Diagnostic of bone metastasis in patients with breast cancer

Tevzadze M.¹ Jeremic B.² Kakhadze S.¹ Baramia M.² Aleksishvili T.³

Abstract

Breast cancer is the most commonly occurring cancer in women population. 70% of patients with breast cancer have evidence of skeletal involvement. Early detection of bone metastasis is very important for accurate staging, optimal treatment as well as prognosis of patients with cancer. In the last several decades various radiologic and nuclear medicine tools have been developed and extensively employed in the detection of bone metastasis, including those of breast cancer. Owing to wide spread availability of these technologies and incidence of breast cancer patients, many of which develop bone metastasis during the course of the disease. This paper reviews major aspects of diagnostic methods of bone metastasis in patients with breast cancer. It describes the available imaging methods to diagnose bone metastasis and its utility without having formal comparison between these technologies. (TCM-GMJ April 2020; 5(1):P11-P14)

Keywords: Bone metastases; Breast cancer; Nuclear medicine diagnostic; SPECT/CT; PET/CT MRI; CT; X-ray.

Introduction

According to the WHO, there were over 2 million new cases in 2018. About 1 in 8 women (12%) will develop invasive breast cancer throughout her lifetime. The skeleton is the third (after the liver and lungs) most common organ to be affected by metastasis, and 70% of patients with breast cancer have evidence of skeletal involvement (1). Any type of cancer that metastasizes via the bloodstream can infiltrate the bone marrow. Different types of bone metastases vary in their anatomic and metabolic appearance and in the reaction they induce in the surrounding bone; Bone metastases are classified as osteoblastic (bone-building), osteolytic (bone-destroying), or mixed. Diagnosis of bone metastasis is crucial to determine the prognosis and to optimize therapy. Significant morbidity may result from skeletal metastases including pain, pathological fracture, spinal cord compression, bone marrow suppression and hypercalcaemia (2). However, in some patients with bone metastasis survival may be relatively long, depending, among many other factors, on their radiological appearance. Hypercalcaemia is a symptom of low specificity for metastatic bone disease; nevertheless, it is a significant complication in oncological treatment and worsens the prognosis of the patient (3).

Therefore, the diagnosis and treatment of bone metastases before the development of significant neurologic and functional deficits might improve the outcome of breast cancer patients. Appropriate imaging can assist in the early detection of bone metastases (4).

In this review, which is based on literature data, and own research material we describe the role of various radiologic and nuclear medical imaging studies in the detection of bone metastases in patients with breast cancer (5). The available studies generally deal with only one tumor type per the study, making the comparisons across imaging modalities generally unavailable (6).

Bone scintigraphy (BS) with technetium-99m-labeled diphosphonates is one of the most frequently performed of all radionuclide procedures over the past several decades. Moreover, some conditions that are not depicted on anatomic images can be diagnosed with bone scintigraphy. BS is a method of imaging with excellent sensitivity (95%) that makes it useful in screening for metastases, and it forms the basis of Radionuclide bone imaging screening (7). Bone metastases usually appear as multiple foci of increased activity (osteoblastic metastasis), although they occasionally manifest as areas of decreased uptake (osteolytic metastasis) (8).

Since bone scintigraphy evaluates changes in bone structure rather than directly imaging the tumor, it can take as long as 6 months to reflect the response to therapy (9). Although the changes in the appearance of bone lesions with effective treatment occur slowly, however, due to sometimes being paradoxical, as exemplified in the phenomenon of bone scintigraphy “flare”, this can make the evaluation of treatment difficult (10) (Fig 1).

Data in the literature shows that SPECT/CT (Single-photon emission computed tomography) can provide true (3D) information. This information is typically presented as cross-sectional slices through the patient but can be freely reformatted or manipulated although not systematically performed. It is usually targeted by the whole body scan and eventually focuses on areas of increased radio-
tracer uptake (11). The potential benefit of carrying out a SPECT/CT, systematically associated with PBS and exploring the whole axial skeleton, would especially be to improve the specificity of focal bone lesions (12) (Fig.2).

**Positron emission tomography (PET)** is a modern and recognized method of detecting cancer cells. The use of a marker 18F-FDG is an effective way of indicating cells with the increased absorption of glucose, such as metastases. By combining PET and CT, high-resolution images can be obtained (13).

