Metastatic mimics on bone scan: “All that glitters is not metastatic”

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ABSTRACT

In this pictorial review, cases where benign diseases caused a diagnostic dilemma on bone scan are illustrated. This review highlights the value of correlative imaging - single-photon emission computed tomography/computed tomography (CT), CT, and magnetic resonance imaging in solving the diagnostic problem by exact localization and characterization of the lesions. All these eventually lead to increased diagnostic confidence, better and more accurate reporting and avoidance of delay in initiation of treatment due to equivocal results. The imaging features of these benign pathologies – which are “mimics of metastatic disease,” are elaborated so that the reader can incorporate them while reporting so as to avoid mis-interpretations.

Keywords: Benign, bone scan, computed tomography, metastasis, methylene diphosphonate, single-photon emission computed tomography

INTRODUCTION

Bone scan is one of the most common and oldest examinations among all nuclear medicine procedures. It is used in the evaluation of benign bone disease like infection/inflammation and also is the standard of care for evaluating metastatic disease in the breast, prostate, and lung cancer.[1] Though the reported sensitivity of bone scan is high, its specificity is low due to increased metabolic activity seen in benign disease such as trauma, infection, inflammation, and degenerative joint diseases. Widespread involvement usually suggests metastatic disease. A single focal lesion is almost always a cause of dilemma in reporting. In all such cases, the dilemma is solved by either doing a single-photon emission computed tomography (SPECT), a SPECT/computed tomography (CT) or a correlative CT or magnetic resonance imaging (MRI).

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MATERIALS AND METHODS

Bone scan in eight cases is discussed. All patients underwent a bone scan with ^{99m}Tc-methylene diphosphonate (MDP) after being injected with 740 MBq (20 mCi), intravenously. All patients were adequately hydrated. The scans were acquired after 3 h in anterior and posterior views on GE S3000 WW Infinia Hawkeye GP3 (Milwaukee, USA).

The imaging features of the bone scans are discussed along with SPECT/CT, CT, or MRI to come to a diagnostic conclusion. The imaging findings were confirmed with a biopsy or a follow-up imaging.

Case 1

A 59-year-old female, a case of carcinoma of the left breast, post left modified radical mastectomy, and chemotherapy, presented a year later with recurrence in left supraclavicular nodes. Bone scan done for restaging showed increased activity in left humerus [Figure 1a and b]. X-ray of the same area showed

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an elongated irregular serpiginous sclerotic lesion in the proximal metadiaphyseal region of the left humerus [Figure 1c]. There was no cortical break, periosteal reaction, or soft tissue swelling. Regional SPECT/CT [Figure 1d] confirmed the findings. These findings were suggestive of a bone infarct. This has remained unchanged on follow-up for 2 years.

A bone infarct is synonymous with osteonecrosis. It implies the ischemic death of cellular elements of the bone and marrow and involves the metaphysis and diaphysis of long bones. When the epiphysis is involved, it is known as avascular necrosis.

The classical radiograph appearance is of sheet-like central lucency surrounded by shell-like sclerosis with serpiginous borders and discrete calcifications. Immediately after the vascular insult a photopenic defect may be seen on bone scintigraphy (BS) for up to 3 days, later than that revascularization together with osteoblastic repair takes place and thus an area of intense activity is visualized. Increased tracer uptake corresponds to revascularization phase. The common causes of bone infarct are prolonged corticosteroid use, sickle cell disease, trauma, Gaucher's disease, and renal transplantation.[2]

Case 2

Bone scan done in an 18-year-old boy for complaints of pain and swelling in the right iliac region revealed an area of increased activity in the right acetabulum and supra-acetabular region of the right iliac bone [Figure 2a and b]. MRI of the pelvis revealed altered marrow signal intensity with cortical expansion and erosion involving the anterior part of the right acetabulum, supra-acetabular part of the ilium, and the superior pubic ramus. The lesion was hypointense on T1-weighted (T1-W) images. On T2-W and short tau inversion recovery images, the lesion showed multiplecystic spaces with thin internal septae. Multiple fluid-fluid levels were seen within the cystic spaces [Figure 2c and d]. These findings were consistent with aneurysmal bone cyst (ABC). The histopathology postcurettage was consistent with ABC.

