

## OSTEORADIONECROSIS ON THE CHESTWALL DUE TO RADIOTHERAPY

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### ABSTRACT

Osteoradionecrosis is a rare, but severe complication of radiation therapy in patients with breast cancer. Radionecrosis developed in a 40-year-old patient 10 months after radiation therapy for breast cancer. The patient was hospitalized and operated on for chest wall necrosis. The results of the treatment were evaluated and discussed under the light of the literature.

**Key words:** osteoradionecrosis, chest wall, breast cancer

### GÖĐÜS DUVARINDA RADYOTERAPİYE BAĐLI OSTEORADYONEKROZ

#### ÖZET

Osteoradyonekroz (ORN), meme kanserinin radyoterapi ile tedavisinden sonra nadir görülen, ancak ciddi bir komplikasyondur. Bu yazıda, meme kanseri tanısı ile radyoterapi uygulanan, bu tedaviden 10 ay sonra ORN gelişen ve kliniđimize yatırılarak tedavi edilen 40 yařındaki bir hasta sunulmakta ve bu komplikasyon ile ilgili bilgiler gözden geçirilerek tarřılmaktadır.

**Anahtar sözcükler:** osteoradyonekroz, göđüs duvarı, meme kanseri.

### Introduction

Osteoradionecrosis (ORN) is a severe complication of radiation therapy in patients with breast and lung cancers. While more frequent in the era when radiotherapy (RT) was carried out through conventional techniques and ortho-voltage devices, ORN is now less commonly witnessed due to the use of modern devices in radiation therapy and better planned treatment regimens (1-4). The treatment of ORN is difficult and includes the control of infections via antibiotics, surgical debridement, hyperbaric oxygen treatment, resection of chest-wall, and reconstruction (5).

In this report, the findings of a patient dying of osteoradionecrosis and the treatment developing as a result of adjuvant radiotherapy performed with the diagnosis of breast cancer have been evaluated and discussed.

### The case

In the mammographic, ultrasound, and magnetic resonance imaging (MRI) of the 40-year-old coming into the clinic with a complaint of a mass in her right breast, solid lesions in the sizes of 20x29mm, 16x10 mm, and 7x4 mm in the right breast and lymph nodes in the axillary region were determined. Invasive ductal carcinoma was removed as a result of through-cut biopsy. The patient was clinically diagnosed with stage-III B (cT2multicentric N2 M0) breast cancer. She was discussed at The Council of Breast Cancer, Medical School

of Istanbul University. The Council recommended that neo-adjuvant chemotherapy, surgery, chemotherapy, radiotherapy, and treatment of tamoxifen. After the administration of 3 courses of 5- Fluorourasil, Epirubisin, Cyclophosphamite neoadjuvant treatment (FEC), and the surgical treatment was decided to be carried out with the determination of partial remission (the size of the biggest tumor decreased to 15 mm and all the lymph ganglions in the axillary region could not palpably be felt: cT1N0M0). Because of clinical non-palpation of the axilla, sentinel biopsy of lymph nodule was performed with blue dye and radioisotope due to previously prepared protocol. Although 2 noted sections of sentinel lymph nodules were found to be negative during frozen section investigation, as a result of protocol, axillary dissection and mastectomy were performed, as the cancer was multicentric prior to treatment. In the pathological evaluation of the removed specimen, only one tumor of 15 mm in the breast (the other two disappeared as a result of chemotherapy) and all of 12 lymph nodules in the axilla were found to be negative. In the histopathological evaluation; nuclear grade was reported to be 3, lymphovascular invasion to be present, estrogen receptor (ER) positive at the rate of 10%, progesterone receptor (PR) to be positive at the rate of 20%, and HER-2 to be negative. Adjuvant radiotherapy (RT) given for peripheric lymphatic radiation and thorax wall of the patient administered post-operative 3 cures of FEC was given radiation therapy as 5000 cGy at 25 fractions using linear accelerator, and then tamoxifen treatment of 20 mg/day/5 years started to be administered. As a result of the development of deep vein thrombosis one month after the tamoxifen,



Figure 1. Osteoradionecrosis in the field of radiotherapy.

