

The association of human immunodeficiency virus and skeletal metastases in breast cancer using Tc-99m methyl diphosphonate bone scan

ABSTRACT

Skeletal involvement occurs in 30%–70% of all cancer patients, with breast cancer (BC) being the leading cause for bone metastases in women and prostate cancer in men followed by lung cancer. Human immunodeficiency virus (HIV) is a lentivirus (a member of the retrovirus family) that causes acquired immunodeficiency syndrome. It is yet unknown what is the impact of HIV to the onset and progression of bone disease in BC. The purpose of the study was to determine the association of HIV infection and skeletal metastases in BC using skeletal scintigraphy. A retrospective analysis of 25 female BC patients' bone scans was performed. The 25 bone scans of 12 patients known HIV positive and 13 patients who were known HIV negative, of similar age and histology, were compared. All 13 HIV negative patients had a positive bone scan. Of the 12 HIV-positive patients, 4 patients on highly active antiretroviral therapy (HAART) had positive bone scans for skeletal metastases. The remaining eight HIV-positive patients had negative bone scans, of which six were on HAART and two were not on HAART. In our study, HIV infection was not found to be a contributing risk factor for skeletal metastases. From our small series, it appears that HIV patients and on HAART have a delay in the onset of skeletal metastases in BC.

Keywords: Bone, bone scan, breast cancer, cancer, human immunodeficiency virus, oncology, skeletal metastases

INTRODUCTION

Skeletal involvement occurs in 30%–70% of all cancer patients, with breast cancer (BC) being the leading cause for bone metastases in women and prostate cancer in men followed by lung cancer. Human immunodeficiency virus (HIV) is a lentivirus (a member of the retrovirus family) that causes acquired immunodeficiency syndrome (AIDS).

The radionuclide bone scan is a noninvasive, painless method to assess the entire skeletal system and to detect early bone involvement from BC and monitor patients on therapy.^[1]


It is yet unknown what is the impact of HIV to the onset and progression of bone disease in BC. The purpose of the study was to determine the association of HIV infection and skeletal metastases in BC using skeletal scintigraphy.

HIV over the years has been frequently associated with increased morbidity and mortality. No documentation has been made previously concerning HIV and its impact if any on skeletal metastases in BC. A possibility of a protective factor in HIV and highly active antiretroviral therapy (HAART) therapy against other non-HIV-associated malignancies has been raised.

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Aims and purpose of the report

The purpose of the study was to determine the association of HIV infection and skeletal metastases in BC using skeletal scintigraphy.

MATERIALS AND METHODS

This was a retrospective analysis. Bone scans were performed using single doses of 740–950 MBq Tc-99m methylene diphosphonate injected Intravenous (IVI), with routine scanning done 2–3 h postinjection. All bone scans, indicated for BC, done at Polokwane Provincial Hospital, Pietersburg, South Africa, were analyzed from January 2013 to July 2013. All patients in the study were female. The mean age for all 25 patients was 46 years, range 28–62 years. Twenty-five bone scans were reviewed: 12 patients known HIV positive and 13 patients who were known HIV negative, of similar age and histology, were compared. The inclusion selection criteria were known HIV status, test, and counselling had to be documented. Images of the bone scan were interpreted independently by two qualified nuclear physicians. The findings of the bone scans were either positive [Figure 1] or negative [Figure 2] for skeletal metastases.

RESULTS

In 25 patients, 12 were HIV positive and 13 were HIV negative [Table 1]. All 13 HIV-negative patients had a positive bone scan [Table 1 and Figure 1a]. Of the 12 HIV-positive patients, 4 patients on HAART had positive bone scans for skeletal metastases [Table 1 and Figure 1b]. The distribution of

uptake for skeletal metastases was involving predominantly axial skeleton for both HIV-negative and HIV-positive patients. There were no additional clinical features in the HIV-positive group which could account for the bone scan findings.

The remaining eight HIV-positive patients had negative bone scans [Figure 2], of which six were on HAART and two were not on HAART [Table 2].

