Utility of Radiolabeled Leukocyte and Bone Marrow Scintigraphy with SPECT/CT in the Diagnostic Work-Up of the Painful Prosthetic Joint: A Single-Institution Experience

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ABSTRACT

In the assessment of prosthetic joint pains, differentiating between aseptic loosening and infection can be challenging due to their similarities in clinical presentation and histopathology. Combined radiolabeled leukocyte and bone marrow scintigraphy with SPECT/CT is considered the most suitable nuclear imaging modality for this purpose. However, this is infrequently performed in our local setting. We present two cases where these studies were appropriately performed with different scan outcomes. The first case involved a 67-year-old male with a painful right knee prosthesis and an alleged history of recurrent periprosthetic joint infection (PJI). The leukocyte tagging scan and marrow scan images were found to be congruent, which was more compatible with aseptic loosening. No emergent surgical intervention was done in our hospital, and the patient returned to his home territory for further management. The second case was a 72-year-old male with progressive pain in his left prosthetic hip which began after his surgery a year prior. Scan images were incongruent, suggestive of PJI; this was confirmed on joint aspiration and eventual surgical revision. Despite this imaging study's high sensitivity and high specificity, it has not been well-received in management algorithms of PJIs. Collaboration between clinicians and nuclear imaging specialists is key in increasing the general use of these procedures.

Keywords: *radiolabeled leukocytes, WBC tagging study, bone marrow scintigraphy, prosthetic joints, periprosthetic infection, prosthetic loosening*

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INTRODUCTION

The post-operative course of joint replacement surgery does not always proceed without complications. Fracture, dislocation, aseptic loosening, and infection are among the differentials to consider given a patient with a painful prosthetic joint [1]. Physical examination and standard radiologic imaging may diagnose fractures and dislocations. However, distinguishing between infection and aseptic loosening is challenging due to their identical clinical presentation and histopathology [2]. While aseptic loosening is the more common cause of prosthetic failure, periprosthetic joint infection (PJI) signals more severe morbidity and predisposes to a more turbulent clinical course, hence the importance of differentiating between the two entities [3-4].

Nuclear medicine contributes significantly in the non-invasive evaluation of painful joint prostheses. Imaging with white blood cells (WBCs) labeled with indium-111 or technetium-99m, also called radiolabeled leukocyte scintigraphy or WBC tagging study, is ideal for this purpose. It is helpful in determining neutrophil-mediated inflammation, as in

PJIs, from those mediated by histiocytes, as in aseptic loosening. Multiple retrospective studies have shown a sensitivity and specificity in the 75–100% range [1, 5].

The diagnostic power of WBC tagging can be further enhanced by combining this with bone marrow scintigraphy, typically using ^{99m}Tc-sulfur colloid. Under most circumstances, the distribution of leukocytes and sulfur colloid are the same since both accumulate in the reticuloendothelial cells of the bone marrow. As such, images from the two scans typically appear spatially congruent. However, in cases of osteomyelitis and periprosthetic infections, WBCs may accumulate in areas where sulfur colloid does not, i.e., the two scan images are spatially incongruent. Taking the two scans in combination, procedural sensitivity and specificity increases to a range of 90–100% [6-7]. With the advent of hybrid single-photon emission computed tomography (SPECT/CT), anatomic-physiologic correlation may be described in further detail.

Access to nuclear medicine centers in our country is relatively limited. Not all hospitals have nuclear imaging equipment, costs of nuclear medicine procedures are higher than those of cross-sectional imaging (such as CT and MRI), and clinicians are inadequately versed with nuclear medicine services. Consequently, WBC tagging and bone marrow scintigraphy procedures are not frequently encountered, and even more in cases where prosthetic joints are being evaluated. In the 8 years since our institution opened, less than 20 such procedures have been performed for varying indications.

Given such local experience with these scans, we would like to present two cases of WBC tagging and bone marrow scintigraphy, augmented with SPECT/CT, with different scan outcomes and post-procedural courses.

