Case Report

A Comparative Case Study between Gallium-67 Citrate Scintigraphy and Gallium-68 Citrate Positron Emission Tomography-Computed Tomography in Bone Infection

Abstract

Bone infections are a common problem, and early diagnosis and intervention can lead to better clinical outcomes and prognoses. Here, we compare the well-known tracers Gallium-67 (Ga-67) citrate versus Ga-68 citrate in the diagnosis of infections.

Keywords: *Bone infections, Gallium-67 citrate scintigraphy, Ga-68 citrate positron emission tomography-computed tomography*

Hanna Elizabeth Johnson, Junita Rachel John, Justin Benjamin, Julie Hephzibah

Department of Nuclear Medicine, Christian Medical College, Vellore, Tamil Nadu, India

Introduction

Undiagnosed infections in patients often result in long hospital stay and poorer clinical outcomes. Osteomyelitis is an infection of the bone and can result in chronic debilitating conditions with repeated hospital visits, if undiagnosed or misdiagnosed, due to the resulting inadequate treatment. Infections to the bone can spread through bloodstream or from infected tissue surrounding it. Gallium-67 (Ga-67) citrate scintigraphy has been a promising infection imaging agent for the past 30 years. In this case report, we compared the utility of Ga-67 citrate scintigraphy and Ga-68 citrate positron emission tomography-computed tomography (PET-CT) to determine the incremental value of the latter in infection imaging. To the author's knowledge, only one such comparative study has been published to date by Segard *et al*.[1]

Case Report

We report a case of a 51-year-old gentleman who presented with a history of swelling associated with discharge over the inner aspect of the right thigh 15 days before his visit to orthopedics OPD in our hospital. The discharge was serious with occasional pus and no bony spicules. He also gave a history of pain over the right thigh for 2 months. A year ago, he had sustained a fracture to the right distal femur, following which he underwent surgery for stabilization and internal fixation. He gave a history of recent-onset diabetes mellitus, being managed on oral hypoglycemic agents.

On examination, he was afebrile and other vital parameters were within normal limits. His systemic examination was unremarkable. His gait was aided and unstable with a walker. He had a flexion deformity of ~15° at his knee with external rotation at the hip and ankle at ease. His biochemical parameters revealed leukocytosis with raised inflammatory markers. His pus culture grew methicillin-resistant *Staphylococcus aureus*. For assessment before surgery and to rule out any other focus of infection, he underwent Ga-67 citrate scintigraphy. The patient also underwent Ga-68 citrate PET-CT for structural assessment preoperatively.

Following intravenous (IV) injection of 4 mCi/148 MBq of Ga-67 citrate, whole body and spot view images of the pelvis and thighs were obtained at 3.5 h and at 20 h [Figure 1]. Abnormally increased tracer accumulation was demonstrated in the distal 1/3rd of the right femur at early imaging which also persisted in the delayed images. The rest of the body did not reveal any abnormal tracer accumulation.

How to cite this article: Johnson HE, John JR, Benjamin J, Hephzibah J. A comparative case study between gallium-67 citrate scintigraphy and gallium-68 citrate positron emission tomography-computed tomography in bone infection. Indian J Nucl Med 2022;37:271-3.

Address for correspondence:
Dr. Julie Hephzibah, Department of Nuclear Medicine, Christian Medical College, Vellore, Tamil Nadu, India.
E-mail: drjulsan@cmcvellore.ac.in

Received: 10-10-2021
Accepted: 27-10-2021
Published: 02-11-2022

Access this article online

Website: www.ijnm.in

DOI: 10.4103/ijnm.ijnm_158_21

Quick Response Code:

