AMSER Case of the Month
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Young adult with sickle cell disease presenting with tibial pain and fever

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Patient Presentation

- HPI: 34-year-old male presenting to Emergency Department with shortness of breath, fevers, chills, and pain all over his body.
- The patient has had multiple episodes of sickle cell crisis, typically presenting with pain in his thighs. This episode is different in that he has fevers/chills and pain was all over his body.
- PMH: Hyperlipidemia, sickle cell disease, multiple bone infarcts, sickle cell pain crises, avascular necrosis of right femoral head, and MRSA bacteremia
- Vitals: Tachycardia, febrile

Patient Presentation

- Physical Exam: Normal physical exam except for the following:
- Abdominal distension without tenderness or guarding
- Tenderness to touch all over his lower extremities , especially in tibial area
- Skin was warm to the tough. No open wounds appreciated.

Pertinent Labs

LABS	
WBC - 27.6 k/microliter	(Normal 4.0-12.0 k/microliter)
RBC - 1.99 m/microliter	(Normal 4.30-5.90 m/microliter)
HbG - 6.8 gm/dl	(Normal 13.5-17.5 gm/dl)
Total bilirubin - 3.5 mg/dl	(Normal 0.0-1.5 mg/dl)

Hospital Course

- Patient admitted for sickle cell crisis and pain management.
- Patient met SIRS criteria- sepsis protocol initiated.
- Started on broad spectrum antibiotics.
- Blood culture was positive for candida.
- TTE showed echodensity on aortic valve, suspected vegetation.
- Patient started on micafungin.

- Patient reports persistent severe pain in right tibial area…

What Imaging Should We Order to Evaluate the Tibial Pain?

ACR Appropriateness Criteria

Variant 1: **Suspected osteomyelitis or septic arthritis or soft tissue infection (excluding spine and diabetic foot). Initial imaging.**

Procedure	Appropriateness Category	Relative Radiation Level
Radiography area of interest	Usually Appropriate	Varies
US area of interest	Usually Not Appropriate	O
MRI area of interest without and with IV contrast	Usually Not Appropriate	O
MRI area of interest without IV contrast	Usually Not Appropriate	O
3-phase bone scan area of interest	Usually Not Appropriate	☢☢☢
CT area of interest with IV contrast	Usually Not Appropriate	Varies
CT area of interest without and with IV contrast	Usually Not Appropriate	Varies
CT area of interest without IV contrast	Usually Not Appropriate	Varies

This imaging modality was ordered initially

Variant 2: **Suspected septic arthritis or soft tissue infection. Initial radiographs normal or with findings suggestive of joint effusion or soft tissue swelling. Next imaging study.**

Procedure	Appropriateness Category	Relative Radiation Level
US area of interest	Usually Appropriate	O
Image-guided aspiration area of interest	Usually Appropriate	Varies
MRI area of interest without and with IV contrast	Usually Appropriate	O
MRI area of interest without IV contrast	Usually Appropriate	O
CT area of interest with IV contrast	Usually Appropriate	Varies
CT area of interest without IV contrast	May Be Appropriate	Varies
3-phase bone scan area of interest	Usually Not Appropriate	☢☢☢
CT area of interest without and with IV contrast	Usually Not Appropriate	Varies

ACR Appropriateness Criteria

Variant 3: **Suspected osteomyelitis. Initial radiographs normal or with findings suggestive of osteomyelitis. Next imaging study.**

Procedure	Appropriateness Category	Relative Radiation Level
MRI area of interest without and with IV contrast	Usually Appropriate	O
MRI area of interest without IV contrast	Usually Appropriate	O
3-phase bone scan area of interest	May Be Appropriate	☢☢☢
3-phase bone scan and WBC scan and sulfur colloid scan area of interest	May Be Appropriate	☢☢☢☢
3-phase bone scan and WBC scan area of interest	May Be Appropriate	☢☢☢☢
FDG-PET/CT area of interest	May Be Appropriate	☢☢☢☢
WBC scan and sulfur colloid scan area of interest	May Be Appropriate	☢☢☢☢
CT area of interest with IV contrast	May Be Appropriate	Varies
CT area of interest without IV contrast	May Be Appropriate	Varies
US area of interest	Usually Not Appropriate	O
WBC scan area of interest	Usually Not Appropriate	☢☢☢☢
CT area of interest without and with IV contrast	Usually Not Appropriate	Varies