ABC is a benign, expansile, osteolytic lesion typically involving the long bones of the appendicular skeleton and vertebrae. Only 8–12% are seen in the pelvis. Histologically, these are blood-filled cavities not lined by endothelium.[3] The etiology is unknown. These are seen more commonly in children and adolescents <20 years of age. The plain radiograph usually shows an expansile lesion with a thin cortical rim, which in either central or eccentrically located in the metaphysis and diaphysis of a long bone. MRI demonstrates the characteristic fluid-fluid levels due to blood sedimentation.

Bone scan demonstrates an area of increased tracer activity with central photopenia. At times diffuse tracer uptake may also be seen. However, the appearance of the lesion is nonspecific and does not correlate with size or osteoblastic activity. However, the presence of a solitary bone lesion helps to differentiate ABC from brown tumors.[4]

Case 3

Bone scan done as a part of routine initial work-up in a 48-year-old female with carcinoma of right breast showed an area of increased tracer activity in the left fronto-parietal area of skull [Figure 3a-c]. A correlative CT scan of the brain showed an extra-axial calcified lesion in the left frontoparietal area [Figure 3d and e] with imaging features characteristic of a calcified meningioma.

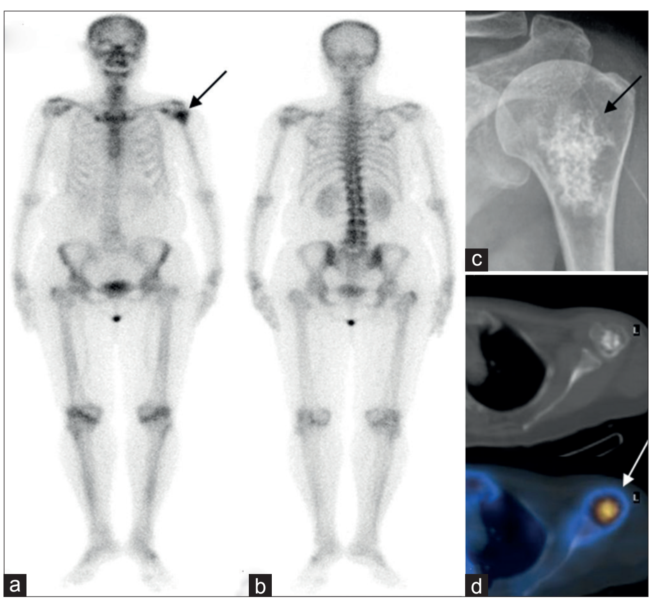

Figure 1: Anterior and posterior views of planar bone scan showing increased activity in the left proximal humerus (a and b) (arrows). X-ray showing elongated, serpiginous sclerotic lesion characteristic of a bone infarct. (c) Single-photon emission computed tomography/computed tomography fused image showing increased uptake in the same (d)

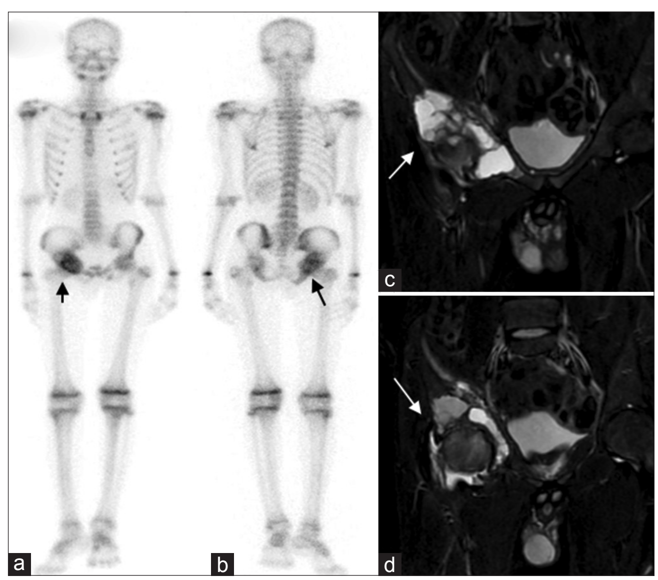

Figure 2: Anterior and posterior views of planar bone scan showing increased activity in the right acetabulum and supra-acetabular region of the right iliac bone (a and b). (c and d) The short tau inversion recovery magnetic resonance imaging images of the pelvis showing altered marrow signal intensity with cortical expansion and erosion involving the anterior part of the right acetabulum, supra-acetabular part of the ilium, and the superior pubic ramus. The lesion shows multiple cystic spaces with thin internal septae and multiple fluid-fluid levels. Findings consistent with aneurysmal bone cyst

