

REVIEW

Nuclear medicine imaging in bone metastases

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Abstract

Nuclear medicine techniques designed to identify bone metastases are reviewed. They include planar and whole body, single photon emission tomography (SPET), F-18 Fluorine and FDG, deoxyglucose, positron emission tomography (PET), bone imaging.

Keywords: *fluorine-18; Tc-99m methylene diphosphonate; single photon emission tomography; positron emission tomography.*

Introduction

Bone is a metabolically active tissue undergoing remodelling in relation to stress and strain with osteoblastic repair and osteoclastic removal of bone. Uptake of an agent depends on the blood supply, the capillary to bone transfer through extra cellular space and the degree of osteoblastic and osteoclastic activity. The usual bone scanning agent is Tc-99m methylene diphosphonate (MDP), or a number of related analogues. The uptake of this agent is primarily at the remineralisation surface of the bone. In bone metastases this is at the repair surface due to osteoblastic activity in response to most adenocarcinomas and sarcomas. However, it can be stated that if the bone infiltration is due to what might be termed a familiar bone marrow component, such as plasma cells in myeloma and white cells in leukaemia or lymphoma, then the response may be muted and only the addition of early pathological fracture may make the bone scan positive. However, for most bone metastases the bone scan is a highly sensitive but not specific technique. Except in myeloma, it is generally a much more sensitive technique than the skeletal survey for bone metastases. A single focal increase of uptake in the context of cancer may be suggestive of a metastases but cannot be taken as diagnostic. Multiple lesions at likely sites of metastases are usually diagnostic. Lung, breast, prostate and renal

cancers account for most bone metastases and over half of these metastases occur in the spine.

Normal and benign changes

The variations in the normal bone scan need to be appreciated, such as the symmetrical epiphysial plates in the child, the increased uptake in joints of the shoulder and hand in the right-handed person on the right side and in the left-handed person on the left side. There are many normal variants: the degree of bone uptake in the skull, increased uptake at the manubrium sternal junction, asymmetry of uptake due to rotation and variations in intensity due to the closeness of the camera to the bone.

There is a range of abnormalities due to benign changes which are usually but not always easy to identify, such as focally increased uptake in the maxilla and mandible due to dental problems, arthropathic changes at the base of the thumb and bunions on the big toes. There are a number of artefacts that may be seen, usually defects due to buckles, jewellery, money, pacemaker or prosthesis. Contamination may be due to active urine, or occasionally contaminated radiographer's fingers, for example on the image of the skull through holding the head. These may be able to be washed off. Renal and urinary activity may cause problems:

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bladder diverticulum, ureterocoele urinary diversion, pelvic retention, or anomalous site and position of a kidney. A poor preparation may contain free Tc-99m in which case the thyroid, stomach and/or salivary gland activity may be seen. Sites of muscle or other soft tissue infarction or necrosis may show focal uptake on the bone scan.

The main problem is the distinction between degenerative change and malignancy in the spine. Typically degenerative change gives uptake on one or other side of the junction of the vertebral bodies which extends outside of the line of the vertebral bodies. It is often seen to the left or the right side of L5, on the vertebral edges on the concavity of scoliosis or relating to weight-bearing joints. Osteoporotic crash fractures are usually seen as a linear change in the vertebra whose intensity relates to the recentness of the event. The occasional rib end may show uptake possibly related to trauma. Cough or osteoporotic fractures may be seen in the ribs and traumatic fractures tend to lie in a line across adjacent ribs. A three-phase scan is usually undertaken to show that a site of osteomyelitis is active on dynamic, blood pool and three-hour images. Investigation of the limbs when there is a specific local complaint is usually undertaken with a three-phase bone scan.