This imaging modality was ordered after initial radiographs

Necessary follow-up imaging to make final diagnosis after inconclusive MRI

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Findings

Tibia and fibula radiographs were normal

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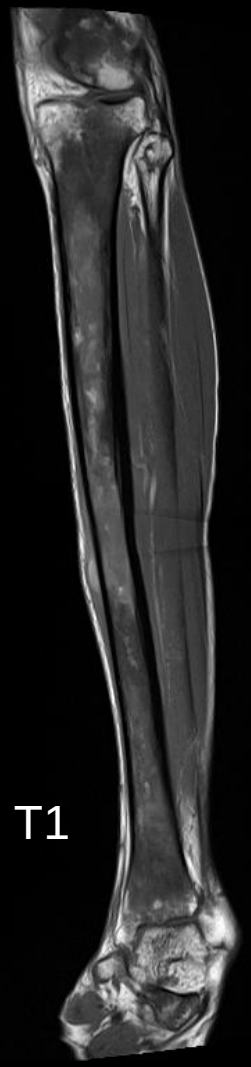
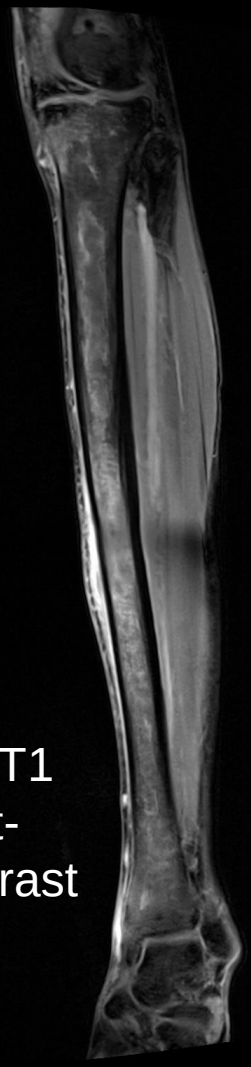
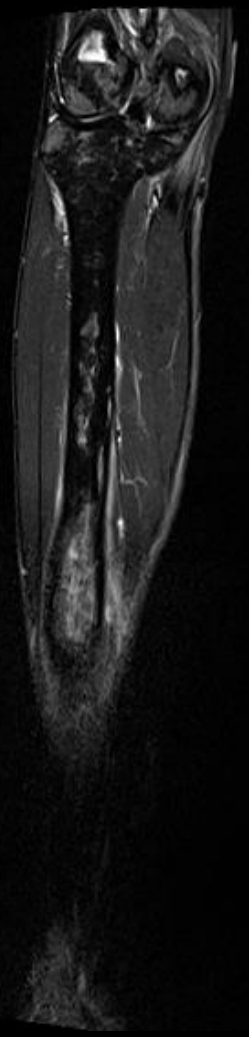
Findings (unlabeled)



