Letter to the editor

DAHUDER
Medical Journal
e-ISSN: 2791-9250

Approach To the Metastatic Bone Lesions; Tumor Investigation in A Patient Without Cancer

Seyit Uyar, Feyzi Bostan

Department of Internal Medicine, Antalya Training and Research Hospital, Antalya, Turkey

ABSTRACT

With the increase in the use of radiological imaging methods, the number of patients with a bone lesion (mostly in the form of a lytic lesion) or metastasis suspicion is also increasing. Patients with such a suspicious bone lesion are referred to internal medicine outpatient clinics for further investigation. However, there is no a standard approach for tumor investigation in incidental bone lesions in the literature. In this article, we mentioned about definition, clinical findings and diagnostic approach to these lesions.

Keywords: cancer, metastasis, bones

With the increase in the use of radiological imaging methods, the number of patients with a bone lesion (mostly in the form of a lytic lesion) or metastasis suspicion is also increasing. Patients with such a suspicious bone lesion are referred to internal medicine outpatient clinics for further investigation. However, there is no a standard approach for tumor investigation in incidental bone lesions in the literature. In this article, we mentioned about definition, clinical findings and diagnostic approach to these lesions.

Lung, breast, prostate, kidney, bladder, thyroid cancers, lymphomas and sarcomas are the main malignancies that metastasize to the bones. Bone metastases have been reported in 30-40% of thyroid, kidney and bronchial cancers in autopsy series and 50-70% of advanced breast and prostate cancers. Osteolytic bone lesions are present in 60% of myeloma patients at the time of diagnosis. Rarely, myeloma may also have osteosclerotic lesions and they are mostly associated with POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal spike, skin changes) syndrome. Metastases are more common in areas such as the skull, vertebrae (more often in the lumbar region), proximal femur, pelvis and sacrum. [1, 2] Bone metastasis are classified as osteolytic or osteoblastic according to their radiological appearance. However, this distinction is not clear and many patients may have both osteolytic and osteoblastic metastasis (Table 1). [1]

Pathophysiology

Bone is the third most metastasized organ (after liver and lung) and metastases of bone are more common than primary bone tumors. Tumors spread to the bone by hematogenous route (venous) or local invasion. The mechanism of bone metastases is not fully understood. Through remodeling, bones try to maintain its strength by dynamic balance between osteoclastic and osteoblastic activity. Once a metastatic focus is located in the bone, tumor cells interact with osteoclastic and osteoblastic cells to increase bone turnover. It is assumed that tumoral cells stimulate osteoclasts via RANKL (receptor activator nuclear

Received: *April 03, 2022****; Accepted:*** *April 24, 2022****; Published Online:*** *April 29, 2022*

How to cite this article: *Uyar S, Bostan F. Approach To the Metastatic Bone Lesions; Tumor Investigation in A Patient Without Cancer. DAHUDER M J 2022, 2(2):33-35.*

Address for correspondence: *Seyit Uyar, Assoc. Department of Internal Medicine, Antalya Training and Research Hospital, Antalya, Turkey. E-mail: seyituyar79@hotmail.com, Phone: +90 242 249 4400*

Table 1. Radiologic presentation of bone metastases

Mostly osteolytic:	Mostly osteosclerotic:	Mix:
- Multiple myeloma	**- Prostate cancer**	**- Breast cancer**
- Renal cell cancer	- Small cell lung cancer	- Gastrointestinal cancers
- Non-small cell lung cancer	- Hodgkin lymphoma	- Squamous cell cancers
- Thyroid cancer	- Carcinoid tumors	
- Non-Hodgkin lymphoma	- Medulloblastoma	
- Melanoma		

*The ones in bold are the tumors that metastasize most frequently to the bones and should be considered initially

factor kappa B ligand). In addition, many cytokines, chemokines and hormones secreted by tumor cells also stimulate osteoblasts and osteoclasts (such as; jagged-1, metalloproteinase-7, parathyroid hormone-related peptide, endothelin-1, bone morphogenic proteins, insulin-like growth factors, platelet-derived growth factors and fibroblast growth factors).[2]

