Bone Scan in Detection of Biological Activity in Nonhypertrophic Fracture Nonunion

Abstract

Biological activity of the fracture site is very important factor in treatment planning of fracture nonunion. If no biological activity is detected, then an autologous bone graft can be supplemented or osteogenic supplementations, such as bone morphogenetic protein is given. If biological activity is present, then secure fixation is sufficient to achieve bony union. Biological activity of nonunions is usually assessed by conventional radiographs. The presence of callus formation is usually assessed as the presence of biological activity. However, high number of radiologically nonhypertrophic nonunion demonstrates intense, uniform tracer uptake on bone scan, a sign of biological activity. Poor or absent callus visualization on radiographs does not always mean a lack of biological activity and it underestimates it. Uptake in bone scintigraphy reflects blood flow and new bone formation and being functional imaging technique, it is more suitable for assessing biological activity.

Keywords: *Biological activity, bone scan, nonhypertrophic nonunion*

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Introduction

Fracture nonunion definition is based on three factors, namely, duration of time since injury, characteristics of fracture on serial X-rays, and lastly clinical parameters assessed by the treating surgeon. Fracture bone that has not completely healed in 9 months since injury and which has not shown any sign of healing over 3 consecutive months on serial X-rays is defined as nonunion.[1] Multiple literatures indicate that optimal time for healing is in between 4 and 12 months, taking into account the type of bone fractured, nature of injury, and quality of the soft tissues around the fractured bone.[2-8] Along with these factors, one more important factor is the physiologic capability of the individual in mounting a healing response. Type of nonunion can be determined by conventional radiological procedures or more accurately on bone scans. Biological activity of the fracture site is very important factor in treatment planning of fracture nonunion. Bone scan being functional imaging technique is most suitable technique for assessing biological activity.

Cases

Case 1

A 52-year-old male patient had a history of fracture intertrochanter right femur following trauma in a road traffic accident (RTA). Open reduction and internal fixation were done 1 year back. He had persistent pain at local site. Local part X-ray was done and fracture nonunion was suspected. He was referred for bone scan. 20 mCi of ^{99m}Tc-methylene diphosphonate was injected intravenous and flow images of upper femoral region were acquired at 1 s/frame for 1 min. Blood pool image was acquired after 10 min. Whole-body anterior and posterior projections were acquired after 3 h using dual head gamma camera GE Discovery NM 630. Regional single-photon emission computed tomography (SPECT) and computed tomography (CT) were also acquired and SPECT-CT fusion was done using Xeleris 3.1. SPECT-CT fusion images showed increased tracer uptake at trochanteric region of right femur corresponding to oligotrophic nonunited fracture site on CT correlation without any cold/photon-deficient area within (pattern Type 1) [Figures 1 and 2]. Hence, it was oligotrophic nonunion with positive biological activity and patient required secure fixation without any osteogenic supplementation or bone grafting.

Case 2

A 48-year-old male patient had a history of comminuted fracture tibia and fibula on the right side following trauma in an RTA.

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External fixation was done 9 months back. He had persistent pain at local site. He was referred for bone scan to see viability of fracture fragments. Three-phase bone scan with SPECT and CT was done according to standard procedure as described in previous case. SPECT-CT fusion images showed photopenic area involving small part of lower shaft of right tibia and fibula corresponding to fracture fragment on CT correlation in a known comminuted fracture [Figures 3-5]. Hence, it was comminuted nonunion with negative biological activity and patient required bone grafting.

Case 3

An 82-year-old male patient had a history of fracture intertrochanter left femur following trauma in an RTA. Open reduction and internal fixation were done 11 months back. Fracture nonunion was suspected and he was referred for bone scan. Three-phase bone scan with SPECT and CT was done according to standard procedure as described earlier. SPECT-CT fusion images showed increased tracer uptake at trochanteric region of left femur corresponding to oligotrophic nonunited fracture site on CT correlation without any cold/photon-deficient area within (pattern Type 1) [Figures 6 and 7]. Hence, it was oligotrophic nonunion with positive biological activity and patient required secure fixation without any osteogenic supplementation or bone grafting.

