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Breast cancer in a male patient with type 1 neurofibromatosis

Tip 1 nörofibromatozisli erkek hastada meme kanseri

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Summary

Neurofibromatosis 1 (NF1) is a neurocutaneous disorder that was known as von Recklinghausen Disease. Patients with NF1 have a propensity to develop malignant and benign nervous system tumors. There are few reported association between male breast cancer and NF1. We herein present the case of a 58-year-old male NF1 patient who presented with breast cancer. The patient is a 58-year-old male who presented with a painful mass in the right breast and back pain. Light microscopic evaluation of the biopsy from the breast mass revealed a malignant component which was considered to be invasive ductal carcinoma. Six cycles of CAF (cyclophosphamide, doxorubicin and 5-Fluorouracil) were administered every three weeks. There are a few cases in the literature about male breast cancer and NF1. Every new breast lump must be carefully examined and if necessary, further evaluation such as mammography, breast USG and breast MRI should be performed.

Key Words: Breast cancer, type 1 neurofibromatosis, male patient.

Özet

Tip 1 nörofibromatozis (NF1) aynı zamanda von Recklinghausen olarak da bilinen nörokutanöz bir hastalıktır. Otozomal dominant geçiş göstermekte olup insidansı 1/2500 ve prevelansı 1/4000 olarak tanımlanmıştır. NF1 hastalarında malign ve benign sinir sistemi tümörleri sık görülür. Meme kanseri NF1 hastalarında nadir görülür.NF1'li erkek hastalarda meme kanseri gelişimi ile ilgili birkaç yayın mevcuttur. Bu makalede meme kanseri gelişen 58 yaşında NF1'li erkek hastayı sunmak istedik. Hasta sağ memede ağrısız bir kitle ve sırt ağrısı ile başvurdu. Tanısal tetkiklerde karaciğer ve multipl kemik metastazları ile sağ memede karsinomu düşündüren kitle tespit edildi. Memedeki kitlenin patolojik değerlendirmesinde invaziv ductal karsinoma tespit edildi. Üç haftada bir 6 kür CAF (siklofosfamid, doxorubicin, 5-fluorourasil) ve kemiklere palyatif radyoterapi uygulandı. NF1'li erkek hastalarda meme kanseri ile ilgili yayınlar sınırlıdır. NF1'li bütün hastalarda memede gelişen her yeni kitle dikkatlice değerlendirilmeli ve gerektiğinde mamografi, meme ultrason ve meme manyetik rezonans görüntülemesi gibi ileri tetkikler yapılmalıdır.

Anahtar Sözcükler: *Meme kanseri, tip 1 nörofibromatozis, erkek hasta.*

Introduction

NF1 is characterized most typically by multiple hyperpigmented skin lesions, known as *café au lait* spots, and neurofibromas. Patients with NF1 have a propensity to develop malignant and benign nervous system tumors. There is a greatly increased relative risk of developing gliomas, malignant peripheral nerve sheath tumors, juvenile chronic myelomonocytic leukemia, rhabdomyosarcoma, and pheochromocytoma (1).

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However, breast cancer is rarely seen in NF1. There are a few cases about association between male breast cancer and NF1 in the literature.

Case Report

The patient is a 58 year-old male who first presented with a painful mass in the right breast and low back pain. The patient had first noticed the breast mass about a year before the presentation. However, he had initially thought it was similar to other tumors in his body.

Physical examination revealed a 5x4 cm mass that was hyperemic and partly ulcerated. There had extensive tumoral masses over his body, which were consisted with neurofibromas (Figure-1).

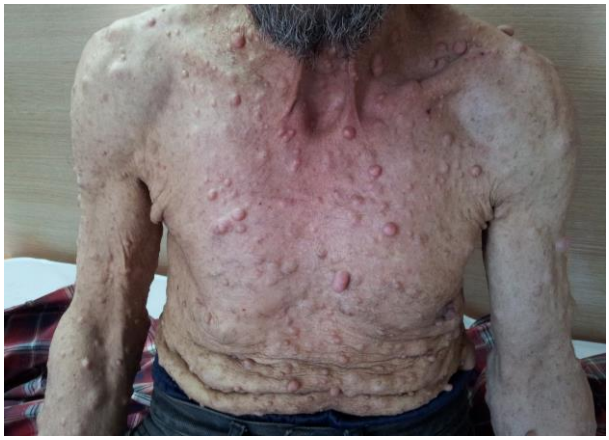

Figure-1. Photo shows the patient with typical clinical signs of type 1 neurofibromatosis.

Mammography could not be performed since the lesion was significantly painful. Breast ultrasound revealed a lesion with irregular borders, an echogenic halo and a posterior shadow within the right breast. An abdominal ultrasound revealed multiple liver masses. The 18F-fluorodeoxyglucose positron emission tomography with computed tomography (PET-CT) study showed pathologic FDG uptake in the right breast lesion, multiple liver masses, bilateral axillary and mediastinal lymph nodes, thoracolumbar vertebrae and other skeletal structures (Figure-2).