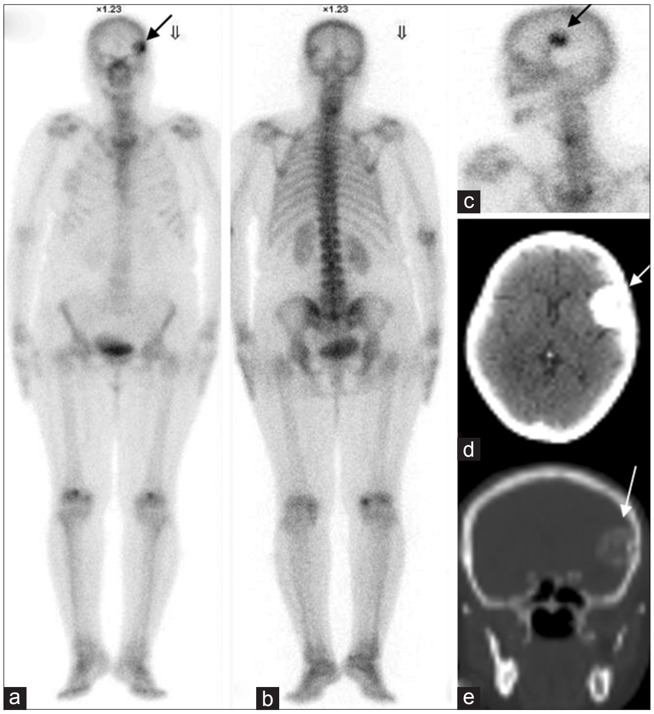

Figure 3: Anterior (a), posterior (b) and sagittal (c) views of planar bone scan showing increased activity in the left fronto-parietal area of skull. Axial (d) and coronal (e) computed tomography scan of the brain showing an extra-axial calcified lesion in the left fronto-parietal area consistent with calcified meningioma

Meningiomas are the most common extra-axial neoplasm of the central nervous system and account for 15–20% of all intracranial neoplasms. These are usually seen in middle-aged females, most common locations being cerebral convexities, parasagittal regions, sphenoid ridge, and olfactory groove. The typical CT features includes a well-circumscribed mass with a broad-based dural attachment with intense homogenous postcontrast enhancement. Uptake of MDP in meningiomas has been reported earlier.[5] SPECT/CT helps differentiate benign tumor like meningioma from primary and metastatic brain lesions.

Case 4

A 60-year-old female a case of carcinoma of right breast underwent a pretreatment bone scan for staging. Her scan revealed increased tracer uptake in L2 vertebra [Figure 4a-c]. Rest of the bones showed normal tracer uptake. A correlative regional CT revealed a polka-dot appearance in right half of L2 vertebral body [Figure 4d] representing a focal hemangioma.

Hemangiomas are asymptomatic benign lesions of the bone, characterized by vascular spaces lined by endothelial cells. The most common location is the thoracic vertebra. The characteristic appearance of a vertebral hemangioma on CT scan is called the "polka-dot" sign produced by the thickened trabeculae. On ^{99m}Tc bone scan, vertebral hemangioma can either be photopenic - not showing any tracer concentration or can show increased tracer uptake.[6]