Radionuclide bone scanning has been the standard initial imaging method for the detection of skeletal metastases because of its great sensitivity and its ability to examine the whole skeleton in a single examination (14). However, some reports indicate that bone scanning is less effective than FDG PET for detecting bone metastases in breast cancer, whereas other reports indicate that FDG PET has a lower sensitivity for detecting breast cancer bone metastases than bone scanning (15). Therefore, FDG PET has not yet found a firm role in the clinical evaluation of bone metastases in breast cancer. Bone SPECT has proven to be superior to planar imaging in detecting various bone diseases. Because no studies comparing bone SPECT and FDG PET have been reported, it is not clear whether FDG PET is a more powerful tool than bone SPECT in the clinical evaluation of breast bone metastases (16).

Fluorine-18 fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography (18F-FDG PET/CT) is reported to be helpful in treatment response assessment and follow-up of metastatic bone disease in breast cancer patients. In metastatic setting (17), 18F-FDG-PET/CT contributes to management optimization by allowing termination of toxic therapies in non-responders. However, the role of this modality in the assessment of the treatment response of bone metastases in breast cancer is not sufficiently established (18).

**Magnetic resonance imaging (MRI)** is the most sophisticated method for imaging bone tumors. This technique is based on the detection of the proton content in the cells. Cancer cells contain more water molecules than healthy bone marrow or cortical bone. Diagnostic images determine not only the degree and type of damage to the bone but also allow assessing the soft tissues adjacent to the tumor. During whole-body MRI examination there is a greater chance of diagnosing (osteoclastic) metastases, than with the use of scintigraphy (19).

New imaging techniques such as MR imaging and positron emission tomography (PET) can identify bone metastases at an earlier stage of growth before host reactions of the osteoblasts occur. Whole-body MR imaging has the potential to visualize the bone marrow (the initial site of neoplastic cell infiltration) directly and to determine abnormalities in bone marrow cell composition with high anatomic resolution. Fluorine-18-fluorodeoxyglucose (FDG) PET depicts early malignant bone marrow infiltration because of its early increased glucose metabolism. In adults, both MRI and PET-CT imaging modalities have been reported to provide sensitivity (up to 100%) for detecting bone metastases superior to that of skeletal scintigraphy (20) (Fig.3).

**Computed tomography (CT)** is a complementary imaging technique used to diagnose bone metastases. It is recommended particularly in dealing with discrepancies between the outcomes of X-ray (negative) and scintigraphy (positive) (21). It allows us to establish the range of destruction of the cortical bone and the presence of periosteal reactions (14). Obtained CT scans give the ability to determine the spatial structure and volume of metastasis. The delectability of metastases is less in CT than bone scintigraphy but due to its collaborative imaging as well as additional information about soft tissue structures CT is useful in this situation (22).

**Classic X-ray** (radiography) in 2 orthogonal projections is most often the first test performed in the early diagnosis of metastases. On the basis of X-ray one can not only obtain information on the size and location of the bone tumour, but also assess the risk of pathological fracture. X-ray shows us to determine whether the tumor is osteolytic, osteoblastic, mixed. Due to its accessibility and popularity, the X-ray examination is quick and cheap, giving it a crucial advantage. In each case, the metastatic tumor diagnosis should strive to clarify the nature of the change with the use of further imaging methods (MRI, CT) (23).

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**Conclusion**

The use of modern imaging techniques allows the exact diagnosis of bone metastases. Standard examination, such as BS, is characterized by adequate sensitivity, is the first-line imaging of bone metastasis. While it is not perfect, its specificity is improved by SPECT/CT (hybrid imaging), becoming very good at detecting bone metastasis. PET/CT appears to have high accuracy and is recommended for further evaluation. F18-fluoride PET/CT (or WB-DW-MRI) may further contribute to BS for staging at diagnosis but may not be appropriate for all forms of therapy. Thus, it remains an important diagnostic tool. In the absence of correlation between clinical status (chronic pain) and radiographic image, the examinations with the high specificity towards metastatic tumors are computed tomography (CT 86%) and magnetic resonance imaging (MRI 97%). Scintigraphy, PET, and whole-body MRI enable imaging of the entire skeletal system within one examination, which makes them an important tool for bone screening in patients with breast cancer.

**Conflict of interest disclosure**

Authors declare no potential conflicting interests related to this paper.
Figure 1: Women 54 y  breast cancer, BS multiple bone metastasis

Figure 2: Women 46y, whit breast cance relapse, SPECT (a) high local uptake in scapula and Th1, according to SPECT/CT (b,c) revealed scapula mts damage and Th1 degenerative changes.

References

Figure 3: Single bone metastasis, BS (a), CT (b), MRI (c)