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CASE REPORT

# Breast Cancer Associated with Von Recklinghausen's Disease: Case Report and Review of Literature

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**Abstract** Breast cancer in association with type- 1 neurofibromatosis (NF1) is a rare clinical entity. Here, we present the case of a 45-year-old woman with typical clinical manifestations of NF1, who presented with a right breast lump, which she had first noticed 8 months back but had disregarded, believing it to be another manifestation of her Von Recklinghausen's disease. Clinical examination and diagnostic workup were suggestive of a breast carcinoma. Subsequently, she underwent modified radical mastectomy, followed by postoperative chemotherapy. Histopathological examination revealed high grade invasive duct carcinoma and multiple neurofibromas. After 7.5 months, she developed recurrence at the drain site with pulmonary and bony metastasis and died 9 months after surgery. Delayed presentation of the patient was the result of her mistaken identification for the breast tumor as a manifestation of NF-1. Early onset, high grade tumor and early recurrence with metastasis place strong emphasis on clinical alertness and to opt for an aggressive treatment option.

**Keywords** Breast cancer · Neurofibromatosis NF-1 · Von Recklinghausen's disease

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## Introduction

In patients with NF-1 there is a high incidence of neoplasm's especially tumors of central and peripheral nervous system including optic gliomas, astrocytomas, meningiomas and schwannomas. Other less frequent malignant tumors such as neurofibrosarcomas, phaeochromocytomas and leukaemias may also occur [1] Very few cases of NF-1 with epithelial malignancies especially breast have been reported [2, 3]. Here we describe a case of 45-year-old female with NF-1 who was diagnosed with invasive duct carcinoma of breast after a delayed presentation. Presenting symptoms, diagnostic evaluation and surgical management are discussed along with a review of the literature.

## Case Presentation

A 45- year- old, premenopausal woman with type-1 neurofibromatosis presented to surgical OPD with painless, slowly growing right breast lump, which she had noticed 8 months back, but had ignored , believing it to be the part of her generalized neurofibromatosis. Her past medical history was unremarkable, and she did not have a family history of breast cancer. Clinical examination revealed a firm deep mass, measuring 3×2 cm in her right breast with multiple cutaneous neurofibromatosis. There was no axillary lymphadenopathy. Left breast and left axilla was essentially normal. Fine-needle aspiration cytology (FNAC) was indicative of malignancy. After cytological confirmation and proper metastatic work-up, she underwent right modified radical mastectomy for stage IIA tumor (T2N0M0, AJCC TNM staging). Histopathological examination revealed an invasive ductal carcinoma with Bloom Richardson score- 7/9 [Figs. 1, 2, 3]. Four out of 9 resected lymph nodes were positive for metastasis. On immunohistochemical analysis the tumor cells were negative for estrogen (ER), progesterone (PR) and c-Erb-B2 receptors. The pigmented papules showed typical features of neurofibromatosis. Postoperatively, she received anthracycline-based chemotherapy and radiotherapy. After 7.5-

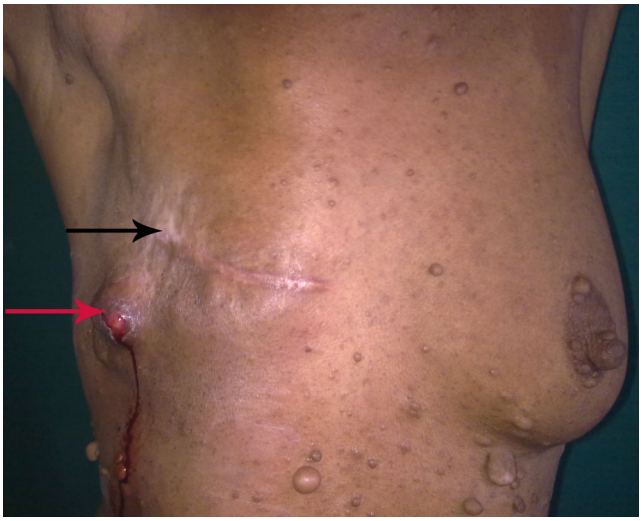

**Fig. 1** Postoperative photograph showing the right modified radical mastectomy scar [*black arrow*] and recurrence at the drain site [*red arrow*]