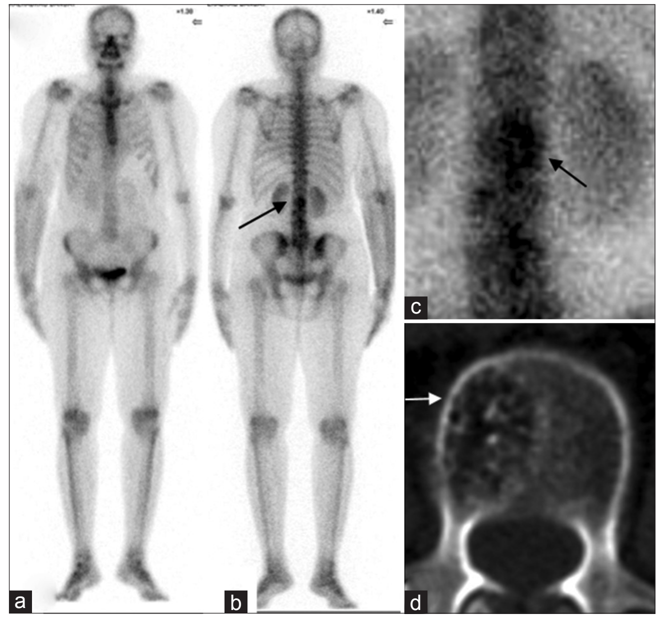

Figure 4: Anterior (a), posterior (b) and regional spot (c) views of planar bone scan showing increased activity in L2 vertebra (seen toward the right of midline in the posterior view [b and c]). Axial computed tomography image (d) showing the classical polka-dot appearance in right half of L2 vertebral body representing a focal hemangioma

Case 5

A 47-year-old female treated for cancer of the cervix with chemotherapy and radiation therapy 8 months back, presented with severe back ache. Bone scan done to look for metastatic disease showed diffuse increased activity in L1–L4 vertebrae [Figure 5a and b]. A correlative CT revealed extensive degenerative changes with reduction in height of the vertebral bodies with no soft tissue component with extensive osteopenic changes in the vertebrae suggesting degenerative collapse [Figure 5c-e].

Radiologically, generalized osteoporosis is seen as decreased bone density or increased radiolucency with cortical thinning. In vertebrae, this is seen characteristically as increased radiolucency, well-defined cortical rim verticalization of the trabeculae. This is known as "picture-framing." These then lead to compression fractures – wedge/endplate fractures.[7]

Case 6

In a 63-year-old female a case of carcinoma of left breast with lung metastases, the bone scan showed two focal areas of increased uptake in L5 vertebra on the posterior view [Figure 6b and c - arrow]. This appearance of bilaterally symmetrical focal areas seen posteriorly in a vertebra is classically seen in facetal arthropathy. However, one should always confirm that a metastatic lesion is not missed, which is commonly seen in the pedicles/posterior elements of a vertebra and would also appear similar, only difference being that metastatic lesions are usually not symmetrical. However, a co-existent lesion and facetal arthropathy may be present in the same vertebra and merits an anatomical correlation. A correlative CT in this case showed loss of cartilage with erosions and vacuum phenomenon in both the facet joints of L5 vertebra [Figure 6d - arrow] confirming facetal arthropathy. Apart from this, a focal uptake was noted in the greater trochanter of left femur [Figure 6a and e - curved arrows] and head of left humerus [Figure 6a and g - block arrows], which were suspicious for metastatic involvement. A correlative CT revealed cortical erosions and reactive sclerosis in the greater trochanter [Figure 6f - curved arrow] as well as in the head of left humerus [Figure 6h - block arrow] which are hall mark of enthesopathy at these sites.

The classical appearance of benign and malignant disease in the spine is that focal hot spots confined to the pedicles are metastatic and those that extend beyond the vertebral bodies or those that are confined to the articular facets and almost always due to benign osteophytes or facetal arthropathy. Active degenerative