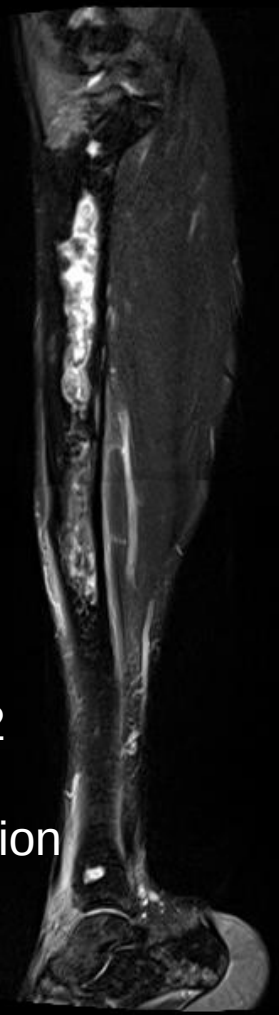
Cor T1



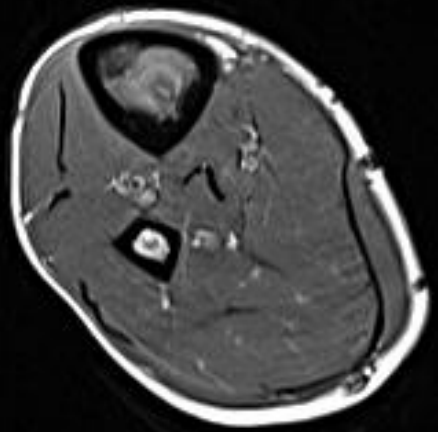
Cor T1
Post-
contrast



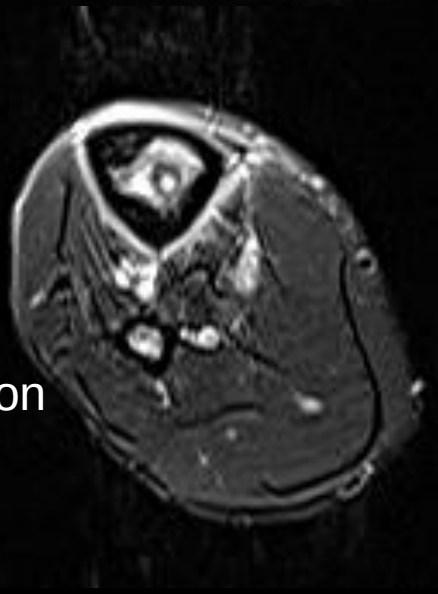
Cor STIR



Sag T2
Fat
saturation



Ax T1



Ax T2
Fat
saturation

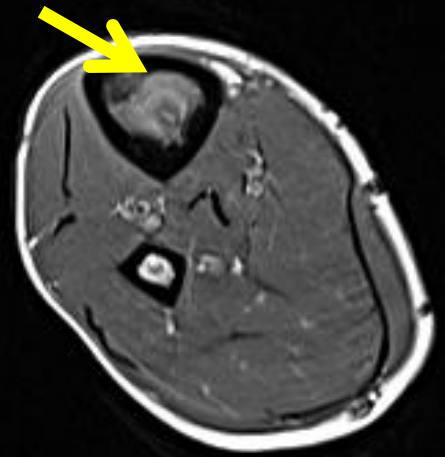
Findings (labeled)

Cor T1

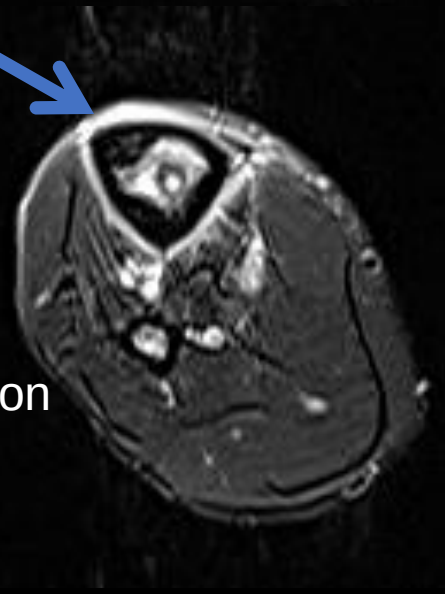
Cor T1
Post-
contrast

Cor STIR

Sag T2
Fat
saturation



Ax T1



Ax T2
Fat
saturation

There is indeterminate intermediate T1 signal (→), contrast enhancement (→), and marrow/periosteal edema (→) in the middle one-third of the tibial diaphysis. Multiple chronic bone infarcts (→) noted.

