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Original article

Is there a Role for Gallium-67 Citrate SPECT/CT, in Patients with Renal Impairment or Who are Renal Transplant Recipients, in Identifying and Localizing Suspected Infection?

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Abstract

To assess the added value of single-photon emission computed tomography/computed tomography (SPECT/CT) in patients with end-stage renal failure (ESRF) or renal transplant recipients in whom focal infection was suspected. Gallium-67 (Ga-67) citrate scintigrams of 18 patients (10 in ESRF and eight with renal transplants) were reviewed. Sites of abnormal uptake seen on the whole body and SPECT were noted. A SPECT/CT was also reviewed to see if additional information could be obtained. Imaging results were compared with the final diagnosis. Overall, 14 out of 18 (78%) patients had a proven cause to explain symptoms while four patients did not have a final cause identified. Infection was proven in the final diagnosis in 12 out of 14 (86%) patients. Of the 10 patients with ESRF, six had confirmed infection with the Ga-67 citrate study correctly identifying five out of six (83%) patients, and SPECT/CT providing additional information in four out of five (80%) patients. In the eight renal transplant recipients, six had a confirmed source of infection (all identified by the Ga-67 citrate study). SPECT/CT provided additional information in two out of six (33%) patients. Ga-67 citrate imaging had an overall sensitivity of 13/14 (93%), with one false negative. SPECT/CT provided an additional contribution in eight out of 18 (44%) patients by better defining the location/extent of infection and differentiating the physiological from the pathological uptake.

Keywords: Gallium-67 citrate, infection, renal failure, single-photon emission computed tomography/computed tomography

Introduction

A major reason why patients with end-stage renal failure (ESRF) have increased morbidity and mortality is infection.[1-3] Patients who have received a renal transplant are also susceptible to infection, primarily as a result of immunosuppression but also due to a shorter ureter predisposing to pyelonephritis.[4-6] Pyrexia of unknown origin (PUO) is a particularly common scenario in this population. Conventional cross-sectional imaging may fail to localize the cause of the fever. A nuclear medicine department serving a hospital with an active renal and renal transplant services may thus be asked to perform imaging in patients with suspected infection and inflammation. In our institution, it has been the practice for many years to opt for gallium-67 (Ga-67) citrate scintigraphy as the technique of choice in this clinical scenario. Ga-67 citrate is a sensitive but nonspecific imaging agent that not only identifies the sites of infection but also detects other causes of PUO such as posttransplant lymphoproliferative disorder (PTLD) or other inflammatory diseases, e.g., sarcoidosis.[7,8] By 48 h postinjection, Ga-67 citrate is not renally excreted and has no physiological uptake in noninflamed and noninfected kidneys. Consequently, it has potential advantages over Tc-99m hexamethylpropyleneamine oxime (HMPAO) labeled white blood cells (WBCs) and F-18-fluorodeoxyglucose (FDG) for imaging possible infections in the renal tract.[9,10]

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The spatial resolution of Ga-67 scintigraphy is poor due to the radionuclide having four photopeaks (93 keV, 185 keV, 288 keV, and 394 keV), all with relatively low abundance. The tracer is also taken up physiologically by various organs, i.e. at sites where there is no disease. Thus, variable uptake may be seen, e.g., in the colon and it can be difficult to identify the exact location of a site of abnormal uptake and determine whether the uptake is pathological or physiological.

The advent of high quality single-photon emission computed tomography/computed tomography (SPECT/CT) has been shown to improve both localization and specificity in orthopedic and oncological conditions.[11-13] In infection, it has been shown that the use of SPECT/CT has resulted in an improved accuracy of reporting, although none of these studies have looked at those patients with a renal transplant or significant renal failure.[14-16]

The aim of this study was to determine whether SPECT/CT could improve the accuracy and the localization of Ga-67 imaging in our institution when compared with our previous standard of whole body imaging (WBI) and SPECT (without CT), which was until recently the standard of care in our institution for patients with suspected infection who had ESRF or were renal transplant recipients.