Discussion

About 5%–10% of fractures are estimated to result in nonunion or delayed union.[9] Biological activity of the fracture site is very important factor in treatment planning of fracture nonunion. If the nonunion shows a lack of biological activity, supplementation of some biological activity is required.[10,11] Biological activity of nonunions is usually assessed by conventional radiographs. The presence of callus formation is usually assessed as the presence of biological activity and the absence or paucity of callus formation is usually assessed as the absence or paucity of biological activity. The nonunions are classified radiologically into the hypertrophic type (elephant foot and horse hoof), oligotrophic type, comminuted type (torsion-wedge, dystrophic, and necrotic), defect type, and atrophic type [Table 1]. Synovial pseudarthrosis is a separate entity and is also an important pathology in fracture nonunion cases. However, assessing biological activity only by radiographic appearance is controversial. Poor callus visualization on radiographs may be due to not only poor biological activity but also inadequate fracture management, including reduction and fixation. Niikura *et al*. described scintigraphic uptake pattern of oligotrophic nonunion, which shows poor or absent callus formation radiologically, is notable. Fifty-six percent of radiologically oligotrophic nonunion demonstrated intense, uniform tracer uptake and only 17% demonstrated a photon-deficient area on bone scan.[12] The authors' results suggest that poor or absent callus visualization on radiographs does not always mean a lack of biological activity and it underestimates biological activity. Bone scan being functional imaging technique is more suitable technique for assessing biological activity. In the era of hybrid imaging, SPECT-CT can be considered as imaging of choice in such cases.

Niikura *et al*. gave scintigraphic uptake pattern for nonunion cases [Table 2].[12] Type 1: A photon-deficient area is absent and intense uniform uptake is observed. Type 2A: A definite photon-deficient cleft is present between two intense areas of uptake. Type 2B: A photon-deficient area is present other than Type 2A. Type 3: Uneven distributed uptake is observed without evidence of a photon-deficient area.

The degree of radiotracer uptake depends primarily on two factors: blood flow and new bone formation.[13-15] Because bone scintigraphy reflects the combination of blood flow and new bone formation, it is useful in assessing

Table 1: Radiological classification of fracture non-union

Fracture Non-Union
Hypertrophic type (elephant foot and horse hoof)
Oligotrophic type
Comminuted type (torsion-wedge, dystrophic, and necrotic)
Defect type
Atrophic type

Table 2: Scintigraphic uptake pattern for fracture non-union

	Fracture Non-Union
Type 1	A photon-deficient area is absent and intense uniform uptake is observed
Type 2A	A definite photon-deficient cleft is present between 2 intense areas of uptake
Type 2B	A photon-deficient area is present other than type 2A
Type 3	Uneven distributed uptake is observed without evidence of a photon-deficient area

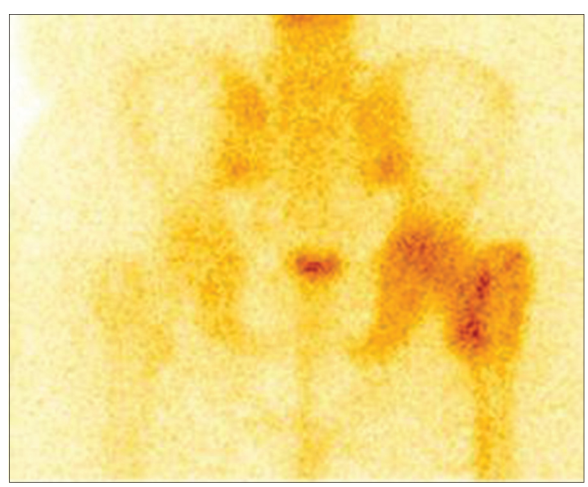

Figure 1: Posterior static image shows increased tracer uptake at trochanteric region of right femur without any cold/photon-deficient area within (pattern Type 1)