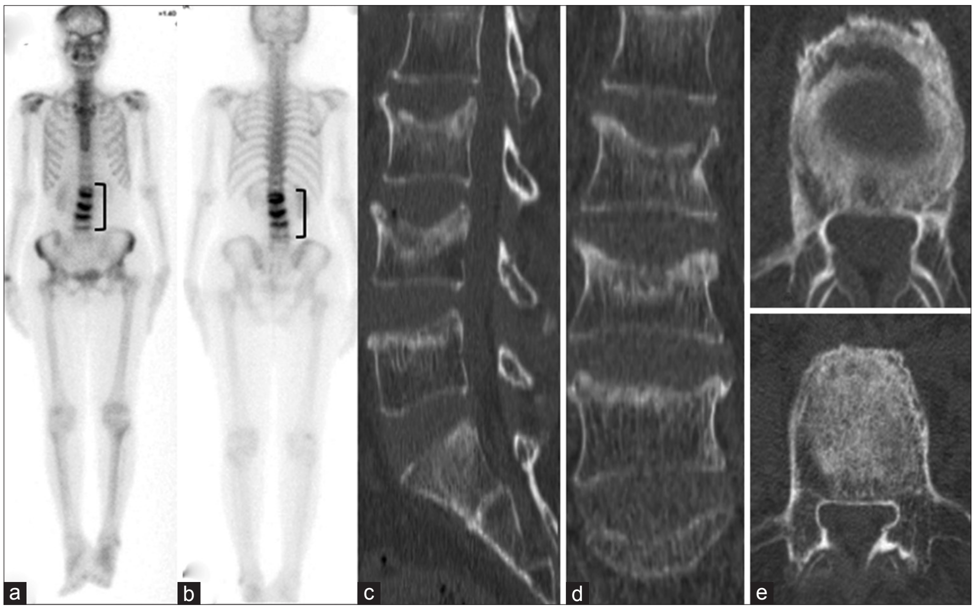

Figure 5: Anterior (a) and posterior (b) views of planar bone scan showing diffuse increased activity in L1–L4 vertebrae. Sagittal (c), coronal (d) and axial (e) computed tomography images showing extensive degenerative changes with reduction in height of the vertebral bodies with extensive osteopenic changes and no soft tissue component, suggesting degenerative collapse

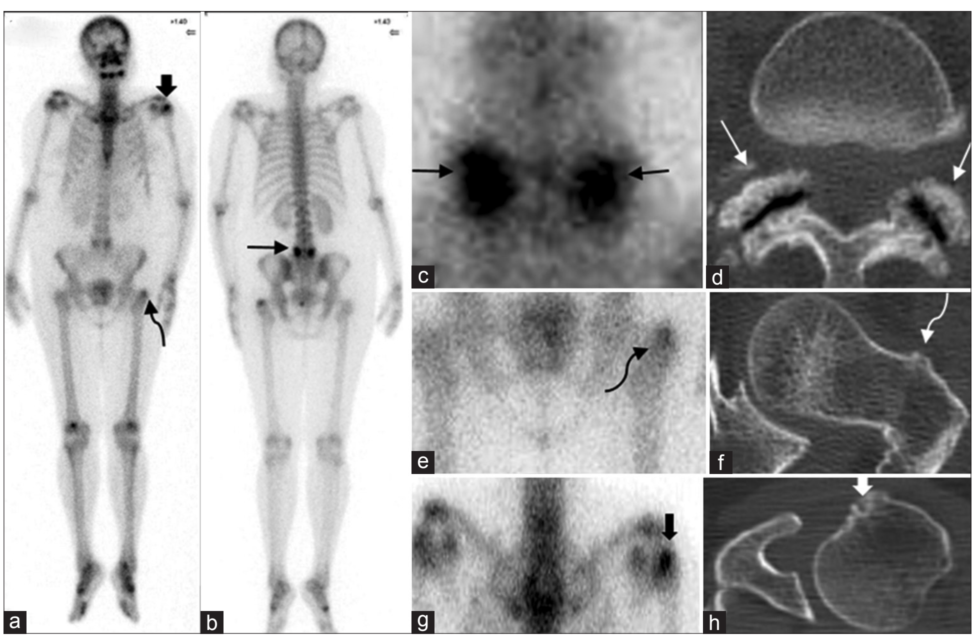

Figure 6: Anterior (a), posterior (b) and regional spot (c) views of planar bone scan showing two focal areas of increased uptake in L5 vertebra (arrow). Axial computed tomography image (d, arrows) showing loss of cartilage with erosions and vacuum phenomenon in both the facet joints of L5 vertebra characteristic feature of facet arthropathy. Focal increased activity is seen in the greater trochanter of left femur (curved arrow) and head of left humerus (block arrow) in a, b, e, g. Axial computed tomography image showing cortical erosion and reactive sclerosis in the greater trochanter of left femur (f) (curved arrow) as well as in the head of left humerus (h) (block arrow) which are hall mark of enthesopathy

osteoarthritis is the cause of increased focal uptake in facet joints. The CT appearance of degenerative facet arthropathy include osteophyte formation, degradation of the cartilage leading to focal or diffuse erosions, sclerosis of subchondral bone, vacuum joint phenomenon and calcification of the joint capsule.[8]

