Role of Bone Scintigraphy and Tumor Marker-Ca 15-3 in Detection of Bone Metastases in Patients with Breast Cancer

Amela Begić[1*], Elma Kučukalić-Selimović[1], Nermina Obralić[2], Osman Durić[3], Nadir Lačević[4], Sadžida Begović[1], Mirela Džubur-Aganović[1]

1. Institute for Nuclear medicine, University Clinics Centre, Bolnička 25, 71000 Sarajevo, Bosnia and Herzegovina
2. Institute for Oncology, University Clinics Centre, Bolnička 25, 71 000 Sarajevo, Bosnia and Herzegovina
3. School of Medicine, University of Sarajevo, Čekaluša 90, 71 000 Sarajevo, Bosnia and Herzegovina
4. Clinic for Gastroenterohepatology, University Clinics Centre, Bolnička 25, 71 000 Sarajevo, Bosnia and Herzegovina

* Corresponding author

Abstract

Breast cancer is one of the most frequent types of cancer affecting women. After hematogenous spreading of cancer, axial skeleton is most frequently involved. Bone scintigraphy is commonly performed in detection and evaluation of bone metastases. In breast cancer, marker Ca 15-3 is widely accepted in follow-up and detection of disease recurrence. Aim of the study was to correlate levels of tumor marker Ca 15-3 and presence of bone metastases detected by bone scintigraphy. Study included 25 patients with breast cancer, previously surgically treated. All patients underwent total body scintigraphy. Ca 15-3 was measured by radioimmunoassay. Presence, number and location of bone metastases were correlated with Ca 15-3 levels. Bone scintigraphy revealed bone metastases in 16 (64%) patients. 11 (44%) patients with metastases and 1 patient (4%) without scintigraphically visible metastases had elevated Ca 15-3 levels. Significant difference in distribution of metastases was found for spine (t=3.930, p=0.008). Correlation between intensity of radiopharmaceutical uptake and level of Ca 15-3 in patients was positive (r =0.405). A weak correlation was found between number of metastases and level of Ca 15-3 (r=0.139). Significant differences in Ca 15-3 level was found in patients with metastases compared to patients without metastases (chi square 0, p =1.0). Since no significant correlation was found between level of Ca 15-3 and number of metastases, we consider scintigraphy an appropriate method for assessment of bone metastases in breast cancer.

KEY WORDS: breast cancer, bone metastases, bone scintigraphy, Ca 15-3

Introduction

Breast cancer is one of the most frequent types of cancer affecting women with incidence peak between age 40-60 (1,2). The most common site of distant metastases is skeleton, which is affected in about 8% of all patients.

After hematogenous spreading of cancer, axial skeleton is most frequently involved with pattern that resembles red bone marrow distribution.

Complications associated with skeletal metastases including pain, pathological fractures, hypercalcemia, myelosupresion, spinal and cord compresion, lessions of nerve roots, are demanding for patients and health care resources in general (3,4) Early detection of bone metastases is mandatory in the evaluation and managament of these patients.

In diagnosis of breast cancer metastases several procedures and tests are available such as: tumor markers (CEA, Ca 15-3), x-rays, CT scan, magnetic resonant imaging, bone scintigraphy. These investigations aim to establish location of dissemination, make a specific diagnosis, prevent complications by early diagnosis and finally to assess patients response to treatment (5).

Although not the latest method, bone scintigraphy is still often requested and commonly performed in detection and evaluation of bone metastases. This investigation allows highly sensitive detection of osteoblastic activity.

Tumor markers are present in healthy individuals as well as in patients with malignant diseases but in different concentrations. In breast cancer, breast-associated mucin marker Ca 15-3 is widely accepted as a serum tumor marker in follow-up and detection of disease recurrence (5,6). This study was undertaken in order to correlate levels of tumor marker Ca 15-3 and presence of bone metastases detected by bone scintigraphy.

Patients and Methods

25 patients with pathologically verified and previously surgically treated breast cancer were included in study. All patients underwent total body scintigraphy using double-head gamma camera equipped with low energy high resolution collimator 3 hours after I.V. injection of 740MBq Tc-99m MDP (methylen diphosponate).

Ca 15-3 was measured by radioimmunoassay using microparticle Enzyme-Immunoassay technology (MEIA, Abbott AXSYM system). Presence and number of bone metastases together with their location were correlated with levels of Ca 15-3 tumor marker. Statistical analyses were performed with chi-square test, Student t-test, standard deviation. Study was approved by Ethical Committee and informed consent in written was obtained from all subjects in advance.

