A Comparative Study of Bone Scan Findings and Serum Levels of Tumor Marker CA15-3 in Patients with Breast Carcinoma

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Abstract Breast cancer is one of the most frequent malignancies in the world. Available staging procedures to detect breast cancer are bone scan, chest X-ray, liver ultrasonography, computerized tomography, estimation of tumor markers like carbohydrate antigen (CA15-3) and carcino embryonic antigen. These procedures are expensive and may not be required in all cases. Out of 70 patients studied, 55 had normal CA15-3 and 15 had elevated levels of CA15-3. Eight (14.5%) of the 55 patients with normal CA15-3 had abnormal bone scan. Fifteen patients had CA15-3 levels above the normal range and among these 9 (60%) had abnormal bone scan. While *prima facie* it would appear that a high level of CA15-3 correlate with abnormal bone scan, it is also true that the numbers are small at present and conclusions about the validity of CA15-3 as marker of bone metastasis may be premature.

Keywords Tumor marker · Breast cancer · CA15-3 · Metastasis · Bone scan

Introduction

Breast cancer actually presents the most common form of cancer disease in women and the second cause of death by a malignant disease in female after lung cancer [1–8].

However the treatment of breast cancer patients with bone metastases is completely different. Many studies have reported that the incidence of bone metastasis differs according to the clinical stage of breast cancer [2, 4–8, 15]. Autopsy studies of breast cancer [9–14] have demonstrated a high proportion of breast cancer patients with bone metastasis (50–85%). The affinity of breast cancer to spread metastases in bones is one major reason for high mortality rate of breast cancer surgery is the treatment of choice for breast cancer patients without metastases.

Therefore, accurate determination of disease stage is important to determine the proper treatment to improve the patient's prognosis. Coleman et al. [15], Koizumi et al. [1] in their study concluded that bone scan in primary breast cancer was very useful to evaluate initial clinical stage and to perform the follow up examination. Presently large number of markers exists for breast cancer. These include MUC-1 (e.g. CA15-3), carcino embryonic antigen (CEA), oncoproteins, milk proteins and cytokeratins. Of these CEA and CA15-3 are the most commonly used.

CA15-3 is a protein that is a normal product of breast tissue and it does not cause breast cancer. If a cancerous tumor (cell growing out of control) is present in breast, the levels of CA15-3 may increase as the number of cancer cells increase. Not every breast tumor caused a rise in CA15-3 so for patients with tumors that do not produce CA15-3 or with early stage breast cancer, this test is not useful. Only about 30% of patients with localized breast cancer will have increased levels of CA15-3. In patients

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with metastatic breast cancer, CA15-3 can be found increased in 50–90% of all cases.

Bone scan is radionuclide imaging of whole body skeleton at a time. It detects osseous involvement of malignancy much earlier than X-ray, CT and MRI. It is reliable and widely used in the management of patients with confirmed breast cancer but non specific.

Aim of Study

The objective of the present study was to correlate CA15-3 with bone scan results of patients with breast cancer in the early detection of skeletal metastases.

Materials and Methods

The prospective study consisted of patients with confirmed breast cancer referred to Radiation Medicine Center for bone scan. CA15-3 analysis was done on patient serum samples collected on the same day when they reported for bone scan. Total seventy patients in the age group of 25–67 years were studied.

CA15-3

The blood drawn was allowed to clot and serum was separated by centrifuging the samples at 4000 rpm for 10 min.

Tumor Marker assay CA15-3 was performed on fully automated immunoassay analyzer ARCHITECT 2000i system. CA15-3 assay is a two step immunoassay to determine the presence of DF3 defined antigens in human serum and plasma, using chemiluminescent microparticle immunoassay (CMIA) technology.

Biological reference interval of CA15-3 is 0–28 U/ml [16, 17].

Bone Scintigraphy

Bone scanning was performed after 3 h of intravenous injection to each patient with ~900 MBq ^{99m}Tc methylene diphosphonate (^{99m}Tc -MDP) using picker dual head gamma camera (Picker AXIS, Odysee FX) equipped with low energy parallel hole collimator. Whole body anterior and posterior views were obtained on the same film. Evaluation of bone scan images were done by experienced nuclear medicine physicians.

