

Docetaxel-induced Scleroderma in A Breast Cancer Patient: A Case Report

Meme Kanserli Bir Hastada Dokataksele Bağlı Gelişen Skleroderma

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ABSTRACT

Paclitaxel and docetaxel are antineoplastic drugs derived from the yew tree, *Taxus brevifolia*. They are the members of the taxane family and act by inhibiting mitotic activity due to the suppression of microtubule depolymerization. They are used in the treatment of ovarian cancer, breast cancer, gastric cancer, small cell lung cancer, and head and neck cancer. In addition to side effects such as cardiotoxicity, neutropenia, arthralgia, and myalgia, they may also cause alopecia, urticaria, mucositis, acral erythema, pustular dermatitis, erythema multiforme, and scleroderma-like mucocutaneous lesions. Scleroderma is among the uncommon side effects of taxane antineoplastic agents. As was the case in few cases in literature, it usually begins with edematous changes in the proximal aspect of the extremities, and subsequently, sclerosis is developed in the skin. Scleroderma, which usually regresses with the discontinuation of the drug and with steroid therapy, may lead to severe contractions that require physical therapy and rehabilitation in some patients. In this paper, we presented a 60-year-old female patient in whom scleroderma developed due to docetaxel chemotherapy for breast cancer, because of its rarity.

Keywords: Taxoids, scleroderma, breast cancer

ÖZ

Paklitaksel ve dokataksel, *Taxus brevifolia* denilen yew ağacından üretilen, mikrotübül depolimarizasyon supreyonu sonucu mitotik aktivitenin inhibisyonu ile etki gösteren, taksan ailesine mensup antineoplastik ilaçlardır. Over, meme, mide, küçük hücreli akciğer kanseri, baş ve boyun kanserlerinin tedavisinde kullanılmaktadır. Kardiyotoksisite, nötropeni, artralji, miyalji gibi yan etkilerin dışında alopesi, ürtiker, mukozit, akral eritem, püstüler dermatit, eritema multiforme ve skleroderma benzeri mukokutanöz lezyonlara da neden olabilir. Skleroderma taksan grubu antineoplastik ilaçların sık görülmeyen yan etkilerindedir. Literatürdeki az sayıdaki olgularda olduğu gibi genellikle ekstremitelerin uç kısımlarında ödematöz değişiklik olarak başlar ve ardından ciltte skleroz gelişir. Çoğunlukla ilacı kesmek ve steroid tedavisi ile gerileyen skleroderma bazı hastalarda fizik tedavi ve rehabilitasyon gerektirecek kadar ciddi kontraktürlere neden olabilir. Bu yazımızda meme kanseri nedeniyle dokataksel kemoterapisi verilen 60 yaşındaki bayan hastada gelişen skleroderma olgusunu, nadir görülmesi nedeniyle, sunduk.

Anahtar sözcükler: Taksoidler, skleroderma, meme kanseri

Introduction

Paclitaxel and docetaxel are antineoplastic agents of the taxane family and act by inhibiting mitosis. They are used in the treatment of solid tumors such as ovarian cancer, breast cancer, small cell lung cancer, and head and neck cancers. In many recent studies on adjuvant therapy of breast cancer, it has been demonstrated that chemotherapy regimens including taxane improve survival and decrease recurrence compared with standard FAC (5-fluorouracil, doxorubicin, and cyclophosphamide) chemotherapy (1, 2). Nevertheless, in addition to side effects such as neutropenia, arthralgia, and cardiotoxicity, they may cause acral erythema, pustular dermatitis, erythema multiforme, and scleroderma-like mucocutaneous lesions (3). Scleroderma is an autoimmune disease of connective tissue with an unknown etiology and courses with increase in connective tissue and fibrosis. Scleroderma-like mucocutaneous lesions are rare adverse events encountered because of docetaxel, and we think that this should be kept in mind during the follow-up of breast cancer patients.

Case Presentations

A 60-year-old female patient underwent modified right radical mastectomy and axillary dissection due to multicentric invasive ductal carcinoma of the right breast. The pathology report revealed that the tumor consisted of numerous millimetric multiple foci, the largest being 3.5 cm in diameter. In addition to extensive lymphovascular tumor emboli and millimetric satellite foci in all quadrants, there were tumor emboli in the lymphatics of the areola and breast skin. Furthermore, the tumor showed extensive perineural invasion. The immunohistochemical examination demonstrated that estrogen and progesterone receptors were diffuse nuclear (-) and *CerbB-2* was (-). Invasive ductal carcinoma metastasis and extracapsular adipose tissue invasion were detected in 6 of 14 lymph nodes obtained from the axillary specimen. Chemotherapy, radiotherapy, and hormonal therapy were decided to be initiated for the patient. A chemotherapy regimen consisting of docetaxel, doxorubicin, and cyclophosphamide (TAC) was started. After the second cure of docetaxel, the patient