Results

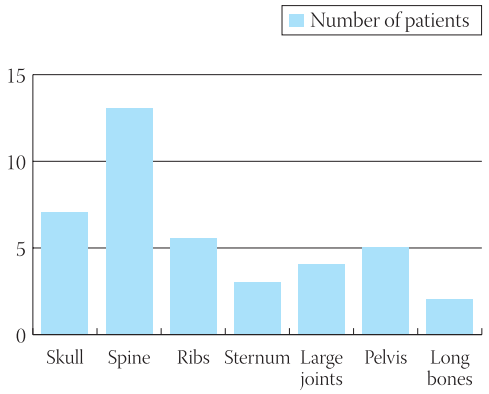
Median age of patients included in study was 50 varying from 30 to 67. 15 patients (60%) had pathologically verified cancer on the left breast, the rest of 10 patients (40%) had the right breast cancer. Bone scintigraphy revealed bone metastases in 16 (64%) patients. Scintigraphy was negative for metastases in 9 (36%) patients. 11 patients (44%) with scintigraphically proven metastases and 1 patient (4%) without scintigraphically visible metastases had elevated Ca 15-3 marker. In 9 patients with normal scintigraphy (36%) only 1 patient (4%) had elevated Ca 15-3 marker, (Table 1.).

Multiple bone metastases were found in 12 (75%) patients. Four patients (25%) had solitary bone metastases. Analyzing the distribution of bone metastases the highest frequency was found for spine (34.09% of all metastases).

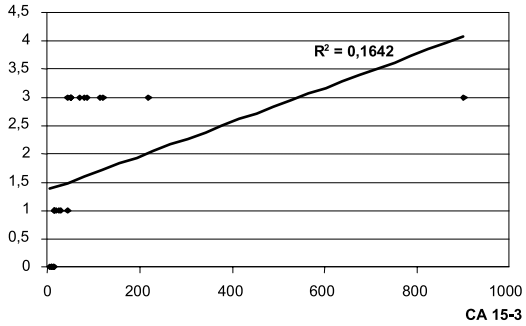
The difference is significantly higher compared to other bones, (t=3.930, p=0.008), Graph 1. The most intensive radiopharmaceutical uptake was found in spine (score 2-3).
Difference was significant (t=3.083, p=0.022), Graph 2.

Correlation between the intensity of radiopharmaceutical uptake and level of Ca 15-3 in patients with breast cancer was positive (r=0.405). Graph 3.

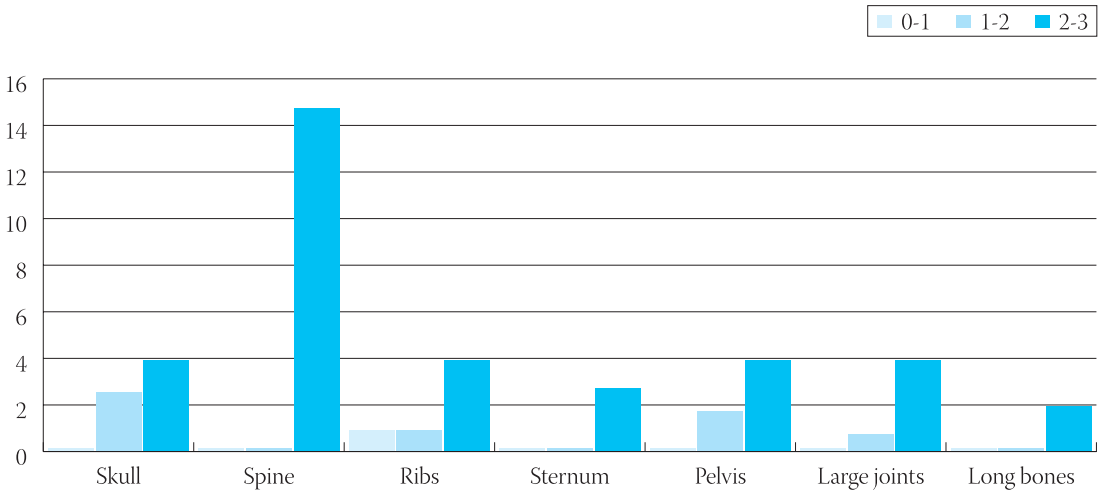
A weak correlation was found between number of metastases and level of Ca 15-3 (r=0.139)- Graph 4. However, statistically significant correlation in level of Ca15-3 was found in patients with bone metastases revealed scintigraphically in relation to patients without bone metastases (chi square 0, p=1.0)