Results

Table 1 gives the bone scan results, the percentage elevated, the age and the levels of CA15-3.

Table 1 Patients with normal CA15-3

Bone scan	Number (%)	Age (years)	CA15-3 (U/ml)
Normal	47 (85.5)	47 ± 8	14.3 ± 5.8
Positive	8 (14.5)	51 ± 9	14.3 ± 5.9
Total number of patients 55			

Table 2 Patients with elevated CA15-3

Bone scan	Number (%)	Age (years)	CA15-3 (U/ml)
Normal	6 (40)	45 ± 11	74.8 ± 47.8
Positive	9 (60)	47 ± 11	346.6 ± 313.7
Total number of patients 15			

Table 3 CA15-3 levels and bone scan results

CA15-3 range (U/ml)	Bone scan findings (number of patients)		Total number of patients
	Positive	Normal	
0–28	8	47	55
29–50	1	2	3
51–100	2	1	3
101–500	3	2	5
>500	3	1	4
Total	17	53	70

The bone scan reports were normal in 47 (85.5%) patients with the age range of 47 ± 8 and CA15-3 levels in the range of 14.3 ± 5.8 U/ml. However, the bone scan results were positive in 8 (14.5%) patients with the age range of 51 ± 9 and CA15-3 levels in the range of 14.3 ± 5.9 U/ml.

Table 2 gives the bone scan results, the percentage elevated, the age and the elevated levels of CA15-3.

The bone scan reports were normal in 6 (40%) patients with the age range of 45 ± 11 and CA15-3 levels in the range of 74.8 ± 47.8 U/ml. However, the bone scan results were positive in 9 (60%) patients with the age range of 47 ± 11 and CA15-3 levels in the range of 346.6 ± 313.7 U/ml.

Table 3 gives the range of CA15-3, the number of patients with positive and negative bone scan results, and the total number of patients.

With CA15-3 values lying in the range of 0–28 U/ml, 8 patients showed positive and 47 showed normal bone scan results, total number of patients accounting to 55.

With CA15-3 values lying in the range of 29–50 U/ml, one patient showed positive and two showed normal bone scan results total number of patients accounting to three.

With CA15-3 values lying in the range of 51–100 U/ml, two patients showed positive and one showed normal bone scan results total number of patients accounting to three.

With CA15-3 values lying in the range of 101–500 U/ml, three patients showed positive and two showed normal bone scan results total number of patients accounting to five.

With CA15-3 values greater than 500 U/ml, three patients showed positive and one showed normal bone scan results total number of patients accounting to four.

Discussion

Bone metastasis is a common event in patients with breast cancer. Several studies have shown that women who are older than 50 years are more likely to develop breast cancer than younger ones. Data reported in our study confirm this high probability of breast cancer in women older than forty. This increase in risk is attributed to the possibilities that the net half life of collagen is slightly decreased after menopause [12].

In our study, out of 55 patients, 47 patients (85%) had normal values of CA15-3 and normal bone scans. 9 patients (60%) were found with elevated CA15-3 and positive bone scans. Number of subjects studied is small to establish a definite correlation between CA15-3 and bone scan findings. But many reported data from other authors support our results and suggests that elevated value of CA15-3 and bone scintigraphy are useful for early identification of bone metastasis in patients with breast cancer [1, 2, 9, 11].

The study by Mohammadzadeh et al. showed that the serum level of CA15-3 antigen is higher in the patients with bone metastatic breast cancer [18]. The preliminary study results of Rame Miftari et al. suggests that application of bone scintigraphy in primary breast cancer, before surgical intervention is very useful to evaluate initial stage and to perform the follow up examination [19].

Conclusion

Although higher levels of CA15-3 suggest the diagnosis of skeletal metastasis, it does not correlate with bone scan results often. Therefore avoiding a bone scan on the basis of a normal CA15-3 result would not be justified in newly diagnosed patients which needs further exploration.

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