CASE 1

A 67-year-old Pacific Islander underwent total right knee replacement in 2007 due to chronic knee pain attributed to osteodegenerative changes. Since then, he underwent two further surgeries in 2010 and 2014 to replace his prosthesis, allegedly due to recurrent infection. Prior to imaging, he just completed 6 weeks of oral antibiotic treatment due to another infection recurrence. Erythrocyte sedimentation rate (ESR) was 114 mm/hr (reference range: 0–20 mm/hr) and C-reactive protein (CRP) was 12 mg/L (reference range: < 6 mg/L). Pain persisted in his right knee, and he was referred to the Department of Nuclear Medicine for further evaluation.

Anterior and posterior planar images of the knees, as well as SPECT/CT images, were acquired at 1 hour and 3 hours after intravenous injection of 547.6 MBq (14.8 mCi) of white blood cells labeled with technetium-99m hexamethylpropyleneamine oxime (^{99m}Tc-HMPAO). Bone marrow scintigraphy using 373.7 MBq (10.1 mCi) of ^{99m}Tc-sulfur colloid was performed 20 hours after the WBC scan to evaluate the bone marrow in the distal femur and proximal tibia. Anterior and posterior imaging was done at 1 hour and 3 hours post-injection, along with SPECT/CT imaging of the knees.

Images from the WBC tagging study showed diffuse radioactivity in the right distal femur (Figures 1A and 1B). On SPECT/CT, increased activity was noted anterior to the prosthesis (Figure 1C), as well as posterior to the femoral component (Figure 1D).

Uptake was persistent, with no significant interval change at the 3rd hour of imaging.

Diffuse tracer accumulation anterior to the right knee was noted on bone marrow scintigraphy (Figure 2), albeit not as intense as in the radiolabeled leukocyte scan. Uniform tracer distribution was seen in both the femoral and the tibial components of the prosthesis. Intense radioactivity in the left femoral bone marrow appeared physiologic. o significant change was noted on static imaging on the third hour.

The WBC tagging and bone marrow scans were deemed to be congruent, compatible with aseptic prosthetic loosening. Based on the scans, no definite evidence of bone involvement or osteomyelitis was reported. After the imaging study, the patient returned to his home territory for further management of his condition. No further intervention was done by the patient's attending orthopedic physician in our hospital.

CASE 2

A 72-year-old male underwent intramedullary nailing of the left proximal femur in 1981 due to a vehicular crash. Total left hip arthroplasty was performed in 2016, with reports of progressive hip pain and difficulty in ambulation after the surgery. ESR was 16 mm/hr (reference range: 0–20 mm/hr) and CRP was 0.47 mg/dL (reference range: < 0.8 mg/dL). Persistence of symptoms prompted referral to the Department of Nuclear Medicine for further evaluation.

Anterior and posterior planar images of the pelvis, as well as SPECT/CT images, were acquired at 1 hour and 3 hours after intravenous injection of 592.0 MBq (16.0 mCi) of WBCs labeled with ^{99m}Tc-HMPAO. Bone marrow scintigraphy using 384.8 MBq (10.4 mCi) of ^{99m}Tc-sulfur colloid was performed 20 hours after the WBC scan to evaluate the bone marrow in the pelvis and hips. Anterior and posterior imaging of the pelvis was done at 1 hour and 3 hours after tracer administration, along with SPECT/CT imaging.

Images from the WBC tagging study showed mildly increased focal uptake in the peri-acetabular region and neck of the femur, more evident on SPECT/CT (Figure 3); this persisted on the 3rd hour of imaging. Bone marrow scintigraphy (Figure 4) revealed two foci of increased tracer uptake adjacent to the prosthesis in the region of the lesser trochanter and proximal third of the left femoral shaft. No undue tracer activity was seen in the left peri-acetabulum and area of the left femoral neck.