Clinical and laboratory findings

Bone metastases are usually asymptomatic and diagnosed at the staging after a tumoral diagnosis. Pain is the most common symptom. Symptoms such as motor deficit, paralysis, loss of sensation, stool and urinary incontinence due to spinal cord compression can be seen in vertebral metastases. [2]

There is no a specific blood test in the diagnosis of bone metastases. However, elevated alkaline phosphatase (ALP) or calcium may be a finding of bone metastases. Osteolytic lesions can often cause hypercalcemia. On the contrary, in osteoblastic metastases, hypocalcemia may be seen with an increase in ALP. It increases significantly in bone metastases of lung, prostate, breast cancers and osteosarcoma. Acid phosphatase, on the other hand, may be increased with ALP by osteoclastic activity. There may be an increase in acid phosphatase especially in prostate cancer. [2]

Since bone metastases can be confused with osteoporosis in elderly women, care should be taken in these people. While the cortical bone is preserved in osteoporosis, it is generally destroyed in metastatic bone lesions.

Diagnosis

a) Screening for bone metastasis in a patient with known cancer

There is no a consensus in the screening and diagnosis of bone metastases in patients with cancer. Firstly, bone metastasis can be screened by direct radiological imaging. If lytic lesions are larger than 1 cm, they may be seen better than lesions smaller than 1 cm on direct radiological imaging. If there is no finding on direct radiography imaging, non-contrast computed tomography (CT) and magnetic resonance imaging (MRI) should be used. MRI is more sensitive than CT in detecting bone metastases, therefore it should be performed when MRI is contraindicated. The advantage of MRI is that bone marrow infiltrates can be evaluated. Bone scintigraphy (Technetium-99m) and positron emission tomography (PET) can be used as secondary imaging techniques. Bone scintigraphy is reliable for detecting metastases in tumors with increased osteoblastic activity, such as prostate and breast cancer. However, it is less sensitive to detect tumors with little or no osteoblastic activity (such as multiple myeloma). PET has high sensitivity and specificity for detection of distant metastases, also bone metastases. PET is superior to bone scintigraphy due to the advantages of detection all distant metastases and clinical staging of cancer. [2-4] Sensitivity and specificity of imaging techniques to detect bone metastasis are shown on Table 2. [3]

Table 2. Sensitivity and specificity of imaging techniques to detect bone metastasis

Imaging technique:	Sensitivity (%)	Specificity (%)
- Computed tomography	77.1	83.2
- Bone scintigraphy	75.1	93
- Magnetic resonance imaging	90.4	96.0
- Positron emission tomography	94.2	97.2

b) Detection of primary tumor without a diagnosis of cancer

First of all, it should be directed to the organ system where the patient has complaints and/or physical examination findings, if any. If there are no complaints and/or physical examination findings, a search for cancer, which is common according to gender and age, should be performed. For this purpose, first of all, solid internal organ cancers should be screened by using contrast-enhanced CT of the lung, abdomen and pelvis, and breast screening should be performed if female. Evaluation for multiple myeloma should also be done simultaneously. If the results of these techniques are negative, bone biopsy should be planned.[2, 3]

Authors' Contribution

Study Conception: SU,; Study Design: SU,; Supervision: SU, FB,; Literature Review: SU, FB,; Manuscript Preparation: SU,FB,; and Critical Review: SU.

REFERENCES

1. UpToDate. Mechanisms of bone metastases. Available at: https://www.uptodate.com/contents/mechanisms-of-bone-metastases?sectionName=Osteoblasts&search=bone%20metastasis&topicRef=91912&anchor=H2047254803&source=see_link#H2047254803. Accessed March 29, 2022.
2. UpToDate. Epidemiology, clinical presentation, and diagnosis of bone metastasis in adults. Available at: https://www.uptodate.com/contents/epidemiology-clinical-presentation-and-diagnosis-of-bone-metastasis-in-adults?search=-bone%20metastasiz&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1. Accessed March 29, 2022.
3. Maillefert JF, Tavernier C, Tebib J. Determining the site of the primary cancer in patients with skeletal metastasis of unknown origin: A retrospective study. Cancer. 2000 Apr;88(7):1759-61.
4. Özer H, Durmaz MS. Kemik Metastazları. Trd Sem 2021; 9: 137-155. (in Turkish)