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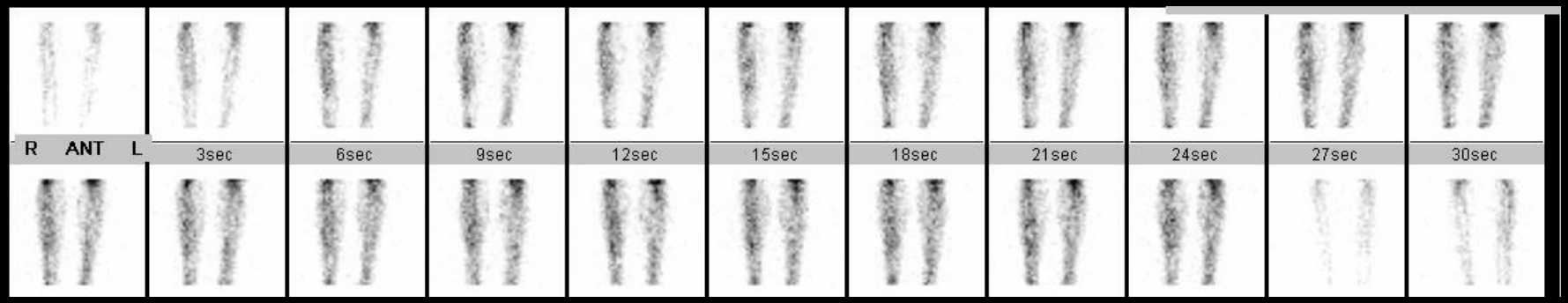
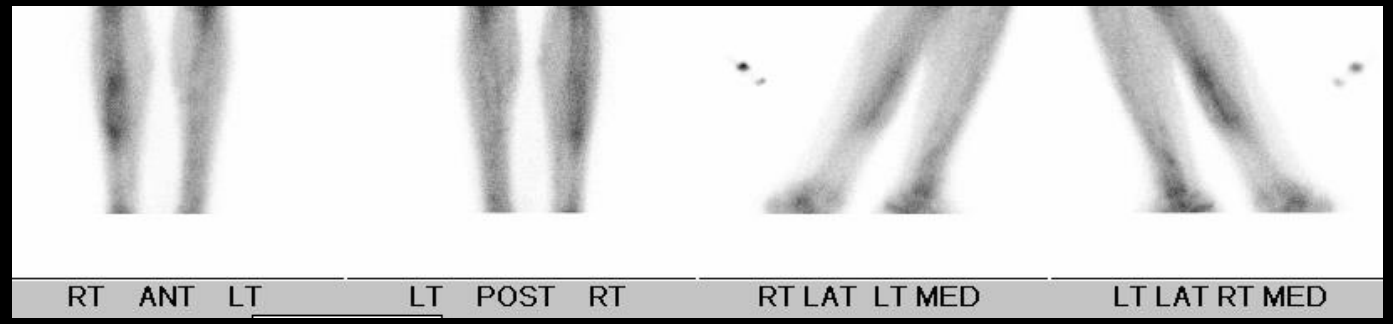
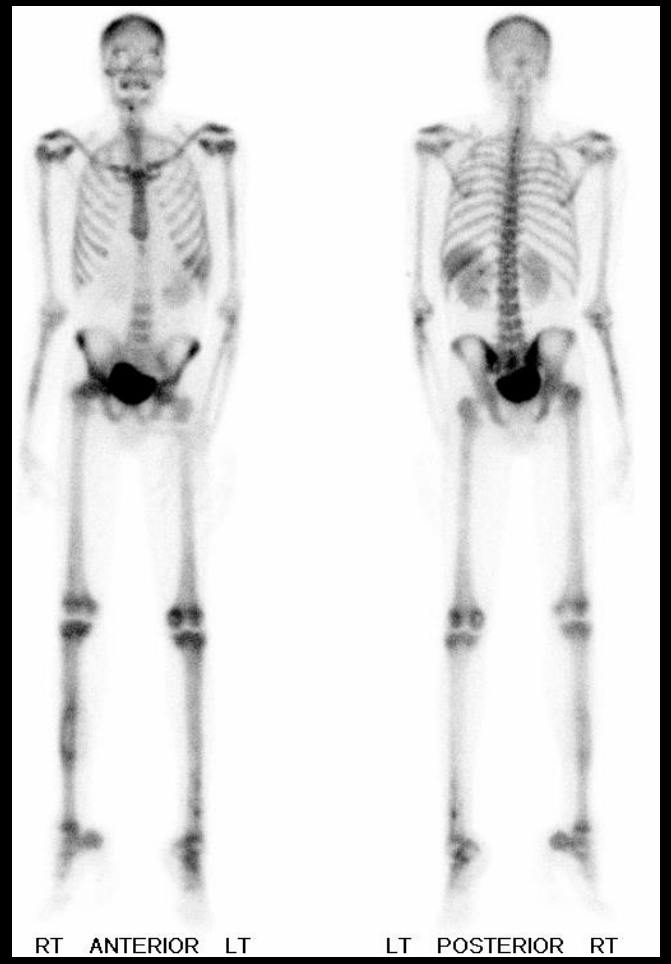
3-Phase Bone Scan Findings: (unlabeled)