The WBC tagging and bone marrow scans were read as incongruent. Mild tracer activity in the area of the left femoral neck and peri-acetabular region, seen only on the radiolabeled leukocyte scan, was suggestive of chronic infection or inflammation. Tracer uptake in the left proximal femoral shaft on the bone marrow scan with no corresponding defect in the WBC tagging study was thought to be reactive marrow secondary to the prosthesis.

Aspiration of fluid in the left trochanteric bursa done after the imaging study revealed purulent discharge. Medical pain management was attempted in the following months, but with little to no relief of symptoms. Eventually, the implant was surgically removed, debridement was done, and an antibiotic cement spacer was applied. Intraoperative findings included significant loosening of the hip prosthesis and purulent material within the screw tracts of the acetabular component. This was post-operatively signed out as a case of septic loosening secondary to PJI.

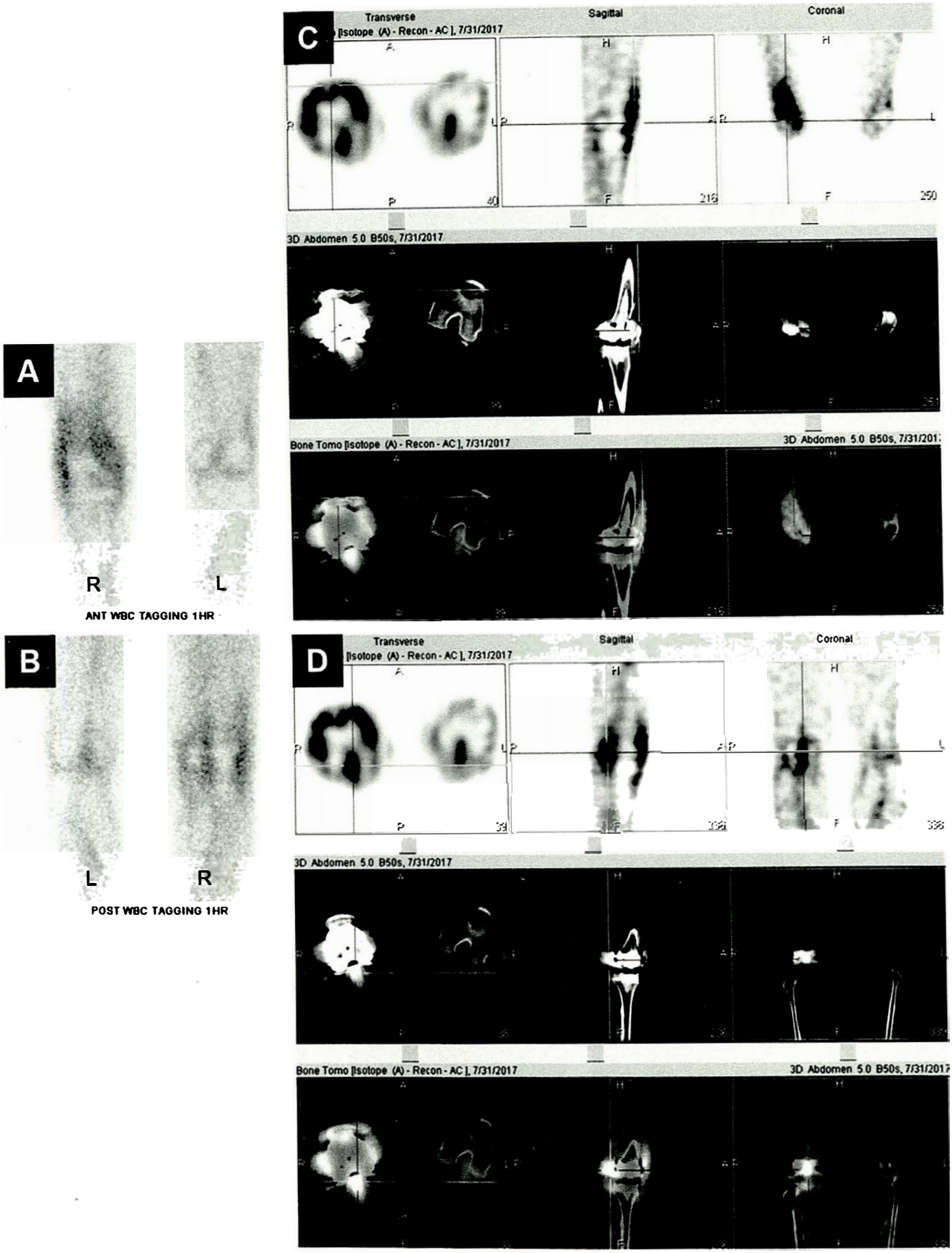

Figure 1. Planar images from the WBC tagging study obtained 1 hour after ^{99m}Tc-WBC injection [A-B] showed increased tracer uptake in the periprosthetic areas of the right knee. On SPECT/CT, this was localized anterior [C] and posterior [D] to the femoral component of the knee prosthesis.

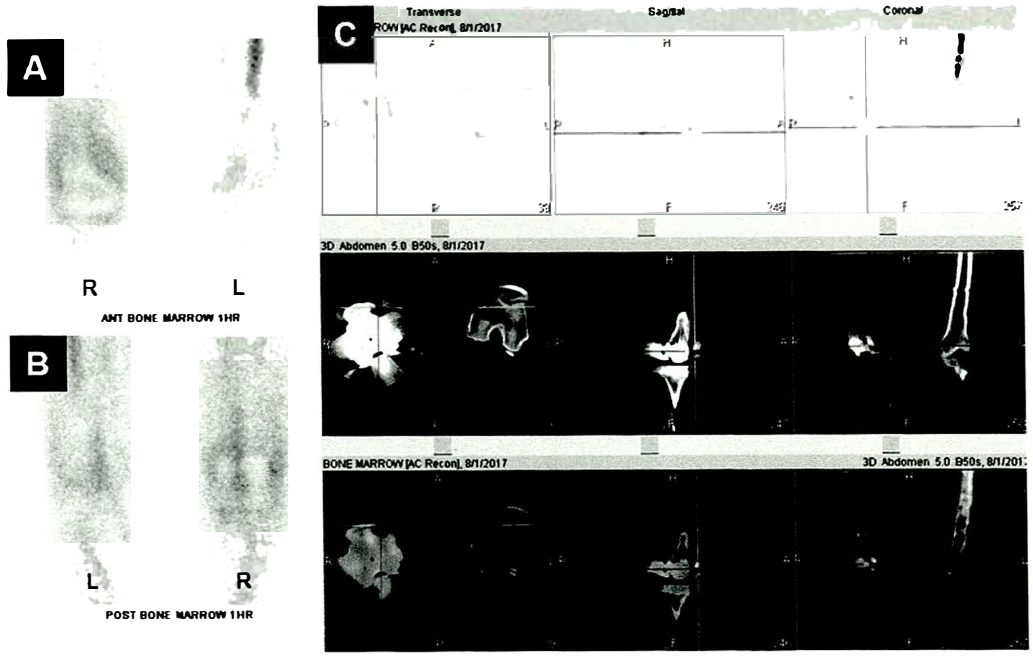

Figure 2. Planar [A-B] and SPECT/CT [C] images from bone marrow scintigraphy obtained 1 hour after ^{99m}Tc-sulfur colloid injection showed diffusely increased tracer uptake anterior to the right knee. The femoral and tibial prosthetic components exhibited uniform tracer distribution.

DISCUSSION

We presented two cases of WBC tagging and bone marrow scintigraphy with SPECT/CT in patients complaining of prosthetic joint pain. While both involved prosthetic joints, the imaging outcomes were different, and in one case, proven to be consistent with post-operative findings.