months, she came to the hospital with breathing difficulty and recurrence at the drain site of previous surgery in the form of very hard skin nodule measuring 2×2 cm [Fig. 1]. After stabilizing her condition, she was properly worked-up. FNAC from the nodule was positive for malignancy. X-ray chest and bone scan showed multiple pulmonary and skeletal secondaries. Wide excision of the nodule was performed and she was discharged on 10th postoperative day. She refused to any further adjuvant treatment and died after 1.5 months.

## Discussion

Neurofibromatosis type-1 is an autosomal dominant genetic disorder, mainly caused by mutations of the NF1 gene, which is located on chromosome 17q11 [4, 5]. The NF-1 gene is a large tumor suppressor gene that encodes the 327-d protein known as neurofibromin. The predominant features of the disease are benign cutaneous neurofibromas and caf'e-au-lait spots. The overall risk of cancer is 4 to 5 times higher than the general population [4]. Frequently associated cancers are malignant peripheral nerve sheath tumors, rhabdomyosarcoma, phaeochromocytoma, somatostatin-producing carcinoid tumors of the duodenal wall, medullary thyroid cancer, and hypothalamic or optic nerve tumors that cause precocious puberty. Majority of the tumors are from connective tissue, endocrine glands and brain parts. But, NF-1 association with breast cancer remains uncommon. Interestingly, these tumors behave in a different manner and have a different natural history from those occurring sporadically. Majority of the breast cancer patient's are not only young but also present their disease at an advanced stage with more negative prognostic factors.

In a review of 37 cases of breast cancer associated with NF-1, Murayama et al. [6] found that most of the cases had lesions greater than T2 (advanced stage) with invasive duct carcinoma histology. They conclude that the late stage presentation was probably because of the presence of numerous skin neurofibromas that has hindered the discovery of the breast lumps.

In a Japanese review, Nakamura et al. [7] found that in 18.5 % of the cases of NF1, the breast cancer patients were younger than 35 years old. Two recent series have shown a significantly higher risk of developing breast cancer in women with NF-1 younger than 50 years of age.

Recent scientific data support a possible association between breast cancer and NF1. It has been suggested that there may be genes that could interact with the NF1 gene, particularly in relation to the BRCA1 subset. They could share a common gene location (both NF1 and BRCA1 are on human chromosome 17q) [5]. Ceccaroni et al. [5] observed five members of a family affected by both NF1 and breast or ovarian cancer, and they showed that three individuals shared

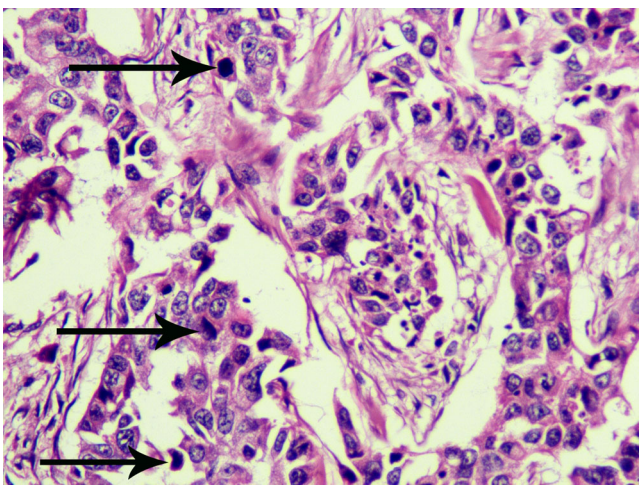

**Fig. 2** Histological findings of invasive duct breast carcinoma showing mitotic figures [*black arrow*] and moderate nuclear pleomorphism (H&E stain, X 100)