Blood Flow Phase



Blood Pool Phase



Delayed Phase

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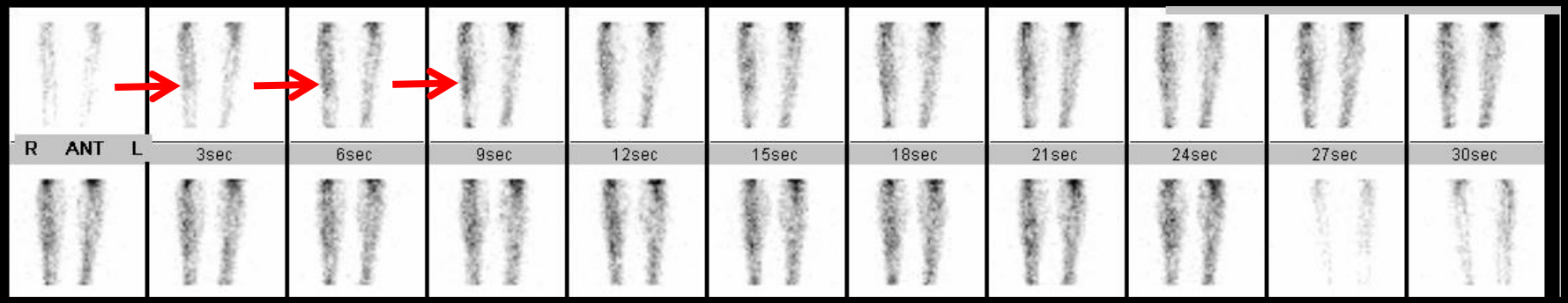
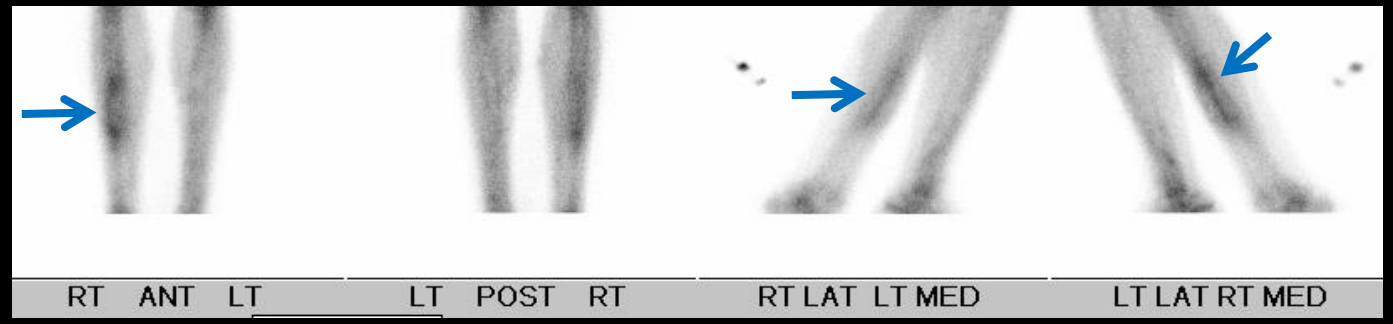
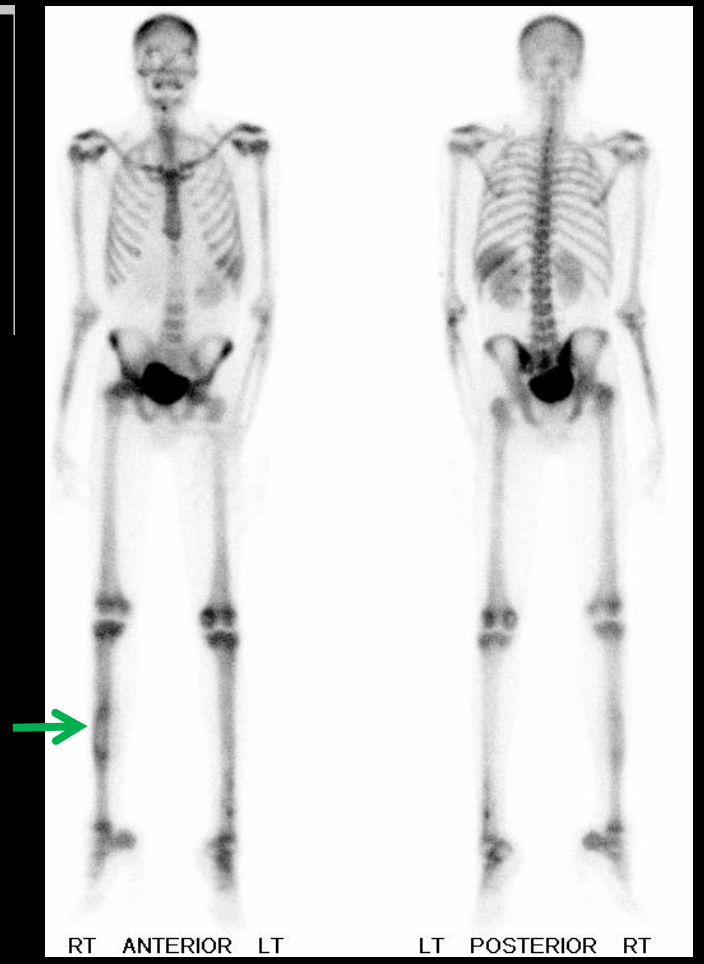
3-Phase Bone Scan Findings: (labeled)