The first case depicted congruent radiolabeled leukocyte and bone marrow scans in a patient with prosthetic knee joint pain and an alleged history of recurrent PJI. The last surgical revision of prosthesis was done 3 years prior to the scan. Based on the resulting images, aseptic loosening was the primary consideration. No additional management was done by the attending doctor in our institution, which may imply the lack of need for emergent medical or surgical intervention as a result of the scan. He was able to fly back to his home territory for continuity of care.

This contrasts with the incongruent set of scans that were obtained in the case of the second patient. Total hip arthroplasty was performed just over a year prior to the scan, with pains persistent in the interim. The resulting images showed focal ^{99m}Tc-WBC uptake in the peri-acetabular and femoral neck regions, and focal ^{99m}Tc-sulfur colloid uptake in the lesser trochanter and proximal femoral shaft. The presence of leukocytes in an area with absent bone marrow activity was indicative of an infectious etiology. This was proven on joint aspiration and on peri-operative findings, as purulent material was noted around the acetabulum.

The use of radiolabeled leukocyte and bone marrow scintigraphy with SPECT/CT for evaluating PJIs is supported by its high sensitivity and specificity compared to other nuclear imaging modalities, as well as by the cases discussed. Nevertheless, current literature does not explicitly endorse this in the

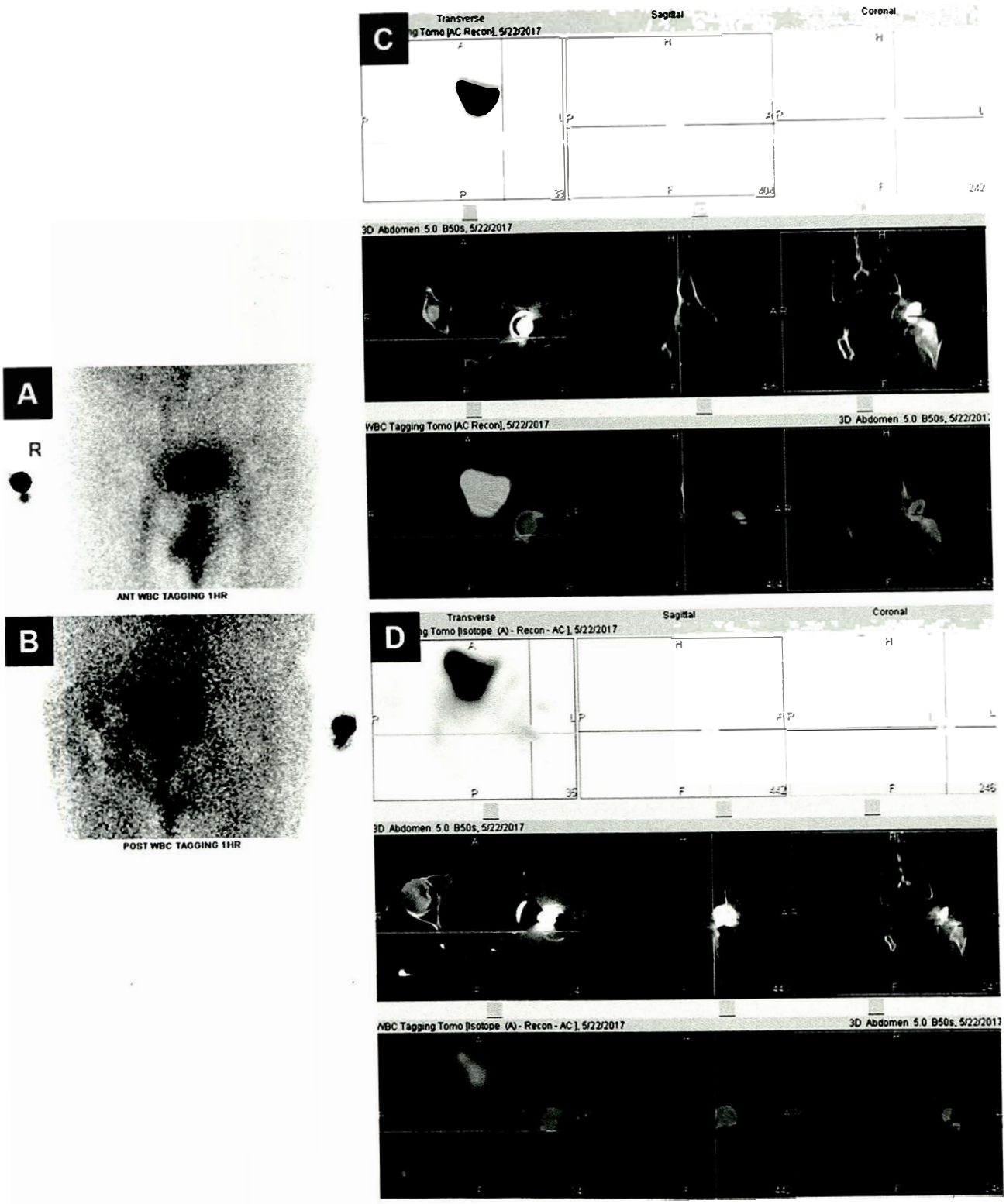

Figure 3. Planar images from the WBC tagging study obtained 1 hour after ^{99m}Tc-WBC injection [A-B] showed increased tracer uptake in the periprosthetic areas of the left hip. On SPECT/CT, this was localized to the left peri-acetabular region [C] and left femoral neck [D].

