childhood and a gradually enlarging painless lump in

the right breast for three months. There was no other medical history of relevance. There was no history of cancer in his family.

On examination multiple soft to firm nontender, skin colored nodules with size ranging from 0.5 to 5cm and many well circumscribed brown macular patches i. e café-au-lait spots were found all over the body (Figure-1). On ophthalmology evaluation the iris and retina were normal. In the right breast a lump of about 6×4 cm size was noted which was hard, mobile, nontender on palpation. Rest of the clinical examination was normal. Genetic analysis couldn't be conducted for logistic reasons and diagnosis of NF1 was made on clinical criteria. True cut biopsy of the right breast lump was suggestive of infiltrative duct carcinoma. X-ray chest posterior-anterior view and ultrasound of abdomen and pelvis was within normal limit. Based on histopathology he underwent modified radical mastectomy of right breast (Figure-1).



**Figure-1:** Clinical photograph showing right modified radical mastectomy scar in a patient of neurofibromatosis type-1.

Postoperative histopathology revealed invasive duct carcinoma of Bloom & Richardson score 7, grade II, base involved by tumor. The pathological stage was pT3N0M0. On immunohistochemistry

ER, PR & HER2 receptors were negative. He was planned for adjuvant chemotherapy followed by radiotherapy based on histopathological report. He received 6 cycles of CAF (Cyclophosphamide, Adriamycin, 5-FU) that was followed by external beam radiotherapy with tangential pair portal of 50 Gy in 25 fractions to right chest wall by cobalt-60 over 5 weeks. At present patient is on regular follow up with clinically controlled disease since last nine months.

## DISCUSSION

Neurofibromatosis type 1 is an autosomal dominant disorder with high penetrance and a wide variability in expression. It is characterized by presence of at least two of the following features i. e 6 or more café-au-lait spots, 2 or more neurofibroma, freckling in the axilla or groin, 2 or more iris lisch nodules, optic glioma, a first degree relation with NF-1 and specific osseous dysplastic lesions. [4]

NF-1 gene is located on pericentromeric region of long arm of chromosome 17 which also houses the BRCA1 gene and regulates conversion of active Ras-GTP to inactive Ras-GDP. Ras is an essential component of signal transduction pathway that regulates growth, proliferation, differentiation and apoptosis. NF-1 gene is a tumor suppressor gene which encodes the neurofibromin protein, a negative regulator of Ras oncogene. The impairment of this hydrolytic process leads to an increased risk of malignancy. [5] It has been associated with certain type of malignancies such as pheochromocytoma, neurofibrosarcoma, leukemia, malignant schwannoma, rhabdomyosarcoma, optic glioma. Though breast cancer has been associated with NF-1, it is rare in literature. As breast cancer is one of the most common tumors in women it is difficult to establish whether coexistence of NF-1 and breast

cancer is a coincidence or a real predisposition.

Sharief et al. evaluated risk of breast cancer in a cohort of 304 women with NF1 aged older than 20 year. [6] The study showed women with NF1 have five-fold risk of breast cancer by the age of fifty year. Invasive duct carcinoma is the commonest type, which is also seen in our case. The author suggested affected women should be considered for screening for breast cancer from age of 40 years. Murayama et al. reported 37 cases of NF1 associated with breast cancer, most are diagnosed at an advanced stage. [7] This may be due to numerous neurofibromas obscure the breast lesion. In a retrospective study of 212 NF1 patients followed over 42 years Sorensen et al. found a relative risk of breast cancer of 4(CI 2.8-5.6) in NF 1. In another retrospective study of 126 women with NF1 who were 20 years or older Madanakia et al reported 4 cases of breast cancer and observed a trend for almost 3 fold increase in the risk of breast cancer in women with NF1 who were less than 50 years old. [8] Different studies i. e Wang et al, Seminog and Goldacre et al also establish increase risk of breast cancer in female patients with NF 1 less than 50 years. [9,10] All these studies concluded that women with NF1 are at a greater risk for breast cancer than the general population particularly when they are younger than 50 years. Studies also showed that these patients may have a delay in diagnosis as breast mass may be misdiagnosed as NF 1 manifestation. Men with NF-1 are at risk of breast cancer but there is few case reports have been published in this contest.

## CONCLUSION

It should be emphasized that NF1 can obscure or delay the diagnosis of breast cancer not only because skin neurofibromas can masks the sign of malignant lesion but

also because patient and physician may mistakenly consider breast lump to be a manifestation of primary disease. Physician should be aware of the coexisting breast malignancy in male as much as to females. Every new breast lump should be evaluated carefully and if necessary further evaluation should be carried out in the line of breast malignancy so that early diagnosis and better management can be achieved.

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