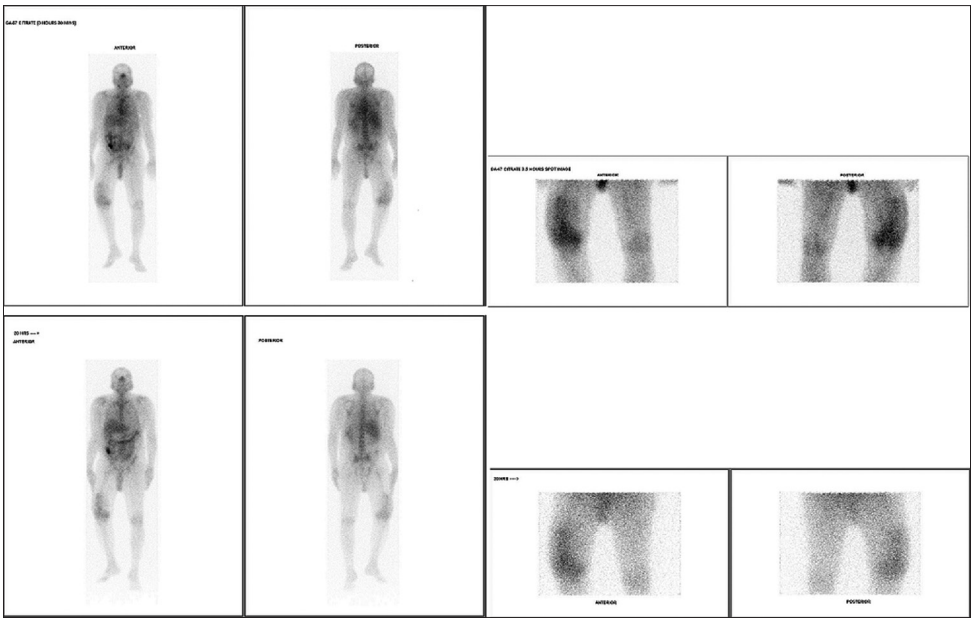

Figure 1: Top row: Gallium-67 citrate scintigraphy images of the whole body in anterior and posterior view at 3 h and 30 min; bottom row: Gallium-67 citrate scintigraphy images of the whole body in anterior and posterior view at 20 h

This was followed by Ga-68 citrate PET scan of the pelvis and lower limbs. Contrast CT and PET images were acquired at 36 min and 90 min after IV injection of 4.6 mCi/170.2 MBq of Ga-68 citrate. Fused PET and CT images were reviewed [Figure 2]. The scan showed Ga-68 citrate avid foci in the fracture involving the metaphyseal region of the right distal femur with associated irregular callous formation. He was diagnosed with nonunited right distal femur fracture due to infection. He was taken up by the orthopedic team for debridement, implant removal, and external fixator application. The histopathological features showed ulceration of epidermis with necrosis of superficial dermis displaying edema, infarcted and congested blood vessels, and aggregates of neutrophils. The viable deep dermis was replaced by inflammatory granulation tissue composed of moderate to dense infiltrates of lymphocytes, plasma cells, and foamy histiocytes, foci of fibrosis, and proliferated vascular channels confirming osteomyelitis.

Discussion: Osteomyelitis can result in acute or chronic inflammation. There are three modes of spread; either hematogenous, local spread from adjacent infected tissue, or direct inoculation during a surgical procedure/trauma.[2] Host-related factors that predispose patients to osteomyelitis include diabetes mellitus,[3] sickle cell anemia,[4] and chronic granulomatous diseases.[2] It can lead to high rates of morbidity if missed or left untreated.

Radiological investigations such as X-ray and CT often do not show changes in the early stages of infection. Despite its high sensitivity, magnetic resonance imaging is of limited value in the presence of metallic implants. Biochemical markers such as erythrocyte sedimentation rate, C-reactive protein, and total counts are useful but lack specificity.[5]