Patients and Methods

General

This study is a retrospective review looking at a consecutive series of patients referred to nuclear medicine to identify the possible sites of sepsis. All these patients had had multiple previous radiological investigations without a cause being identified.

Patient population

A total of 18 patients were referred for Ga-67 citrate SPECT/CT from the renal unit over a 14-month period [Table 1]. There were 10 patients in Group A comprising patients with ESRF attending a predialysis clinic or who were already on dialysis. Three of these patients had suspected infection of adult polycystic kidney disease (APCKD); three had suspected bone infections; three had a persistently raised C-reactive protein (CRP), the cause of which had not been elucidated from other investigations; and one patient had a suspected graft infection.

Group B comprised eight patients all of whom had received a renal transplant, which was functioning in six patients. In three of these patients, an infected graft was suspected (although in one of these patients, the clinicians were unsure if the site of infection was native or due to transplant). In the fourth patient, the site of infection was thought to be within a cyst in a native polycystic kidney. Another patient was suspected of having a vascular graft infection. In three patients, the site was unknown although one of these patients was suspected of having PTLD.

Table 1: Patient characteristics

Age/gender	Dialysis	Clinical presentation
Group A patients with ESRF if on dialysis		
63/Female	PD	PUO; APCKD
57/Male	Nil	APCKD Infected kidney
47/Male	Nil	APCKD? Left hip infection
86/Male	Nil	CRF, PUO, raised CRP
50/Male	HD	CRP raised
82/Male	HD	Lumbar spine pain? Infection
81/Female	Nil	? Lumbar discitis
90/Female	HD	? Discitis
83/Female	HD	? Vascular graft infection
65/Male	HD	CRP raised; unexplained abdominal pain
Group B patients with renal transplants		
47/Male	No on HD	? Infected transplant
27/Female	Yes	? Infected transplant
52/Female	Yes	? Infected transplant/native kidney
45/Male	Yes	APCKD? Infected cyst
40/Female	No on HD	? infected vascular graft
37/Male	Yes	PUO
50/Male	Yes	PUO
61/Male	Yes	PUO? Infection? PTLD

APCKD: Adult polycystic kidney disease; CRF: Chronic renal failure; CRP: C-reactive protein; HD: Hemodialysis; PD: Peritoneal dialysis; PTLD: Posttransplant lymphoproliferative disorder; PUO: Pyrexia of unknown origin

Imaging protocol

Whole body Ga-67 citrate scintigraphy was performed 48 h after injection of 150 MBq Ga-67 citrate using a dual-headed, variable-angle gamma-camera (Siemens Healthcare, Erlangen, Germany) fitted with a medium-energy collimator. The three main energy peaks of Ga-67, such as 93 keV, 184 keV, and 300 keV, were chosen. Whole body images were acquired at 8 cm/min. After inspection of the whole body images by a trained nuclear medicine physician, a SPECT/CT was performed of the body region that was suspected to contain the site of infection, or which had been suspicious on WBI.

SPECT images were acquired in a 60-step (20 s/stop), 360° noncircular orbit and reconstructed in a 128 × 128 matrix, using a three-dimensional ordered subsets expectation maximization algorithm. Data were reconstructed iteratively using Siemens Healthcare, Erlangen, Germany with four subsets and eight iterations, and applying a Gaussian filter.

SPECT studies were viewed in the coronal, axial, and sagittal planes and in a reprojection.

A low-dose CT transmission scan was acquired after the SPECT study. The CT parameters used were a voltage of

130 kVp and an electric charge of 40-65 mAs (40 mAs for the thorax and 65 mAs for the abdomen) modulated with a "dosecare package." The CT was reconstructed using a 512 × 512 matrix at a slice thickness of 5 mm. Transmission data were registered with the emission data using the Siemens Healthcare, Erlangen, Germany. CT correction for attenuation was applied to the SPECT images.

Matching pairs of X-ray transmission and nuclear medicine emission images were fused using the Siemens Healthcare, Erlangen, Germany, and hybrid images of overlying transmission (CT) and emission (SPECT) data were generated.