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Figure 1. Cutaneous fibrosis in the dorsum of the right hand and arm



Figure 2. Cutaneous fibrosis in the palms of the right hand and arm

developed redness and edema followed by induration on the skin of the left lower extremity first, and after a while, the same lesion appeared on the right arm, and the photos of the lesions were taken after the patient provided informed consent (Figure 1-3). Dermatology and rheumatology consultations performed for this reason suggested that these lesions were due to a connective tissue disease. Drug eruptions, urticaria, eczema, local dystrophy, and other diseases with Raynaud's phenomenon were also observed in the differential diagnosis, and then various diagnostic tests were performed. On blood analysis, ANA (antinuclear antibody-centromere antibody) was positive (1/320). Anticardiolipin, antiphospholipid, ANCA, ENA, CCP antibodies, and other rheumatological parameters were found to be negative. Based on all clinical and laboratory findings and the 2013 ACR/EULAR Classification Criteria for Scleroderma, the patient was diagnosed with scleroderma. Skin biopsy was not performed because the patient was receiving chemotherapy and because of the probability of poor wound healing. Cyclophosphamide and prednisolone were commenced. Five thousand centigray radiotherapy was delivered in 25 fractions to the right chest wall and axillary fossa at the radiation oncology unit. However, femara was commenced at a single dose daily. Approximately a year later, the lesion on her left leg completely disappeared, but the one on her right arm partially regressed.

Discussion and Conclusions

Taxanes are antineoplastic agents derived from the yew tree, *Taxus brevifolia*, and they act by inhibiting mitosis. They are used in the treatment of ovarian cancer, breast cancer, small cell lung cancer, and



Figure 3. Scleroderma affecting the right hand and arm. Improvement in erythema, dyspigmentation, and skin thickness demonstrated over a 3-month period

head and neck cancers. Recently, numerous studies were performed on taxane-based chemotherapies. Multicenter studies such as BCIRG 001 and GEICAM/2003-02 demonstrated that chemotherapy regimens including taxane improve survival and reduce recurrence rates compared with the standard FAC chemotherapy (1, 2). Taxanes, as well as other antineoplastic agents, have many toxic effects. In addition to side effects such as cardiotoxicity, mucositis, neutropenia, arthralgia, and myalgia, they may also lead to some mucocutaneous lesions. Although hypersensitivity lesions such as urticaria are more common, there are patients in literature who developed erythematous and edematous skin reactions, erythema multiforme, and systemic lupus erythematosus after taxoid administration (3-6). Scleroderma-like skin lesions following docetaxel have rarely been reported in literature (7-10). There is no case reported from Turkey. Battafarano et al. (7) presented three patients who developed sclerotic skin lesions in the lower extremities following docetaxel administration. Cleveland (8) reported extensive edema followed by fibrosis after docetaxel in a metastatic breast cancer patient in whom the signs were rapidly improved when the drug was discontinued. Likewise, Hasset (9) also identified scleroderma-like skin lesions due to docetaxel in a breast cancer patient. In their study that included 5 patients with metastatic breast cancer who developed scleroderma following taxane administration, Itoh et al. (11) reported edema in the distal aspect of the extremities followed by sclerosis in the skin. While all these patients received steroid therapy, three required rehabilitation. It is known that similar skin lesions also develop with paclitaxel, another taxane agent (12-15). Tanaka et al. (16) also presented a patient with metastatic breast cancer who developed cystoid macular edema due to paclitaxel and emphasized the importance of mucocutaneous lesions as a rarely seen side effect that could substantially affect the quality of life. Sclerotic skin lesions may either be limited to a certain region of the body or be extensive (8, 9). In the present case, extensive sclerotic skin lesions appeared in the lower left and upper right extremities after docetaxel administration. Restriction occurred in the hand, arm, and foot movements of the patient. This condition quite unfavorably influenced the patient's quality of life. The lesions began to regress after the chemotherapy was ended and steroid therapy was commenced.

Taxoid antineoplastic agents, which are being increasingly used in the adjuvant therapy of breast cancer, have mucocutaneous adverse events in addition to their many toxic effects. Although scleroderma is rarely encountered, it should always be kept in mind that it may develop af-

ter docetaxel administration. Moreover, a systemic approach is needed in the diagnosis and treatment of these cutaneous lesions.

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