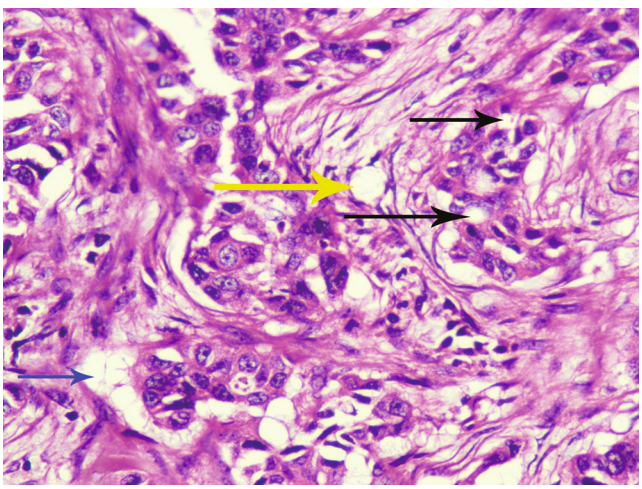

**Fig. 3** Histological findings of invasive duct breast carcinoma showing tubule formation [*black arrow*] and adipose tissue with infiltration [*blue arrow*]. *Yellow arrow* shows blood vessel (H&E stain, X 100)

a common haplotype, including the NF1 and BRCA1 loci on chromosome 17 and a BRCA1 mutation. They concluded that the concurrence of NF1 and hereditary breast or ovarian cancer in the family was likely because of the two linked mutations at the NF1 and BRCA1 loci.

Veronesi et al. [8] in a study of familial breast cancer showed that BRCA1-positive patients tended to be more often premenopausal, and they had more frequently negative prognostic factors. Similarly, most cases of breast cancer in NF1 occur in women aged less than 50 years [9].

Similar to these published reports, we also observed that our patient had advanced disease at young age. She had high grade invasive duct carcinoma with negative ER/PR status and died early because of metastatic disease.

## Conclusions

Breast cancer occurrence in the background of NF-1 is a rare phenomenon. Multiple cutaneous lesions in NF-1 may obscure breast lumps leading to delayed detection of cancer. Early onset, aggressive behavior and different natural history of these tumors require a specific approach to their detection and management. Increasing awareness of this rare possibility needs to be transferred to the patients and treating doctor both, to pick-up more and more tumors at a very early stage.

## References

1. Kumar K, Abbas AK, Fausto N. Neoplasia.In: Robbins and Cotran Pathologic Basis of Disease.7th Ed.Philadelphia: WB Saunders.2004; 305
2. Walker L, Thomson D, Easton D et al (2006) A prospective study of Neurofibromatosis type1 cancer incidence in the UK. Br J Cancer 195: 233–238
3. Roberta I, Barbara M, Graziella P (2008) Association of GIST, breast cancer and Schwannoma in a 60- year old woman affected by type-1 von Recklinghausen's neurofibromatosis. Tumori 194:126–128
4. Zoller ME, Rembeck B, Oden A, Samuelsson M, Angervall L (1997) Malignant and benign tumors in patients with neurofibromatosis type 1 in a defined Swedish population. Cancer 79:2125–2131
5. Ceccaroni M, Genuardi M, Legge F, Lucci-Cordisco E, Carrara S, D'Amico F et al (2002) BRCA1-related malignancies in a family presenting with von Recklinghausen's disease. Gynecol Oncol 86: 375–378
6. Murayama Y, Yamamoto Y, Shimojima N, Takahara T, Kikuchi K, Iida S et al (1999) T1 breast cancer associated with von Recklinghausen's neurofibromatosis. Breast Cancer 6:227–230
7. Nakamura M, Tangoku A, Kusanagi H, Oka M, Suzuki T (1998) Breast cancer associated with Recklinghausen's disease: report of a case. Nippon Geka Hokan 67:3–9
8. Veronesi A, de Giacomi C, Magri MD, Lombardi D, Zanetti M, Scuderi C et al (2005) Familial breast cancer: characteristics and outcome of BRCA 1–2 positive and negative cases. BMC Cancer 5:70
9. Sharif S, Moran A, Huson SM, Iddenden R, Shenton A, Howard E et al (2007) Women with neurofibromatosis 1 are at a moderately increased risk of developing breast cancer and should be considered for early screening. J Med Genet 44:481–484