In total, 34 regions (16 abdominal, 15 pelvic, and three chest) were evaluated. The SPECT/CT images were also visually inspected to exclude any misregistration using the reference landmarks. No misalignment was identified in the SPECT/CT studies of the 18 patients.

Interpretation criteria

Because many of these patients were frequent attenders at the department of nuclear medicine for multiple scintigraphic tests, a truly "blind" read of the results could not be achieved as these patients were well-known to all the staff. Therefore, readings by two experienced nuclear medicine specialists were performed in a clinical scenario and they were aware of the patients' clinical history and the results of previously performed conventional imaging tests before they reviewed the scintigraphic data, including the planar and the SPECT images, recording any sites of suspected pathology. After the results of the planar and the SPECT images had been recorded, the SPECT/CT images were subsequently evaluated and interpreted in the same manner. Any focus of increased uptake not related to normal physiologic biodistribution of radiopharmaceutical in the suspicious region was considered to represent pathology. Any disagreements on the interpretation were settled by a consensual agreement between the two specialists.

SPECT/CT was considered contributory when it provided data that could not be obtained from the assessment of the planar and the SPECT images alone concerning the presence of pathology or its precise location. The results were then compared with the final diagnosis, which was derived from the microbiological findings (n = 11), histology (n = 1), and/or correlative imaging data (n = 14).

Results

Patients with renal failure/on dialysis (Group A)

In the 10 patients with severe renal impairment (Group A), infection was confirmed in six (60%) patients [Table 2]. In five out of six (83%) patients, the whole body and SPECT study identified the site of infection correctly. In one out of six (17%) patients (patient 7), the final diagnosis of discitis was not identified on the Ga-67 study. In four out of five (80%) patients (patients 2, 3, 6, and 10), SPECT/CT was able to localize and define the extent of infection more precisely than the planar and the SPECT alone. Of the remaining four patients, no infection was found in three patients (patients 1, 4, 8), with SPECT/CT adding value in one patient, confirming the focal uptake on conventional scintigraphy to be physiological (patient 1). The last patient (patient 5) had inflammatory disease identified.

Patients with transplants (Group B)

There were six (75%) confirmed infections in the eight patients with renal transplants that were imaged. All the six patients were diagnosed using the Ga-67 citrate scan. SPECT/CT provided additional information for two out of six (33%) patients (patients 15 and 17). In patient 15, the uptake was confirmed to localize to a soft tissue collection (and not bowel uptake) while in patient 17, the extent of infection was better defined on SPECT/CT.

One of the remaining patients had myositis (which was seen equally well with conventional scintigraphy and SPECT/CT). The last remaining patient had PTLD, and SPECT/CT helped raise the suspicion of this diagnosis as lymph node uptake was not identified on the whole body or SPECT alone.

Summary

Of the 18 patients imaged, 14 (78%) had a proven cause to explain the symptoms while four patients did not have a final cause identified. Infection was proven as the final diagnosis in 12 out of 14 (86%) patients. Ga-67 imaging had an overall sensitivity of 13/14 (93%), with one false negative. SPECT/CT provided an additional contribution in eight out of 18 (44%) patients by better defining the location/extent of infection and differentiating the physiological from the pathological uptake.

Discussion

The results of this retrospective study show that SPECT/CT can improve the accuracy of Ga-67 citrate imaging in this patient group. In our study, like that of others reported in the literature, the main improvement is of specificity.[10-16] The site of tracer uptake could more accurately be defined [Figures 1 and 2]. In addition, a contemporaneous CT (albeit noncontrast and of reduced mAs) may enable a diagnosis to be established even if there is no Ga-67 uptake at that site.[14,15]

This study demonstrated that SPECT/CT contributed additional information that was clinically useful in over 40% of the patients imaged. This additional