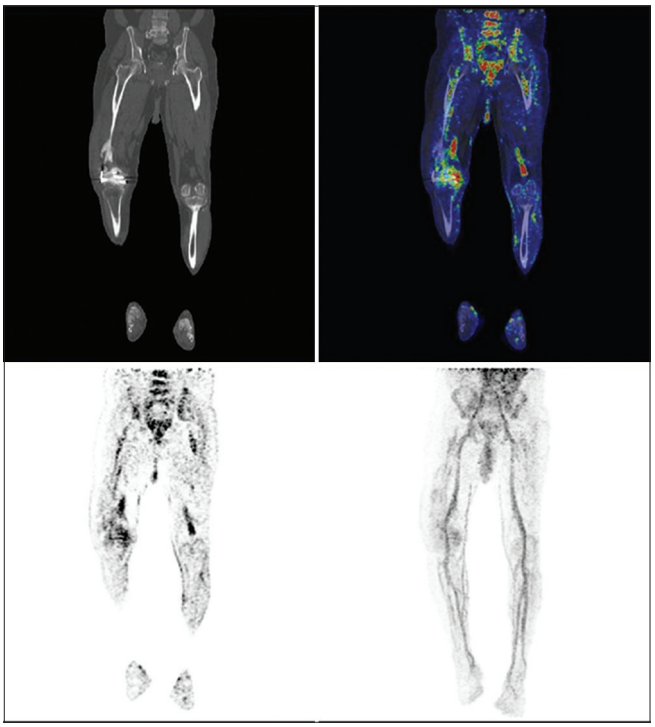

Figure 2: Views of coronal section of both thighs from a Ga-68 citrate positron emission tomography-computed tomography scan. (Top left) computed tomography: Metal implant in the right distal femur with fracture; (top right) Fused positron emission tomography-computed tomography: Avid infectious focus in the right distal femur; (below left) positron emission tomography: Avid infectious focus in the right distal femur; (below right) maximum intensity projection image: physiological uptake with the focus of increased tracer activity in the right distal thigh

Functional imaging in nuclear medicine utilizing tracers that bind to cells specific to infections can be used in diagnosis at any stage. Early diagnosis and management enable better outcomes. Both Ga-67 and Ga-68 citrate

have a similar mechanism of uptake in infections. In patients with infections, gallium leaks into the site of inflammation from the vascular epithelium or is taken up by pathogen themselves. It then binds to lactoferrin that is present in abundance in leukocytes. The gallium-bound lactoferrin finally binds to macrophages at the inflammatory site. Organisms grown in a low-iron environment produce siderophores. These siderophores have a high affinity for iron as well as gallium. Most tissues have very little free iron; hence, these pathogens produce siderophores. The siderophore-gallium complex enters the cell directly.[6]

Ga-68 citrate PET-CT has several advantages over Ga-67 citrate scintigraphy. Ga-68 is produced through an on-site generator.[5] It is a positron-emitting radionuclide; hence, suitable for imaging using a PET scanner. When combined with CT, it has the advantage of superior imaging quality and resolution. It has a shorter half-life of 68 min leading to faster imaging due to shorter uptake time. The imaging can be completed in a days' time with a lower radiation dose[7] as compared to Ga-67 which has a much longer half-life of 78 h with imaging protocols up to 72-h. Ga-67 also requires a high-energy cyclotron for production which makes it expensive and not readily available.

The study done by Nanni *et al*. evaluated the utility of Ga-68 citrate PET-CT in a population of patients with suspected bone infections and reported an overall accuracy of 90% with a sensitivity of 100% and a specificity of ~76%.[8]

In our case report, imaging with both tracers showed comparable results for the diagnosis of infection with superior imaging quality and resolution provided by Ga-68 citrate PET-CT, which further guided the surgical plan for management. Ga-68 citrate has not only shown promising results in diagnosing skeletal infections but with the added advantage of a quicker preparation time, lower cost, and lower radiation dose.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Segard T, Morandeau LM, Dunne ML, Robinson JO, Murray RJ, Geelhoed EA, *et al.* Comparison between gallium-68 citrate positron emission tomography-computed tomography and gallium-67 citrate scintigraphy for infection imaging. Intern Med J 2019;49:1016-22.
2. Calhoun JH, Manring MM, Shirtliff M. Osteomyelitis of the long bones. Semin Plast Surg 2009;23:59-72.
3. Moutschen MP, Scheen AJ, Lefebvre PJ. Impaired immune responses in diabetes mellitus: Analysis of the factors and mechanisms involved. Relevance to the increased susceptibility of diabetic patients to specific infections. Diabete Metab 1992;18:187-201.
4. Epps CH Jr., Bryant DD 3rd, Coles MJ, Castro O. Osteomyelitis in patients who have sickle-cell disease. Diagnosis and management. J Bone Joint Surg Am 1991;73:1281-94.
5. Xu T, Chen Y. Research Progress of [68Ga]Citrate PET's Utility in Infection and Inflammation Imaging: a Review. Mol Imaging Biol. 2020;22:22-32. doi: 10.1007/s11307-019-01366-x. PMID: 31076971.
6. Bernstein LR. Mechanisms of therapeutic activity for gallium. Pharmacol Rev 1998;50:665-82.
7. Palestro CJ. The current role of gallium imaging in infection. Semin Nucl Med 1994;24:128-41.
8. Nanni C, Errani C, Boriani L, Fantini L, Ambrosini V, Boschi S, *et al.* 68Ga-citrate PET/CT for evaluating patients with infections of the bone: Preliminary results. J Nucl Med 2010;51:1932-6.