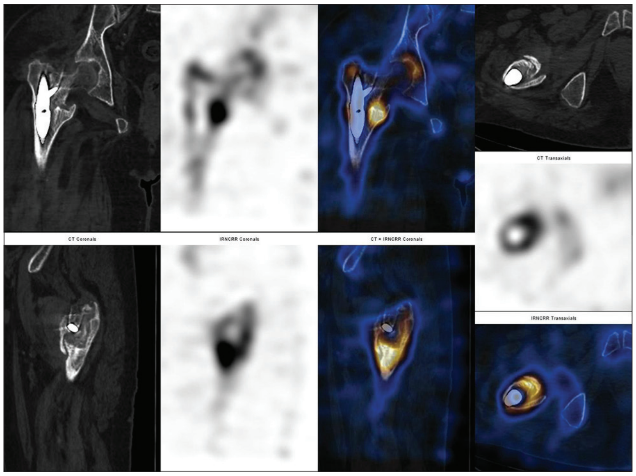

Figure 2: Single-photon emission computed tomography-computed tomography fusion images show increased tracer uptake at trochanteric region of right femur corresponding to oligotrophic nonunited fracture site on computed tomography correlation without any cold/photon-deficient area within

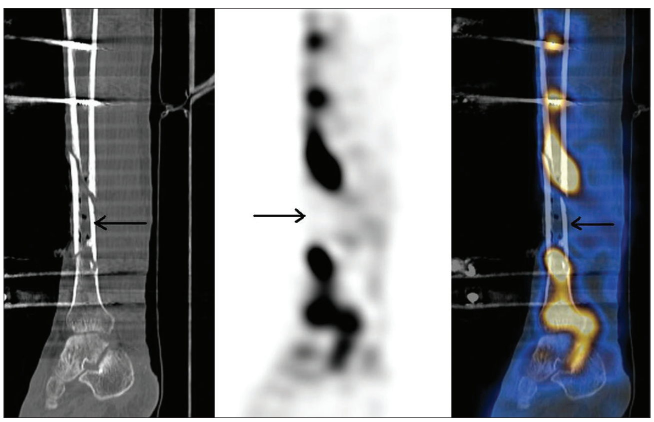

Figure 4: Single-photon emission computed tomography-computed tomography fusion images showed photopenic area involving small part of lower shaft of right tibia corresponding to fracture fragment on computed tomography correlation in a known comminuted fracture

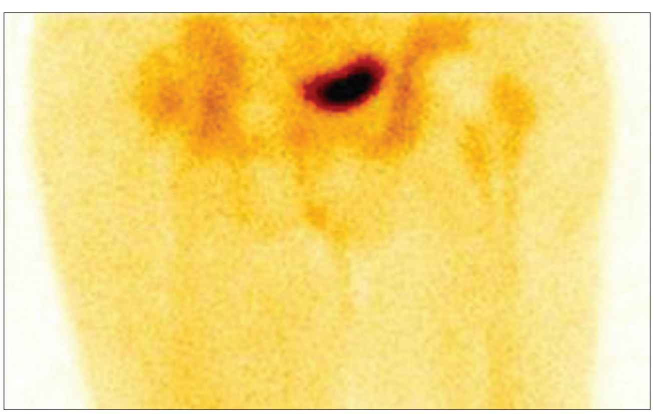

Figure 6: Posterior static image shows increased tracer uptake at trochanteric region of left femur without any cold/photon-deficient area within (pattern Type 1). Photopenic area is noted in right hip region (h/o right hip hemireplacement arthroplasty)

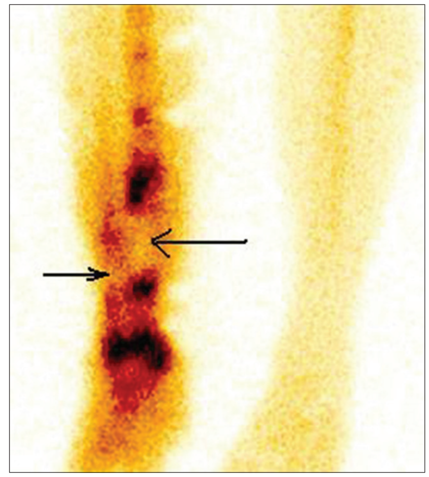

Figure 3: Anterior static image shows photopenic area involving small part of lower shaft of right tibia and fibula with patchy increased tracer uptake proximal and distal to fracture site (pattern Type 2B)