Table 2: Clinical results

Patient no.	WB+SPECT	SPECT/CT	Contribution of SPECT/CT	Final diagnosis
Group A patients with end-stage renal failure if on dialysis				
1	Uptake adjacent to kidney (bowel)	Negative	Excluded uptake as physiological	No infection
2	Uptake in one kidney	Upper pole one kidney cyst	Defined level/extent of abnormality	Infection in kidney cyst
3	Uptake in left hip	Left hip infection	Defined level/extent of abnormality	Infected left hip
4	Negative	Negative	None	AAA: Noninfected
5	Uptake I SCJ	Degenerative left SCJ	None	Inflammation left SCJ
6	Uptake I3	Uptake I3-I4 disc	Define level/extent of abnormality	Discitis
7	Negative	Negative	None	Discitis
8	Physiological large bowel	Physiological activity	None	No infection/inflammation
9	Uptake right lung	Right lower lobe	None	Pneumonia
10	Left abdomen	Splenic collection	Defined location and confirmed as a soft tissue collection	Pancreatitis and splenic collection
Group B patients with renal transplants				
11	Uptake in transplant	Uptake in transplant	None	Infected transplant
12	Uptake in thigh muscles	Uptake in thigh muscles	None	Myositis
13	Uptake in native kidney and transplant	Uptake in native kidney and transplant	None	Infected native kidney and transplant
14	Uptake in native kidney	Uptake in native kidney	None	Infected native kidney
15	Uptake RIF	Abscess RIF	Defined focal uptake as infection	Abscess RIF
16	Uptake in lungs	Uptake in lungs	Nil	Chest infection
17	Uptake in right flank	Infection: Right psoas extending into right pelvis	Defined extent of infection	Psoas and pelvic abscess
18	Uptake in spine and left ilium	Uptake in spine, left ilium and abdominal nodes	Lymph node not seen on planar/SPECT	PTLD

AAA: Abdominal aortic aneurysm; AVN: Avascular necrosis; PTLD: Posttransplant lymphoproliferative disorder; SCJ: Sternoclavicular joint; RIF: Right iliac fossa

information may justify the additional radiation burden of 1-2 mSv in these patients attributed to the use of CT. The additional financial cost of SPECT/CT versus SPECT alone may also be justified if a diagnosis is reached more promptly.

Despite these patients being recognized as a clinically challenging group, the results of this study are similar to that obtained in other studies looking at different patient groups. For example, in 82 patients with a mixture of soft tissue and bone infections imaged with In-111 leukocytes or Ga-67 citrate, additional information was found in 48% of patients by the additional use of SPECT/CT.[17] In a group of 28 patients with orthopedic infections imaged with Tc-99m HMPAO-labeled WBCs, SPECT/CT produced an improved accuracy of reporting in 36% of patients.[16] In addition, there are case reports that show the utility of Ga-67 citrate SPECT/CT in suspected adult with infected polycystic kidneys and perirenal transplant infections.[8-10]

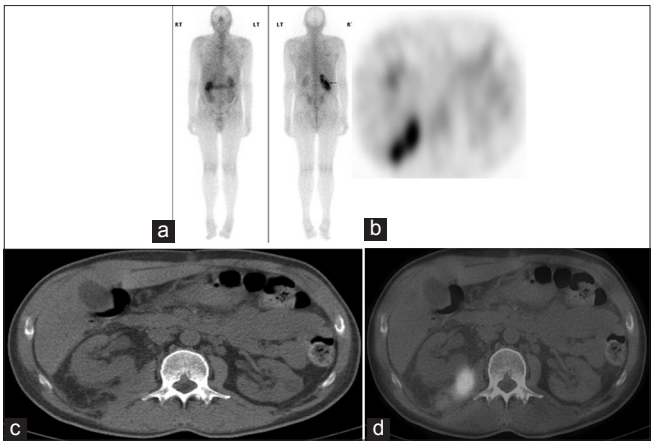

Figure 1: Ga-67 citrate study in a renal transplant recipient with fever of unknown origin (patient 17). The whole-body study (a) suggests uptake in the right posterior upper abdomen suspicious of infection in the native right kidney. A transverse SPECT (b), low dose CT (c), and fused SPECT/CT (d) were viewed. On SPECT/CT, abnormal uptake lies within the right psoas muscle and posterior pararenal space and is separate from the right kidney