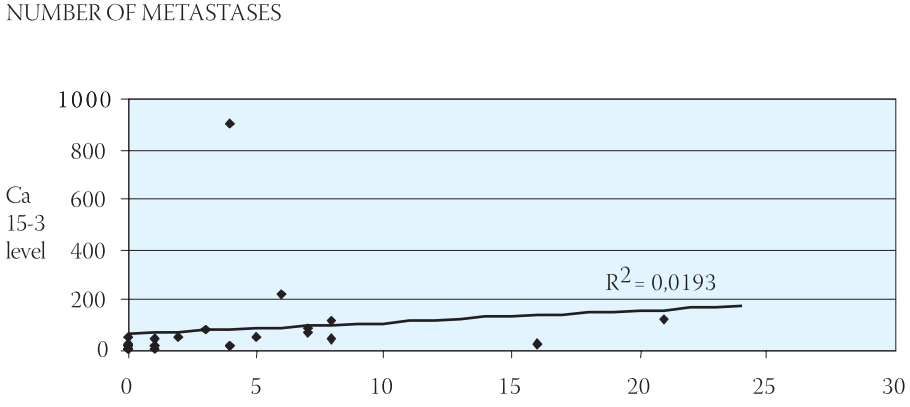
GRAPH 1. Distribution of metastases in the skeleton



GRAPH 3. Correlation between
the uptake intensity and Ca 15-3 with trendline



GRAPH 2. Intensity of radiofarmaceutical uptake



GRAPH 4. Correlation between number of metastases and Ca 15-3 level

Discussion

Breast cancer is the leading cause of death in women aged 35-54 (7). Although bone scan is frequently performed in evaluation of breast cancer metastases, precise role of bone scanning at different stages of the disease is still contentious. Clinical areas in which the bone scan has been evaluated include staging, systematic follow-up of asimptomatic patients, and assessment of response to therapy. In breast cancer, metastases are most often distributed in the axial skeleton, reflecting the distribution of red bone marrow, with the vertebrae being the most commonly involved site (4). In our study, most common site of bone metastases was spine.

Tumor markers sensitivity is also related to the site of recurrence, with the lowest sensitivity for locoregional relapse and highest for liver metastases (8). The disease extent of patients with bone metastases correlated significantly with elevated Ca 15-3 levels. Higher Ca 15-3 levels were found for larger disease extent. Consequently, longer survival was observed in patients with limited disease extent (8). In our study we found significantly higher levels of Ca 15-3 in patients with bone metastases, however, we found no significant correlation between level of Ca 15-3 and number of bone metastases.

References

(1) Coleman R.E., Rubens R.D. The clinical course of bone metastases from breast cancer.Br. J. Cancer. 1987; 55: 61-66.
(2) Richards M.A., Braysher S., Gregory W.M., et al: Advanced breast cancer: use of resources and cost complications. Br. J. Cancer. 1993; 67: 856-860.
(3) Galasko C.S.B. Tumors. In: Galasko C.S.B.,Weber D.A. (eds): Radionuclide scintigraphy in orthopaedics, New York; Churchill Livingstone. 1984; 65-110.
(4) Gary J.R.C., Fogelman I. Skeletal Metastases From Breast Cancer: Imaging With Nuclear Medicine in Seminars in Nuclear Medicine. 1999;vol XXXIX,No 1:69-79.
(5) Shering S.G., Sherry F., McDermott E.W., O'Higgins N.J. Preoperative Ca15-3 concentrations predict outcome of patients with breast carcinoma. Cancer.1998; 83(12): 2521-2527.
(6) Parkin D.M. et al. Cancer incidence in five continents. (SSSEER-Surveillance, Epidemiology and End Results program). Vol. VI. Lyon: IARC Scientific Publications 1992;120.
(7) Bombardieri E., Pizzichetta M., Veronesi P. et al. Ca 15-3 determination in patients with breast cancer: Clinical utility for the detection of distant metastases. Eur. J. Cancer. 1993; 29:144-146.
(8) Tarkan K., Nazan G., Zafer A. The use of Ca 15-3 and Estrogen Receptor in Breast Cancer Patients With Bone Metastases. Gazi Med. J. 1998; 9:149-153.