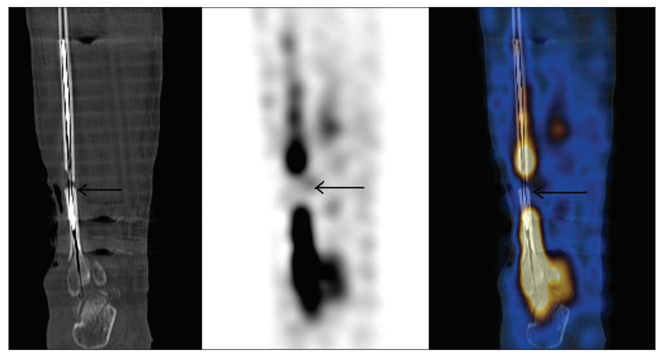

Figure 5: Single-photon emission computed tomography-computed tomography fusion images showed photopenic area involving small part of lower shaft of right fibula corresponding to fracture fragment on computed tomography correlation in a known comminuted fracture

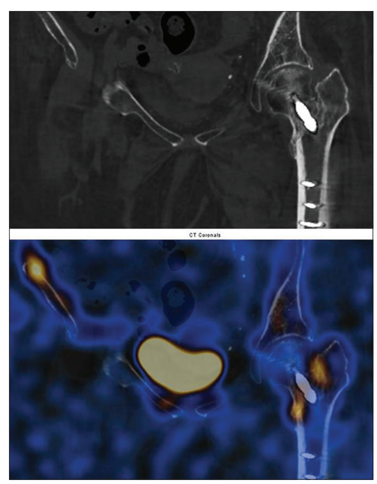

Figure 7: Single-photon emission computed tomography-computed tomography fusion images show increased tracer uptake at trochanteric region of left femur corresponding to oligotrophic nonunited fracture site on computed tomography correlation without any cold/photon-deficient area within

biological activity in nonunion cases. Bone scintigraphy is very useful and helps in guiding management in specific subset of cases such as nonhypertrophic nonunions. If a photon-deficient area is detected on bone scintigraphy, then an autologous bone graft can be supplemented in such cases. Other osteogenic supplementations, such as bone morphogenetic protein, are optional. If a photon-deficient area is not detected, then secure fixation is sufficient to achieve bony union. Hypertrophic nonunions do not need bone scintigraphy and secure fixation will lead to bony union.

Niikura *et al*. showed a correlation between the surgical findings and the photon-deficient findings on bone scintigraphy.[12] Nonhypertrophic nonunions with photon-deficient areas on bone scintigraphy demonstrated bone-deficient areas induced by comminution, gaps, or bone defects on surgical findings. Fibrous tissue was formed at the bone-deficient area. Therefore, these findings suggest that the fibrous tissue formed at the bone-deficient area is deficient in biological activity. The authors suggest that the deficiency of biological activity comprises a deficiency of both blood flow and osteogenic activity because little bleeding from the fibrous tissue was detected when it was excised. The degree of photon deficiency seen on bone scintigraphy correlates with the extent of the bone-deficient area. However, Reed *et al*.[16] reported that atrophic nonunions were not avascular by a histological investigation of biopsied human nonunion tissue. Garcia *et al*.[17] reported that in atrophic nonunions, the expression of vascular endothelial growth factor, which is an important inducer of angiogenesis, was not reduced and the expression of bone morphogenetic protein, which is an osteogenic mediator, was reduced compared with united fractures in an animal study. Hence, it is believed that blood supply is preserved, but osteogenic activity is decreased at the photon-deficient area; therefore, the supplementation of osteogenic activity is necessary and appropriate for the treatment approach in atrophic nonunions. Hence, it is unclear that the decrease in uptake indicates a decrease in blood flow, new bone formation, or both as reflected by bone scintigraphy. There are some limitations of bone scintigraphy in assessing biological activity.[18,19] Uptake in bone scintigraphy reflects blood flow and new bone formation;[13-15] however, it is difficult to know the ratio of these two factors based on single 3 h bone phase images. The flow image gives idea about blood flow while 3 h image shows the new bone formation activity. Hence, a reasonable idea about both these factors can be obtained by a three-phase bone scan. In addition, the presence of biological activity can be established if uptake is observed; therefore, qualitative assessment can be performed. However, quantitative assessment is difficult. This limitation should be considered when bone scintigraphy is used for the assessment of biological activity in fracture nonunion cases.

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Conflicts of interest

There are no conflicts of interest.

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