

99m-Tc-ubiquicidin scintigraphy in diagnosis of knee prosthesis infection and comparison with F-18 fluorodeoxy-glucose positron emission tomography/computed tomography

Koramadai Karuppusamy Kamaleshwaran, Rajkumar N¹, Vyshak Mohanan, Radhakrishnan Kalarikal, Ajit Sugunan Shinto

Department of Nuclear Medicine, PET/CT and Radionuclide Therapy, Kovai Medical Center and Hospital Limited, ¹Department of Orthopedics, Ganga Medical Centre and Hospitals Private Limited, Coimbatore, Tamil Nadu, India

ABSTRACT

Total knee arthroplasty has witnessed a significant increase in recent years. Despite the advantages of this surgical procedure, it has some complications, the most serious of which is prosthetic infection. The discrimination of bacterial infections from sterile inflammatory processes is of great importance in the management of periprosthetic infection (PPI). Ubiquicidin (UBI) is a synthetic antimicrobial peptide fragment reported to be highly infection-specific. Tc99m-UBI has recently been reported to be a promising radiotracer for infection imaging. We report a case of left knee PPI diagnosed using 99mTc-UBI scintigraphy and compared with F-18 fluorodeoxy-glucose positron emission tomography.

Keywords: Knee joint, prosthetic infection, Tc99m-ubiquicidin, fluorodeoxy-glucose-positron emission tomography

INTRODUCTION

As the number of orthopedic procedures continues to rise, there is a substantial increase in surgical implantation of internal devices and prostheses. Accordingly, the diagnosis of orthopedic implant infections, as one of the most important complications of the procedure, is becoming an increasingly common challenge. The noninvasive diagnostic differentiation between periprosthetic infection (PPI) and sterile inflammation is problematic, while clinical management decisions need to be made promptly in order to avoid subsequent serious complications.^[1] The current available imaging approaches, despite having high sensitivity, lack specificity for infections.^[2] Therefore, advances in the noninvasive differentiation between PPI and sterile inflammation are needed. Ubiquicidin (UBI) is a synthetic cationic antimicrobial peptide

that preferentially binds to bacterial cell membrane at the site of infection. Considering its affinity for bacterial components, UBI has been labeled with Tc99m and tested as a potential scintigraphic agent for diagnosis of suspected PPI.^[3] We report diagnostic value of Tc99m-UBI scintigraphy in differentiation of bacterial infection from sterile inflammation in suspected orthopedic knee implants.

CASE REPORT

A 55-year-old woman underwent bilateral knee replacement before 1-year. She developed left knee pain and swelling. In view of suspected PPI, she was referred for three phase bone scintigraphy. Blood pool phase showed increased tracer pooling in the left knee region [Figure 1]. Delayed whole body images show increased uptake in the left knee prosthetic bone interface [Figure 2]. Whole body Tc99m-UBI scintigraphy showed pooling of tracer in the same area of left knee region as in bone scintigraphy [Figure 3]. Static images of knee joint at 2 h showed interval increase in pooling of tracer [Figure 4]. ¹⁸F fluorodeoxy-glucose positron emission tomography (F-18 FDG PET/CT) images of the knee joint also show increased uptake in the left knee prosthesis-bone interface [Figure 5]. In view of increased uptake in all three scans, scan findings

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Address for correspondence:

Dr. Koramadai Karuppusamy Kamaleshwaran, Department of Nuclear Medicine, PET/CT and Radionuclide Therapy, Comprehensive Cancer Care Center, Kovai Medical Center and Hospital Limited, Coimbatore - 641 014, Tamil Nadu, India. E-mail: dr.kamaleshwar@gmail.com

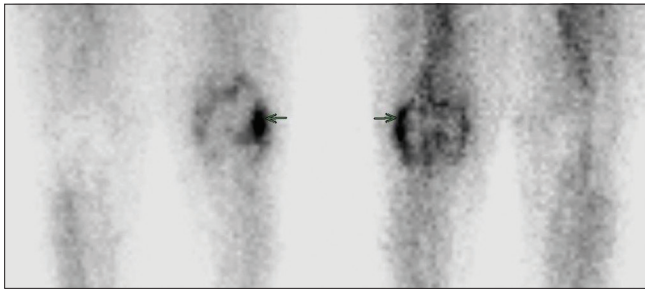


Figure 1: Tc99m-methylene diphosphonate blood pool phase showed increased tracer pooling in the left knee region (arrow)