An alternative method would be to use F-18 FDG positron emission tomography-CT (PET-CT). A series of studies has shown that this modality can be accurate in patients with a wide range of infections including PUO.[18-21] While there are no studies in the same patient groups like that of our study [chronic renal failure (CRF) and postrenal transplant], the incidence of infection lying within the renal tract itself was high (29%). Using F-18 FDG PET-CT, the route of tracer elimination (i.e. renal) can lead to difficulties in the interpretation of the images, as the pathological tracer uptake is much more difficult to distinguish than the physiological. In a few reports, there has been limited evidence that F-18 FDG PET may still be useful in the infected renal cyst.[22,23] In addition, the

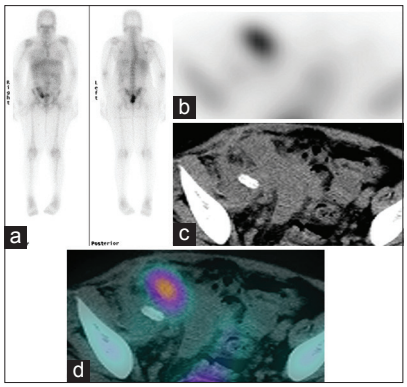

Figure 2: Ga-67 citrate study in a renal transplant recipient with fever of unknown origin and a suspected vascular graft infection (patient 15). The whole body study (a) suggests uptake within the right iliac fossa. A transverse SPECT (b), low dose CT (c), and fused SPECT/CT (d) were viewed. The SPECT/CT demonstrates that the abnormal uptake of tracer localized to a soft tissue collection in the right iliac fossa, which was confirmed as an abscess on ultrasound aspirate

use of F-18 FDG for infection imaging is not universally funded or reimbursed.

Therefore, it would appear from this retrospective review that SPECT/CT in Ga-67 citrate imaging may have a role in imaging infection in patients with advanced renal disease, on dialysis or having received a renal transplant. Further work needs to be done to determine if SPECT/CT can be combined with other single photon imaging agents such as radiolabeled leukocytes.