Blood Flow Phase



Blood Pool Phase

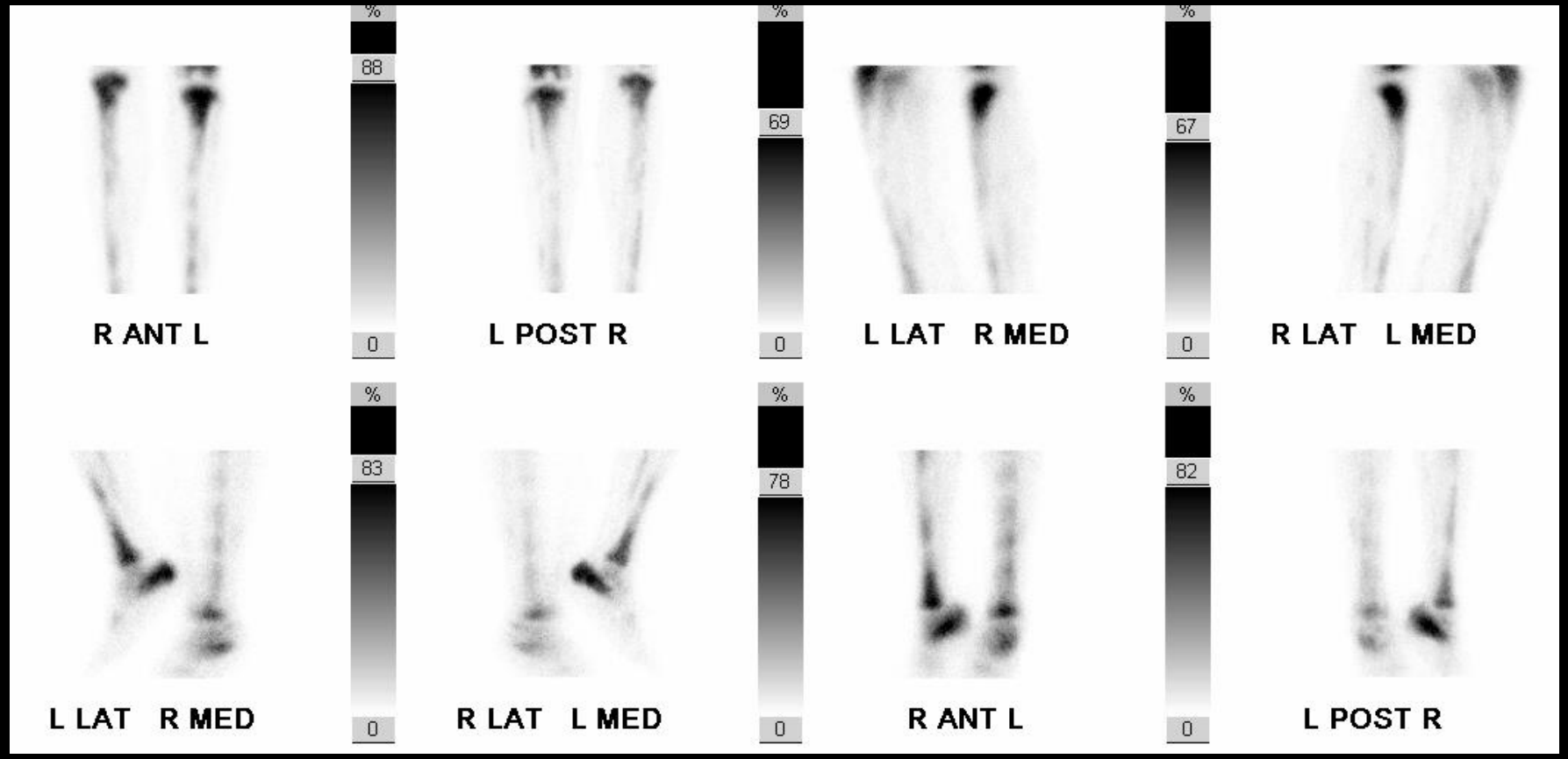


Delayed Phase

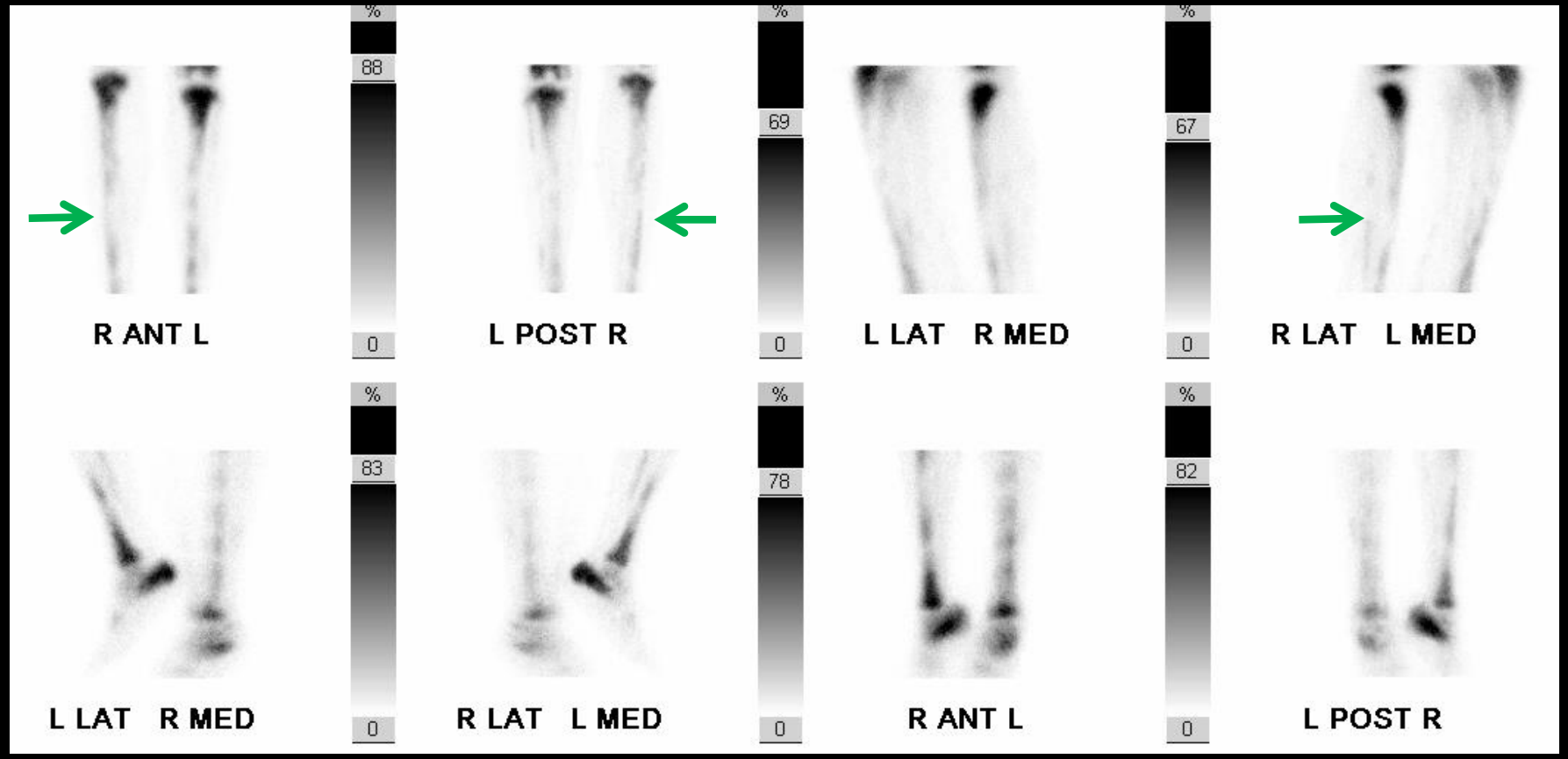
Positive 3-phase bone scan with increased uptake in the middle third of the tibia on flow phase (→), blood pool phase (→), and delayed phase (→).