Table 1: Bone scan result by HIV status

Bone scan result	HIV status		Total
	Positive	Negative	
Negative scan	8	0	8
Positive scan	4	13	17
Fischer's Exact test			
$P_{r<=P}$			0.00458

Table 2: Bone scan result by HIV therapy (HAART)

Bone scan result	HIV therapy (HAART)			Total
	HIV negative	HIV on HAART	HIV not on HAART	
Negative scan	0	6	2	8
Positive scan	13	4	0	17
Total	13	10	2	25
Fischer's Exact test				
$P_{r<=P}$				0.000236

Table 3: Bone scan result by mean age

Bone scan result	Number	Mean age
Negative scan	8	42.375
Positive scan	17	47.941176

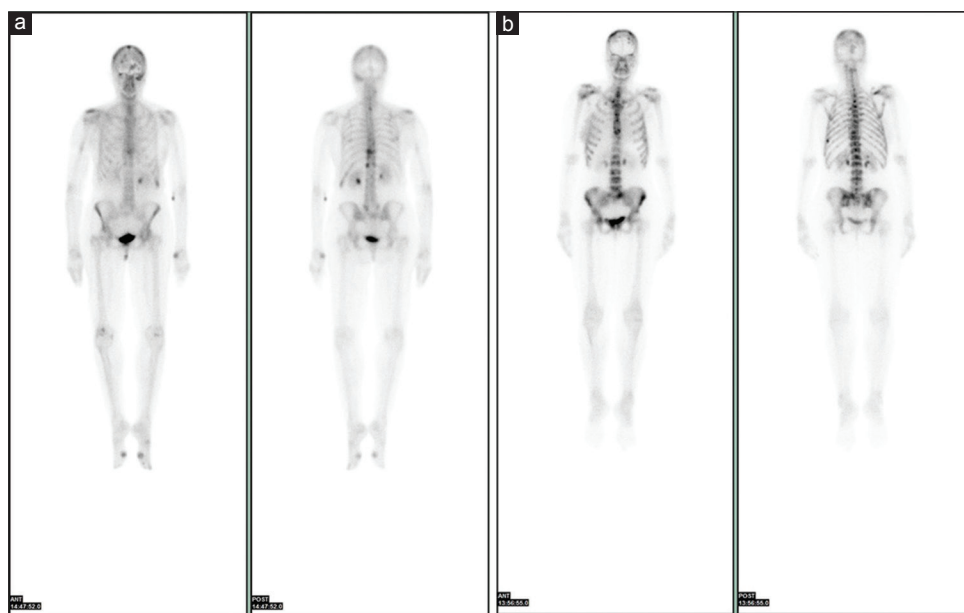


Figure 1: Bone scan positive for skeletal metastases. (a) Positive bone scan for skeletal metastases human immunodeficiency virus negative patient. (b) Positive bone scan for skeletal metastases human immunodeficiency virus positive patient

The association with HIV-positive patients and on HAART with negative bone scans was statistically significant ($P < 0.05$) [Table 2]. No significant association was found in HIV-positive versus HIV-negative patients regarding histology characteristics or age distribution [Figure 3 and Tables 3, 4].

DISCUSSION

Bone metastases are the most common malignant bone tumor.^[2] Skeletal involvement occurs in 30%–70% of all cancer patients, with BC being the leading cause for bone metastases in women and prostate cancer in men followed by lung cancer. In 2010, South Africa had an age-standardized BC incidence rate of 25.86/100,000 women.^[3]

A malignant lesion may be detected on a bone scan as early as a year before being detected on anatomical imaging. It has been estimated that 50%–75% of the trabecular bone destruction is required to visualize a metastasis on X-ray.^[4]

The purpose of radionuclide bone imaging is to identify bone metastases as early as possible, to determine the full extent of disease, to evaluate the presence of complications that may accompany malignant bone involvement (including pathologic fractures and spinal cord compression), to monitor response to therapy, and occasionally, to guide biopsy if histological confirmation is indicated.