References

1. Dalrymple LS, Johansen KL, Chertow GM, Cheng SC, Grimes B, Gold EB, *et al*. Infection-related hospitalizations in older patients with ESRD. Am J Kidney Dis 2010;53:522-30.
2. Iseki K, Tozawa M, Yoshi S, Fukiyama K. Serum C-reactive protein (CRP) and risk of death in chronic dialysis patients. Nephrol Dial Transplant 1999;14:1956-60.
3. Akbar SA, Jafri SZ, Amendola MA, Madrazo BL, Salem R, Bis KG. Complications of renal transplantation. Radiographics 2005;25:1335-56.
4. Pourmand G, Pourmand M, Salem S, Mehrsai A, Taheri Mahmoudi M, Nikoobakht M, *et al*. Posttransplant infectious complications: A prospective study on 142 kidney allograft recipients. Urol J 2006;3:23-31.
5. Zukowski M, Bohatyrewicz R, Biernawska J, Kotfis K, Zegan M, Knap R, *et al*. Risk factors for septic complications in kidney transplant recipients. Transplant Proc 2009;41:3043-5.
6. Dupont PJ, Psimenou E, Lord R, Buscombe JR, Hilson AJ, Sweny P. Late recurrent urinary tract infections may produce renal allograft scarring even in the absence of symptoms or vesicoureteric reflux. Transplantation 2007;84:351-5.
7. Chiffoleau S, Chatal JF, Talmant C, Vasseur F, Soulillou JP. The respective roles of gallium 67 citrate scanning and diagnostic ultrasound in detecting suppurations in renal allograft recipients. Pathol Biol (Paris) 1980;28:155-9.
8. Tzen KY, Yen TC, Lin KJ. Perirenal, peripelvic, and upper ureter abscesses in a nearly nonfunctioning kidney demonstrated by Tc-99m DMSA and Ga-67 renal SPECT. Clin Nucl Med 1999;24:68.
9. Tsang V, Lui S, Hilson A, Moorhead J, Fernando O, Sweny P. Gallium-67 scintigraphy in the detection of infected polycystic kidneys in renal transplant recipients. Nucl Med Commun 1989;10:167-70.
10. Amesur P, Castronuovo JJ, Chandramouly B. Infected cyst localization with gallium SPECT imaging in polycystic kidney disease. Clin Nucl Med 1988;13:35-7.
11. Utsunomiya D, Shiraishi S, Imuta M, Tomiguchi S, Kawanaka K, Morishita S, *et al*. Added value of SPECT/CT fusion in assessing suspected bone metastasis: Comparison with scintigraphy alone and nonfused scintigraphy and CT. Radiology 2006;238:264-71.
12. Papathanassiou D, Flament JB, Pochart JM, Patey M, Marty H, Liehn JC, *et al*. SPECT/CT in localization of parathyroid adenoma or hyperplasia in patients with previous neck surgery. Clin Nucl Med 2008;33:394-7.
13. Krausz Y, Keidan Z, Kogan I, Even-Sapir E, Bar-Shalom R, Engel A, *et al*. SPECT/CT hybrid imaging with 111In-pentetreotide in assessment of neuroendocrine tumours. Clin Endocrinol (Oxf) 2003;59:565-73.
14. Filippi L, Schillaci O. SPECT/CT with hybrid camera: A new imaging modality for the functional and anatomical mapping of infections. Expert Rev Med Devices 2006;3:699-703.
15. Horger M, Eschmann SM, Pfannenberg C, Storek D, Vonthein R, Claussen CD, *et al*. Added value of SPECT/CT in patients suspected of having bone infection: Preliminary results. Arch Orthop Trauma Surg 2007;127:211-21.
16. Filippi L, Schillaci O. Usefulness of hybrid SPECT/CT in 99m Tc-HMPAO-labelled leukocyte scintigraphy for bone and joint infections. J Nucl Med 2006;47:1908-13.
17. Bar-Shalom R, Yefremov N, Guralnik L, Keidar Z, Engel A, Nitecki S, *et al*. SPECT/CT using 67Ga and 111In-labelled leukocyte scintigraphy for diagnosis of infection. J Nucl Med 2006;47:587-94.
18. Bleeker-Rovers CP, de Kleijn EM, Corstens FH, van der Meer JW, Oyen WJ. Clinical value of FDG PET in patients with fever of unknown origin and patients suspected of focal infection or inflammation. Eur J Nucl Med Mol Imaging 2004;31:29-37.
19. Bleeker-Rovers CP, Vos FJ, Mudde AH, Dofferhoff AS, de Geus-Oei LF, Rijnders AJ, *et al*. A prospective multi-centre study of the value of FDG-PET as part of a structured diagnostic protocol in patients with fever of unknown origin. Eur J Nucl Med Mol Imaging 2007;34:694-703.
20. Keidar Z, Gurman-Balbir A, Gaitini D, Israel O. Fever of unknown origin: The role of 18F-FDG PET/CT. J Nucl Med 2008;49:1980-5.
21. Balink H, Collins J, Bruyn GA, Gemmel F. F-18 FDG PET/CT in the diagnosis of fever of unknown origin. Clin Nucl Med 2009;34:862-8.
22. Bleeker-Rovers CP, de Sévaux RG, van Hamersvelt HW, Corstens FH, Oyen WJ. Diagnosis of renal and hepatic cyst infections by 18-F-fluorodeoxyglucose positron emission tomography in autosomal dominant polycystic kidney disease. Am J Kidney Dis 2003;41:E18-21.
23. Soussan M, Sberro R, Wartski M, Fakhouri F, Pecking AP, Alberini JL. Diagnosis and localization of renal cyst infection by 18F-fluorodeoxyglucose PET/CT in polycystic kidney disease. Ann Nucl Med 2008;22:529-31.

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