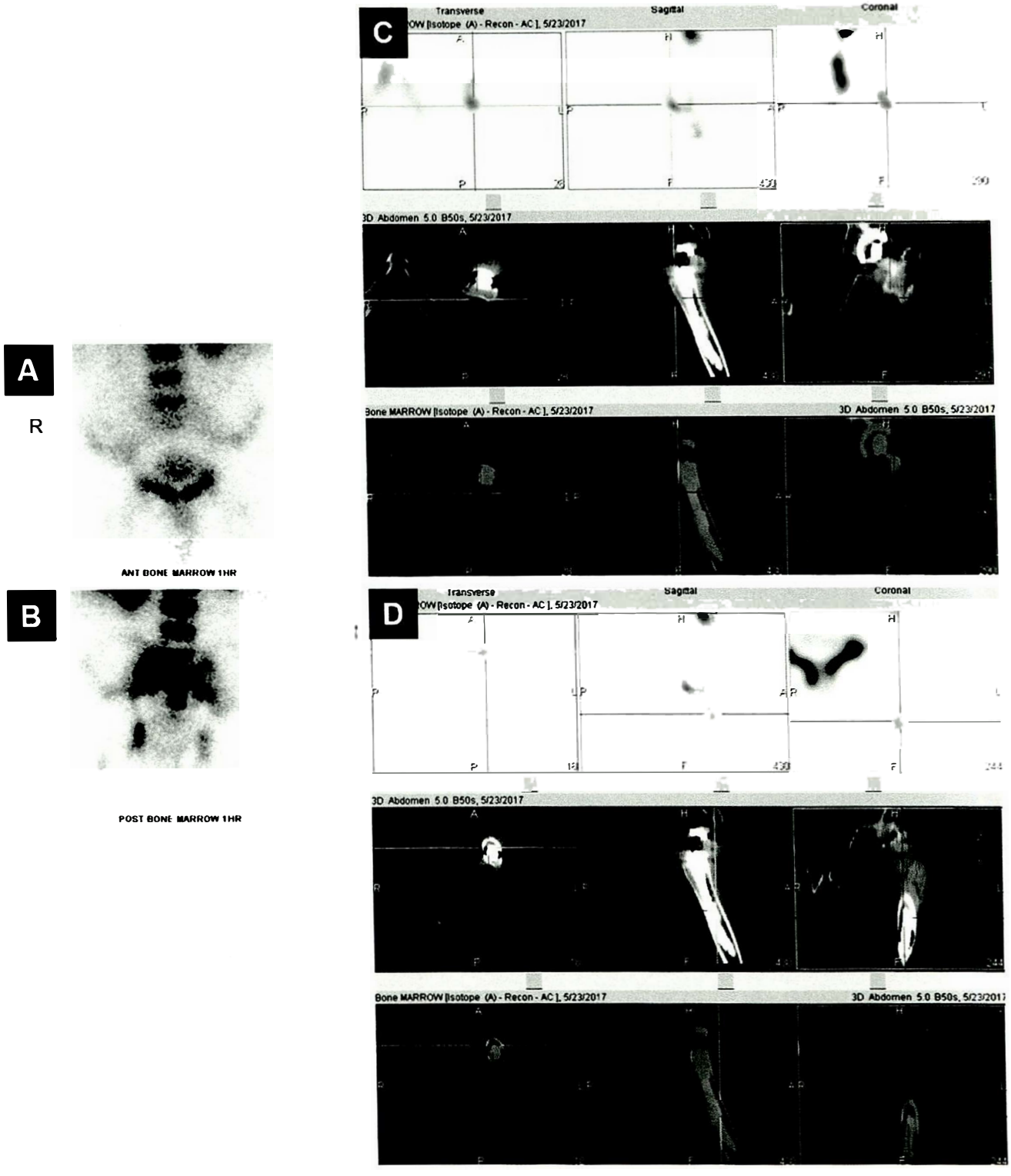

Figure 4. Planar images from bone marrow scintigraphy obtained 1 hour after ^{99m}Tc-sulfur colloid injection [A-B]. On SPECT/CT, two foci of increased tracer uptake are noted adjacent to the prosthesis in the region of the left lesser trochanter [C] and proximal third of the left femoral shaft [D].

management of PJIs. Instead, guidelines and journals tend to generalize nuclear imaging (along with bone scintigraphy, gallium imaging, and positron emission tomography (PET) using ^{18}F-FDG) when giving their recommendations. According to the American Academy of Orthopedic Surgeons, nuclear medicine procedures may be requested, but caution should be exercised as they perceive supporting evidence to be limited [8]. The "algorithm-based approach" by Ting and Della Valle (2017) also lumps together nuclear imaging procedures, alone or in combination, and does not recommend their use, citing time, cost, result variability, and generally low specificity as reasons [9]. Most recently, the article by Li et al. on the management of PJIs does not even mention combined radiolabeled leukocyte and bone marrow scanning; it only cites ^{18}F-FDG PET, which has a relatively lower sensitivity and specificity [10].

The value of combined WBC tagging and bone marrow scintigraphy is perhaps seen among patients (usually the elderly) who refuse to undergo more invasive diagnostic procedures such as joint aspiration. Additionally, as shown in Case 2, the two imaging tests may be useful in the setting of high clinical suspicion but normal ESR and CRP, which were found to be unreliable biomarkers for the diagnosis of PJI prior to second-stage reimplantation, or in metal-on-metal or corrosion cases [11]. Yet, the general lack of awareness by the attending clinicians on the different types and indications for nuclear medicine procedures may also contribute to the underutilization of these imaging modalities despite its proven advantages.

The authors hope that the cases presented may serve as a guide when it comes to requesting, performing, and interpreting this set of imaging studies in the future. Closer collaboration between clinicians and nuclear medicine physicians is suggested to clarify the role of nuclear imaging procedures (specifically the ones presented) in the diagnostic work-up of PJIs.

CONCLUSION

WBC tagging and bone marrow scintigraphy with SPECT/CT may still play a role in the diagnostic work-up of prosthetic joint pain, provided that referring doctors and nuclear medicine specialists have adequate knowledge on their indications and interpretation, respectively.

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