Enthesopathy is a disease occurring at sites of "enthuses" – these are sites of attachment of a ligament or tendon to the bone. The nature of pathology at these sites in elderly is usually degenerative or inflammatory. The other causes being trauma, endocrine, or metabolic. The common sites of involvement are trochanteric region of femur, tuberosity of humerus, olecranon, patella, calcaneus, pelvis, and sometimes vertebrae. The radiological features are hyperostosis, bone erosion, fragmentation, and crystal deposition. It has earlier been reported that these site of attachment show increased tracer concentration on radionuclide BS.[9]

Case 7

Bone scan done for initial staging in a 45-year-old female revealed foci increased activity in the lumbar region posteriorly. Increased activity was seen at the level of L2 vertebra on the right side, which was tracking until L5 vertebra [Figure 7a and b- arrows]. In addition, at the level of L2 vertebra the activity was seen transversely across the vertebra. This appearance was very unusual and a regional SPECT/CT revealed these areas to be present on the skin surface posteriorly in the lumbar area due to urinary contamination [Figure 7c and d].

Contamination, though an unwanted occurrence is quite commonly seen in Nuclear Medicine Departments. The most common being urinary contamination and the others result from extravasation at the injected site, a leaking intravenous tubing or due to bleeding from site of injection.[10] It is necessary to identify these false – positive sites of MDP localization to avoid incorrect reporting. Imaging in multiple projections and SPECT/CT are helpful in avoiding these mis-interpretations.

Case 8

A 31-year-old female, carcinoma right breast, and pretreatment bone scan revealed a focal area of increased activity in D3 vertebra [Figure 8a and b], rest of the scan was normal. A regional CT revealed a prominent venous channel [Figure 8c and 8d].

These prominent channels of the basi-vertebral venous plexus are seen as linear areas of lucency on sagittal plane in CT images. Posteriorly, these areas flare into a trumpet-shaped area as they join the spinal canal. On axial CT images, they appear as notch-like lucent area. These venous plexus are potential channels of spread of infection and malignancy. This lucency of the basi-vertebral venous plexus can often be mistaken for lytic metastatic lesion. The important differentiating point is that a destructive lytic lesions has ill-defined margins, whereas a venous channel has distinct osseous border.[11]

DISCUSSION

Since long bone scan has been used for evaluation of skeletal metastases. Thought it has moderate sensitivity for detection of skeletal lesions, it lacks the needed specificity for detection of metastatic bone lesion. This is because degenerative changes and benign bone lesions also may show increased tracer uptake due to increased bone turnover or increased vascularity. More so a single lesion is always a cause of concern and it is usually a SPECT or a fused SPECT/CT that bails us out to correctly identify a lesion as benign or malignant.

Many reports in the past few years have shown that bone scan is not an effective modality for confirming metastatic disease due to its moderate sensitivity and low specificity ranging from 46–70% and 32–57%, respectively. The addition of SPECT to two-dimensional planar imaging either alone or in combination with CT (SPECT/CT) improves the sensitivity, specificity and diagnostic accuracy.[12]

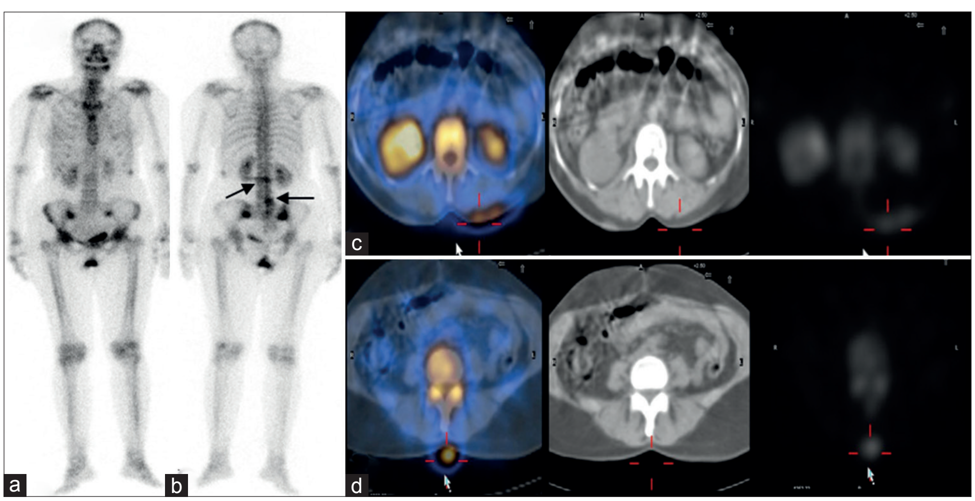

Figure 7: Anterior (a) and posterior (b) views of planar bone scan showing increased activity at the level of L2 vertebra on the right side tracking until L5 vertebra (arrow). Regional single-photon emission computed tomography/computed tomography (c and d) shows these areas to be present on the skin surface posteriorly in the lumbar area due to urinary contamination (cross). Also noted in (d) is increased tracer uptake in bilateral facets suggesting facetal arthropathy