this treatment was discontinued, and the patient was given medical ovarian ablation (goserelin) was routinely followed up. In the patient, a wound not recovering in the radiation area 10 months after the radiotherapy occurred. The finding of the biopsy performed in this area was reported as "chronic infection with necrosis." According to the results obtained from wound debridement, irrigation with physiological saline, and culture from the wound, a treatment regime with antibiotics was started (Picture 1). Due to the slow improvement, the wound was re-debrided and Vacuum Assisted Closure (VAC) was applied. Since the strain of "pseudomonas aeruginosa" was produced in the culture samples taken from the wound, the antibiotics were altered. In the tomography of thorax wall, MRI, and bone scintigraphy; a diffusal increase was determined during vascularization in the lower part of the right hemithorax, and there was no increase in the osteo-blastic activity. These results and histopathologic examination suggested necrosis of radiation. As a consequence of the result that no desired improvement of the wound could be obtained through conservative and minimally invasive treatments given over nearly 3 months, surgical treatment was decided to be performed on the patient with the consultation of the clinics of thorax surgery and plastic reconstructive surgery. The resections of right frontal chest wall and fibrotic lung, the flap of rectus abdominis muscle (TRAM), and free skin grafts, as well as repair operations, were performed in the patient. Histopathology of the removed material revealed common necrosis, chronic infection, and fibrosis in the bone and striated muscle tissue, fibrosis, and pneumonic infiltration in the lung tissue. Eight days after the surgery, the patient had sepsis and died from multiple organ failure.

## Discussion

An important treatment providing local control in the multidisciplinary treatment of breast cancer is radiation therapy (RT). While radiotherapy decreases the rate of local recurrence after conservative surgical treatment of the breast is more than 50%, it is emphasized in various studies that it also provides the patients with a high rate of survival (6, 7, 8). The existence of adjuvant radiotherapy performed after mastectomy is also controversial. Thorax wall and regional lymphatic radiation therapy is almost routinely

performed in the patients with tumors of a size of more than 4 cm and in those with the involvement of four or more lymph nodes the axilla (9-13). In the patients with lymph nodes between 1 and 3 involved in the axilla, there are also centers recommending radiotherapy by evaluating other prognostic factors (14-16).

Unless radiotherapy is performed with modern systems and techniques, thorax wall necrosis, ulceration on skin, brachial plexopathy, cardiac morbidity/mortality, secondary cancer, pneumonitis, edema of the arms, and costa fracture are encountered (17-19).

As the dose of radiation increases, the changes in the target tissue become correspondingly higher and irreversible depending on the increase. In doses over 4000 cGv, permanent changes take place in the bones; however, ORN produced in the doses over 6000 cGv becomes generally more resistant to conservative surgery. Contrary to the ortho-voltage devices leading to an increase of the absorption of radiation in the bone tissue, new megavoltage devices reduce the damage to the tissues in the areas where RT is applied (2,3). The use of fractionated RT techniques hyperfractionated and accelerated was reported to decrease the incidence of ORN (1). With the introduction of intensity adjusted RT (IMRT), the condition is expected to get more decreased. Still, despite all the developments in RT, ORN, even if rare, may also be seen (20).

Predisposing factors for ORN include the following: trauma, infection, inflammation, overdose RT application, involvement of the tumor with bone tissue or its occurrence around the bone tissue, and individual sensitivity and endurance characteristics of the patient (21). Application of radiotherapy after mastectomy may cause more damages in thorax walls and inner thorax organs (lungs, heart etc.), if the radiation technique, the device to be used, treatment planning, and dose of radiation are ignored. In our patient, radiotherapy applied after mastectomy increased this risk. The sensitivity of the patient to radiation is an important risk factor in the occurrence of this complication.

Pathogenesis of ORN is development of vascular necrosis stemming from radiation. Cytotoxic effects of radiation on the osteogenic layer cause soft tissue fibrosis, the blockage of endosseous arteries, hypoxic, hypocellular and hypo-vascular bones, and soft tissue. This decreases the recovery capacity of tissues with a decline in the development of matrices and deformation in the bone mineralization (22). In our patient, the development of deep vein thrombosis as a result of tamoxifen shows that the patient tends to be coagulopative and chemotherapy, and radiation slows down the circulation in the region and causes malnutrition with effects, such as vasculitis, thus it can be responsible from radio-necrosis.

The time in the formation of ORN after the completion of RT is variable and it may take a few months or many years. In a study of 33 cases including head and neck malignancy, the formation period of ORN after RT was between 4 and 228 months (23). It was 10 months in our patient.

The most frequent finding in ORN is pain, infection, or pathologic fractures. ORN can be diagnosed through joint evaluation of clinical findings, pathology, and radiology (20).

Although RT was applied at lower doses with modern devices in our case, the development of ORN may be related to infection seen in the wound after surgery. The infection is accepted as a predisposing factor for ORN (21). Moreover, it is reported that significant acute and chronic complications were formed in those with collagen vascular

diseases after RT (24). Therefore, breast conservative treatment (local excision and breast irradiation) in those known to have collagen vascular diseases are accepted as contraindication (25).

ORN is a late and obstinate complication rarely seen after radiotherapy. Thus, even if modern RT devices and techniques are used, patients administered RT should be closely followed for early and late complications and effective treatment options should be implemented, if necessary.

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