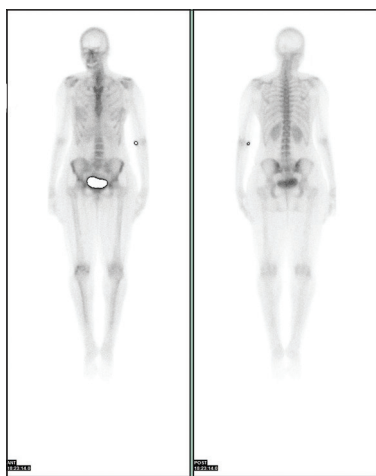


Figure 2: Negative bone scan for skeletal metastases

Generally, people infected with HIV have a higher tendency for developing cancer. This may be due to impaired immune surveillance, dysregulation of growth factors or cytokines, or imbalance between proliferation and differentiation.^[5]

HAART has successfully increased life expectancy in HIV-infected individuals, thus shifting the paradigm of diagnosis of cancer toward non-AIDS defining cancers. BC is considered non-AIDS defining cancer. The risk of BC in HIV-infected and noninfected individuals appears to be variable. This is dependent on the reproductive factors, ethnicity, age, and breastfeeding.^[6,7] In 2001, Frisch *et al.*^[8] found that HIV had a negligible impact on BC incidence compared to HIV-negative patients.

Palan *et al.*^[9] proposed several theories as to why HIV infection may actually protect against breast tumor development in 2010. He cited theories such as reduction in immune function reducing host response to tumor infiltration; HAART-induced restoration of immune function with treatment may decrease the availability/activity of proangiogenic factors and interfere with other oncogenic cytokine and intracellular signaling pathways, used to proliferate and apoptosis; there is some evidence to suggest that HIV viral proteins may induce tumor cell cytotoxicity; and finally, the nutrient redistribution in HIV patients resulting in reduction in peripheral fat stores could reduce peripheral estradiol conversion in these women.

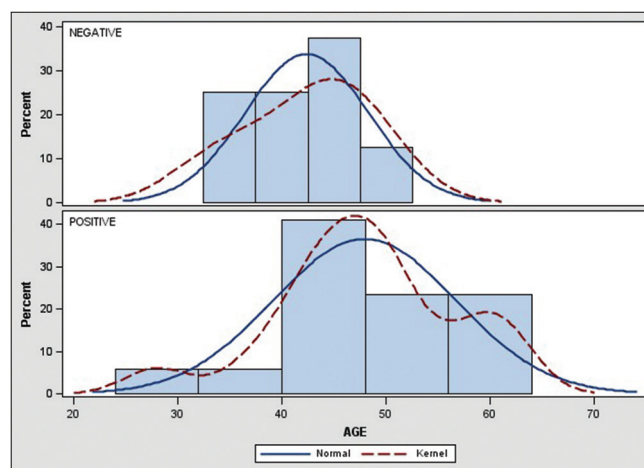


Figure 3: Distribution of age

Table 4: Bone scan result by breast carcinoma histology

Bone scan result	Breast carcinoma by histology				Total
	Grade 1 IDC*	Grade 2 IDC*	Grade 3 IDC*	Invasive Colloid Carcinoma	
Negative scan	2	1	4	1	8
Positive scan	1	9	6	1	17
Fischer's Exact Test					
$P_{r \leq P}$					0.1572

*IDC: Infiltrating Ductal Carcinoma

Cubasch *et al.*^[10] investigated the association of HIV status and tumor characteristics in BC in 1092 patients. They found that HIV status was not associated with tumor characteristics.

In 2015, prompted by South Africa's unique combination of high HIV prevalence, widely available antiretroviral therapy, and advanced facilities for BC diagnosis and treatment in the public sector, Cubasch *et al.*^[11] began the South African Breast Cancer and HIV Outcomes, a 3-year study to further analyze the relationship of HIV-infected individuals and the progression of BC.

CONCLUSION

In our study, HIV infection was not found to be a contributing risk factor for skeletal metastases. From our small series, it appears that HIV patients and on HAART have a delay in the onset of skeletal metastases in BC.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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