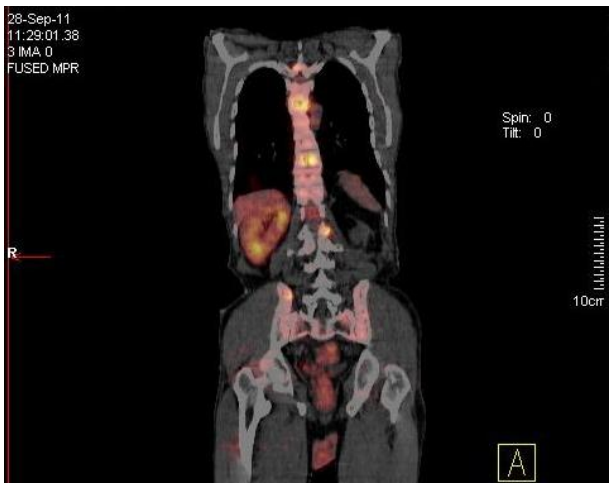

Figure-2. PET-CT demonstrates multipl bony and liver metastases.

Palliative radiotherapy was initiated urgently while awaiting pathology results due to the significantly increased risk of fracture in the lumbar vertebrae.

Light microscopic evaluation revealed a malignant component which was considered to be invasive ductal carcinoma (Figure-3), and a second component which was thought to be consistent with a neurofibroma. Immunohistochemical studies showed strong estrogen receptor positivity (90%), a scattered positivity for GCDFP-15, and c-Erb-B2 negativity.

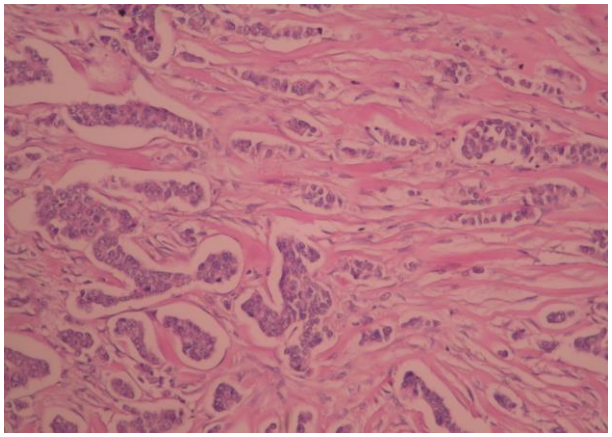

Figure-3. Atypical pleomorphic epithelial tumor cells in solid and adenoid-like structures in a desmoplastic stroma (H&E, x200).

A diagnosis of metastatic breast cancer was made with the findings described above. As first line therapy, 6 cycles of CAF (cyclophosphamide 600mg/m^2 on day 1, doxorubicin 60mg/m^2 on day 1 and 5-Fluorouracil 600mg/m^2 on day 1) were administered every three weeks. Post-treatment PET-CT showed only minimal uptake in the bony lesions. There was no FDG uptake in the liver masses, axillary or mediastinal lymph nodes. The patient benefited from systemic chemotherapy clinically, as well. Following chemotherapy, hormonal therapy was initiated with tamoxifen at 10mg twice a day. At the time of manuscript submission, the patient still alive and there was no progression in disease.

Discussion

The diagnosis of NF1 is made when a patient has at least two of the following characteristics: cafe´ au lait macules, skin-fold freckles, optic glioma, iris Lisch nodules, specific osseous dysplastic lesions and a family history positive for NF1 in a first-degree relative. Since the isolation of the gene responsible for NF1 in 1990, molecular diagnosis can now be made (2). In a total of 212 patients followed up over 42 years, Sorensen et al. reported a relative risk of malignancy of 4.0 (CI 2.8–5.6). In a group of 70 patients with NF1, an overall cancer incidence four times higher than expected in the general population was reported. Other data have indicated overall additional malignancy risks in NF1 of between 5 and 15% (3,4). According to the American Society of Clinical Oncology, the overall lifetime risk of developing cancer in patients with neurofibromatosis type 1 is 7%, about twice the risk of that seen in the general population.

NF1 is a tumor suppressor gene. The NF1 gene product, neurofibromin, stimulates the intrinsic hydrolysis of Ras-GTP to Ras-GDP to diminish signaling through the Ras-MAPK pathway. In the absence of neurofibromin, the active (GTP-bound) form of Ras drives cell proliferation, an important step in tumorigenesis (5).

Breast cancer has also been shown to be associated with NF1. The association of NF1 with breast cancer is rare in the literature (6,7). Compared with breast cancer rates from the general population, women with NF1 had a fivefold increased risk of being diagnosed with breast cancer. A prospective study of cancer incidence in 448 individuals (221 male and 227 female) with NF1 found only five males with breast cancer. Breast cancer was not detected in any male patient in this study. There have been numerous case reports in the literature of patients with NF1 who presented with ductal-type breast carcinomas, including a male patient who was diagnosed with bilateral ductal carcinoma at age 18 (6).

Male breast cancer (MBC) is rare (8). To our knowledge there are few published data and relationship between male breast cancer and NF1 in the literature.

Breast cancer screening guidelines have been established for the general population and for women with known genetic risk factors for breast cancer such asBRCA1 and PTEN syndromes in an effort to decrease mortality from breast cancer through early diagnosis. There are currently no such guidelines for patients with NF1 and general male population.

Most of the patients, like our case, may not be aware of their breast cancer. Manifestations of neurofibromatosis obscure the signs of breast cancer. In conclusion, it should be noted that multiple neurofibromas may obscure breast masses during palpation, however, clinical physicians should always keep the possibility of a coexisting malignancy in mind to men as much as to women.

We report the possibly increased risk of men with Von Recklinghausen's disease for development of breast cancer and we emphasize difficulties in diagnosis. Every new breast lump must be carefully examined and if necessary further evaluation such as mammography, breast USG and breast MRI should be performed.

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