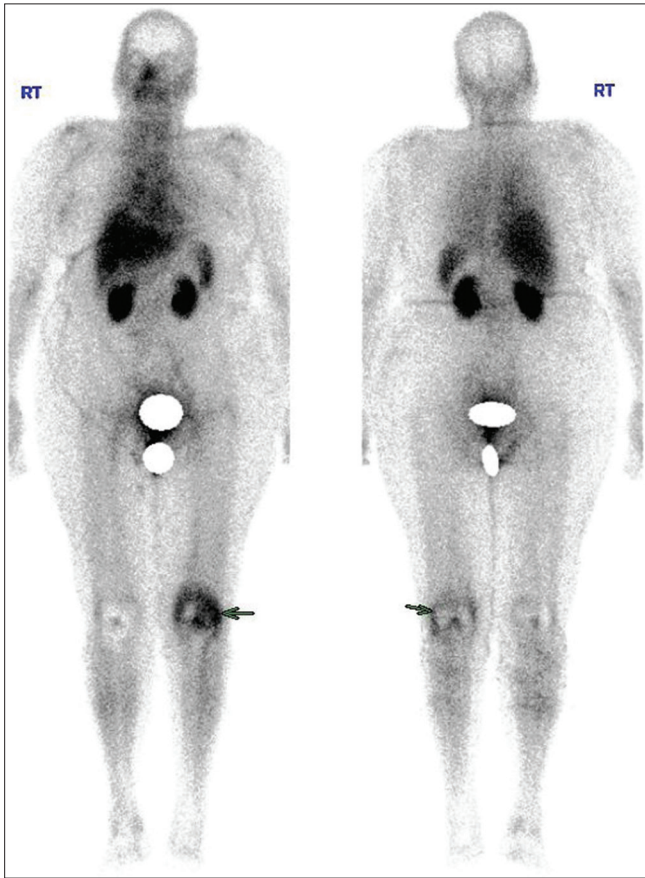


Figure 3: Tc99m-ubiquicidin whole body bone scan increased uptake in the left knee region (arrow). Also physiological uptake noted in liver and spleen

suggestive of infection were raised. Patient underwent debridement of the prosthesis, and bacterial culture was positive. She was started on antibiotics.

DISCUSSION

Total knee arthroplasty (TKA) is a common surgery for end-stage knee arthritis that is associated with significant improvements in pain, function, and quality-of-life. Outcomes following TKA are excellent in the majority of the patients. Perhaps the most challenging complication following TKA is PPI. PPI occurs in 1–2% of primary TKAs and 3–5% of revision TKAs.^[4] The differentiation of infection from aseptic

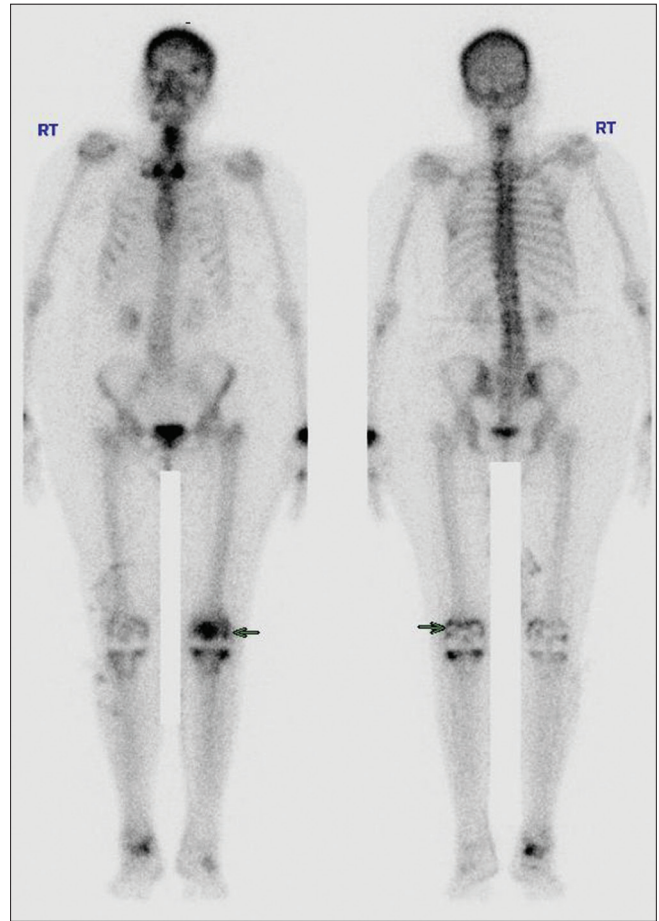


Figure 2: Tc99m-methylene diphosphonate whole body bone scan increased uptake in the left knee prosthetic bone interface (arrow)