Single photon emission tomography (SPET)

This is particularly useful in the lower lumbar spine for distinguishing causes of chronic backache^[1,2]. A metastasis usually affects the whole or the part of the body of the vertebra, or part of the body and a pedicle, or a pedicle alone. Occasionally a defect is seen with the rim of uptake around it. This is commonly noted in renal metastases. The spine of the vertebra is not usually involved in bone metastases. Uptake in the spine of the vertebra may be seen with Paget's disease when there is usually a trefoil appearance of uptake in the spinous process and the two pedicles. Osteoid osteoma may also show uptake in a spinous process. SPET is useful in demonstrating facet joint arthropathy, active pars defect or degenerative changes. SPET is also used for sorting out the relations of focal uptake seen in the skull and in evaluating joint disease, for example cartilage tears in the knee or avascular necrosis in the hip.

Defects in uptake in the bone may be seen with a number of malignancies, typically lung cancer and breast cancer and occasionally in myeloma. Also through a number of benign diseases such as haemangioma, bone infarct associated with haemoglobinopathies and fat infiltration as in Gaucher's disease. More generally, they are due to local radiotherapy.

Management of patients with cancer

It is generally agreed that in stage I cancers a bone scan is not required. However, there are two approaches, the passive and the active. The passive approach likes to have a baseline bone scan, for example in breast cancer^[3] or prostate cancer at initial evaluation of the patient; the bone scan is then repeated, for example at six-monthly intervals independent of symptoms or signs. The active approach, which is preferred as it reduces the number of unnecessary bone scans, is to evaluate the patient from a symptomatic point of view; if bone pain develops a bone scan is performed. Nevertheless, some authorities prefer to undertake a bone scan before cancer surgery, particularly in lung cancer as evidence of metastases would preclude an operation. In breast cancer this is not usually the case, since removal of a breast tumour is usually undertaken whether or not there is evidence of metastases.

The bone scan may be used as part of an evaluation protocol for a new cancer therapy. This may require a bone scan before and at the evaluation time. In prostate cancer a bone scan would normally be done before radical prostatectomy is contemplated as part of the staging procedure. In colorectal cancer bone metastases are rare until liver and lung involvement has occurred, but local bone infiltration may be seen.

Serial bone scans may be used to evaluate the effect of therapy, for example anti androgen therapy in prostate cancer and anti oestrogen therapy in breast cancer.

On occasions, a 'flare' will be seen with local increase of uptake at the metastatic site before reduction, particularly in breast cancer^[4]. Residual bone scan abnormality may persist long after active bone metastases have responded to treatment or stabilised.

F-18 and FDG bone imaging

The increasing availability of bone PET and SPET, with coincidence counting with a two-headed thick-crystal camera, has led to the wider application of F-18 DG, deoxyglucose, and F-18 fluorine in evaluating bone metastases.

FDG does not show normal bone. It identifies active metastases in marrow as focal increases in uptake, in contrast with bone marrow imaging with radiolabelled white cells or colloids, which show defects. It is able to show metastases that do not cause a reaction on the bone scan. It has a higher specificity than Tc-99m MDP for bone metastases as it is less likely to be taken up by benign bone lesions and by degenerative changes^[5-7]. However, in breast cancer a lesser sensitivity for FDG PET than Tc-99m MDP is reported^[8].

F-18 Fluorine does show uptake in normal bone, but much more in bone invaded by metastases. With the higher sensitivity and resolution of dedicated PET systems, its sensitivity and specificity for bone metastases

are greater than that of Tc-99m MDP^[7,9]. Data with these F-18 tracers for SPET coincidence counting and how that compares with dedicated PET are not yet available.

Conclusion

In conclusion, radionuclide bone imaging with Tc-99m MDP is an established method of showing bone metastases, but may be in decline^[10]. The increasing use of SPET bone imaging and the availability of F-18 tracers are leading to improvements in detection and the monitoring of their treatment.

Questions

1. After primary treatment for breast or prostate cancer, should there be: (a) passive serial follow-up bone scans, e.g. annually; or (b) active use, i.e. only when signs or symptoms of bone disorder occur?
2. What is the role of bone SPET?
3. Does F-18 or F-18 DG imaging have a place in symptomatic bone disorder when the bone scan and radiology are negative?

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