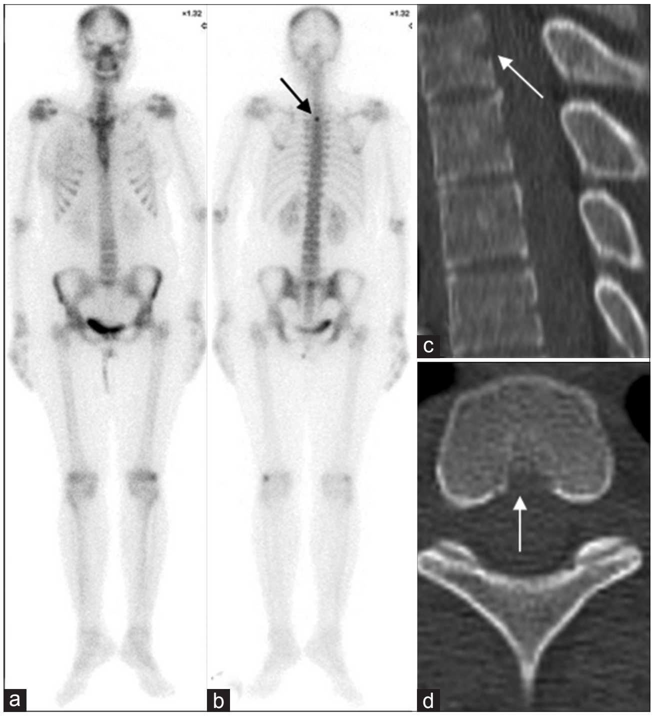

Figure 8: Anterior (a) and posterior (b) views of planar bone scan showing focal increased activity at the level of D3 vertebra (arrow). Sagittal and axial computed tomography image (c and d) showing a prominent venous channel (arrows)

^{18}F-sodium fluoride (NaF) is a relatively new re-emerged positron emission tomography (PET) tracer that is gaining popularity for detection of bone metastases. It is highly sensitive for detection of bone metastases.[13] Increased bone turnover and increase in regional blood flow are the reasons for increased tracer uptake of NaF in malignant lesions.[14] The rate of false-positivity is also decreased in ^{18}F-NaF PET/CT due to characterization of the lesions by the CT component of the study.

In a study by Even-Sapir *et al*., where they compared bone scan with SPECT and ^{18}F-fluoride PET and PET/CT, the authors showed that SPECT was more sensitive than planar BS, but NaF PET/CT had the highest sensitivity of all.[12] The tracer NaF is not tumor specific; it has high sensitivity but is prone to false positivity. The addition of PET to CT while performing ^{18}F-NaF PET/CT helps to characterize the lesions, reduces the false positivity and increases the specificity. Moreover, due to the CT component even the osteolytic lesions are detected on NaF PET/CT as compared to the conventional bone scan which misses osteolytic lesions.

In a recent prospective trial called the SKELETA trial, the authors have shown that both NaF PET/CT and whole body MRI including diffusion weighted MRI have a higher diagnostic accuracy as compared to bone scan and SPECT.[15]

CONCLUSION

Bone scan is a very cost-effective and sensitive test for detection of metastatic disease. Though very sensitive, it lacks in specificity due to the absence of characteristic features for characterization of lesions. This becomes more pronounced when there is a solitary bone lesion. In such cases, it is mandatory that either hybrid imaging is done with SPECT/CT or an anatomic correlation is done with CT or MRI for characterization of the lesion. Skeletal PET/CT imaging with ^{18}F-NaF can also be contemplated. Routine use of SPECT/CT and PET/CT skeletal imaging will help us to avoid incorrect reporting will enhance our confidence while reporting and will also generate a bond of trust with the referring physician.

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Conflicts of interest

There are no conflicts of interest.

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