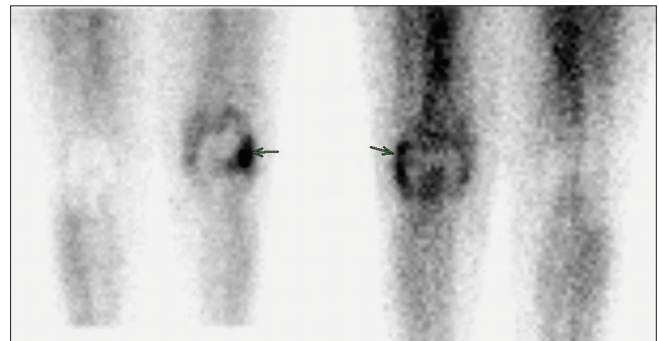


Figure 4: Static images of ^{99m}Tc-ubiquicidin showing increased uptake in left knee localized exactly to blood pool uptake in methylene diphosphonate (arrow)

loosening is of great importance because loosening with PPI is a catastrophic complication. Although the differential diagnosis of the two conditions is essential to the success of further revision surgery, the detection of PPI remains difficult. Although one stage revision surgery is indicated for patients with aseptic loosening, two-stage revision surgery in which implantation after eradication of infection by several surgical steps including removal of the implants, debridement, and antibiotics-loaded cement beads, is usually required for the patients with PPI.^[5]

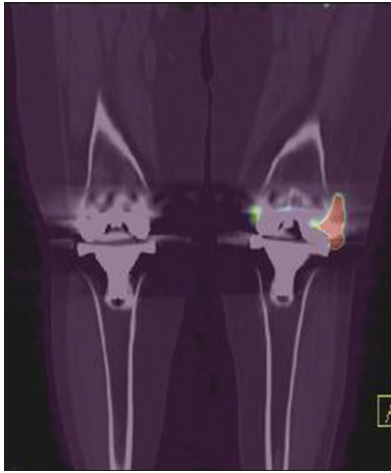


Figure 5: Coronal fused positron emission tomography-computed tomography also showing increased uptake in left knee prosthesis region correlating with methylene diphosphonate and ubiquicidin

Several imaging modalities are available to assist surgeons in diagnosing PPI in TKA. Radiographs showing periosteal new bone formation, scattered foci of osteolysis and subchondral bone resorption are highly suggestive of infection but are typically late findings. Periprosthetic radiolucency may be unrelated to a septic process, and serial radiographs help rule out other conditions like wear, osteolysis or fracture.^[6] Radionuclide scintigraphy may be helpful in the diagnosis of PPI in TKA, because their results are not impacted by the presence of metallic implants. Triple-phase Tc99m-methylene diphosphonate bone scintigraphy (TPBS) is a simple, widely available test which is quite sensitive in detecting bone remodeling changes around TKA components; however, it cannot distinguish between aseptic loosening and TKA infection TPBS does have a high negative predictive value, however, making it a useful initial screening test. Labeled antigranulocyte antibody or labeled leukocyte study has Sensitivity, specificity, and accuracy of 100%, 97%, and 98%, respectively.^[7] Boubaker *et al.* reported that Tc99m-besilesomab was 67% sensitive and 75% specific for diagnosing prosthetic hip infection.^[8]

F-18 fluorodeoxy-glucose PET/CT has been recently evaluated for diagnosis of PPI in TKA. Inflammatory cells express more glucose transporters, resulting in intracellular accumulation of F-18 FDG-6 phosphate which cannot be metabolized by the cell and can be identified by PET imaging. The advantages of a PET scan are that only one injection is required and the results are available within 4 h. However, it is not widely available, is expensive and can produce false positives secondary to uptake of FDG in aseptic inflammation around implants. In their meta-analysis, Reinartz reported that the accuracy of the TPBS, white blood cell imaging, and FDG-PET scan of PPI for TKA was 81%, 84%, and 83% respectively.^[9] Aksoy *et al.* showed sensitivity, specificity, and positive and negative predictive values of FDG-labeled leukocyte PET/CT were 93.3%, 97.4%, 93.3%, and 97.4%, respectively.^[10]

Antimicrobial peptides bind to the bacterial cell membrane. Their expression may be constant or induced on contact with microbes. They also can be transported via leukocytes.^[11] Among all the human-derived antimicrobial peptides tested, the UBI has demonstrated the greatest promise. Tc99m-UBI is a small synthetic peptide, which originated from human UBI and which attaches preferentially to bacteria *in vitro* and not to activated leukocytes.^[12] The Tc99m-UBI scans have depicted the most promising results for delineation between infection and inflammation in animal models and human investigations.^[13,14] Meta-analysis by Ostovar showed that Tc99m-UBI scans had a reasonably high differentiation ability in recognizing an infection among patients who had possible infection in the soft tissue, musculoskeletal system, and prosthesis, and overall accuracy was 93.7%.^[15]

A study by Akhtar *et al.* showed Tc99m-UBI is a highly sensitive and specific agent for localizing infective foci in bone and soft tissues of humans. The optimum imaging time for delineation between infectious and inflammatory process is 30 min after intravenous administration of radiotracer.^[16] In a study by Aryana *et al.* evaluated the feasibility of Tc99m-UBI scintigraphy in the detection of infectious foci in painful hip prosthesis. The sensitivity, specificity, negative and positive predictive values and accuracy of the study were all 100%.^[3] Our case demonstrates uptake in bone scintigraphy, 99mTc-UBI and FDG PET/CT confirming PPI in the knee joint.

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