This raises suspicion for osteomyelitis but the differential includes subacute infarct with an inflammatory response.

WBC Scan Findings (unlabeled)



WBC Scan Findings (labeled)



Technetium 99m HMPAO-labeled WBC scan demonstrates no increased localization in the middle third of the right tibia (→), relative to other sites in the tibia.

This is most consistent with subacute infarct rather than osteomyelitis.

Final Diagnosis:

Subacute bone infarct in tibia mimicking osteomyelitis

Case Discussion

- Sickle cell disease (SCD) is a congenital hemoglobinopathy that results in the formation of sickled red blood cells (RBCs). These RBCs are susceptible to vaso-occclusive events which may result in bone infarcts [1], with the long bones the most common sites of involvement.

- These infarcts present with localized pain, and occasionally swelling or fever in the acute phase due to associated inflammatory response. The presentation can imitate osteomyelitis, and the distinction is clinically important. Complicating the clinical picture, patients with sickle cell disease are also at increased risk of osteomyelitis [1], potentially due to impaired immune response or complications of infarct.

- MRI is considered to be the gold standard for diagnosing acute osteomyelitis. MRI sensitivity is typically reported in the range of 95% and specificity 85-95%. However, the specificity decreases when there is a coexisting bone process such as Charcot arthropathy, bone infarct, tumor, or previous surgery [2]. In these cases, nuclear medicine imaging may play a critical role.

Case Discussion

- A three-phase bone scan is an appropriate first nuclear medicine test in suspected osteomyelitis due to the high sensitivity of approximately 90%. However, the specificity ranges from 50-90% and is lower in the setting of prior surgery, Charcot arthropathy, or infarcts [3-5].

- A three-phase positive bone scan (increased blood flow, soft tissue inflammation, and bone uptake) indicates an acute process, raising suspicion for acute osteomyelitis. However, the differential includes acute/subacute fracture, recent surgery, tumor, subacute bone infarct, tumor, Charcot arthropathy or inflammatory arthropathy [6].

- In cases where these processes remain in the differential, labeled white blood cell (WBC) scintigraphy is recommended for confirmation of infection [7]. In the extremities, the sensitivity and specificity of labeled WBC scan are 80-90% [2,3,5]. Concurrent marrow imaging with technetium sulfur colloid is recommended in the setting of prior surgery or suspected diabetic foot infection. Nuclear medicine imaging may offer additional detail into the size and extent of the infection [7].

- In indeterminate cases, bone biopsy and culture may be required, regardless of the imaging findings.

Case Discussion

- This case illustrates the difficulties in distinguishing subacute bone infarct from osteomyelitis in sickle cell patients, especially when conventional imaging techniques such as an MRI do not yield definitive results.
- In this setting, nuclear medicine imaging, such as the three-phase bone scan and labeled WBC scan, plays a crucial role in clinical decision making.
- Confirmed osteomyelitis requires intravenous and/or long-term antibiotic treatment. Surgical debridement is reserved for recalcitrant infection [8].
- Conversely acute bone infarcts and vaso-occlusive disease are typically managed with supportive care, including hydration and pain control. Epiphyseal involvement (e.g. in the femoral head) carries a higher risk of articular collapse and other complications, which may require surgical intervention such as osteotomy [8].

References:

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2. Lauri C, Glaudemans AWJM, Campagna G, et al. Comparison of white blood cell scintigraphy, FDG PET/CT and MRI in suspected diabetic foot infection: Results of a large retrospective multicenter study. J Clin Med 2020;9(6):1645.
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5. Przybylski MM, Holloway S, Vyce SD, Obando A. Diagnosing osteomyelitis in the diabetic foot: a pilot study to examine the sensitivity and specificity of Tc(99m) white blood cell-labelled single photon emission computed tomography/computed tomography. Int Wound J 2016;13(3):382-389.
6. O'Malley JM and Ziessman HA, eds. Nuclear Medicine and Molecular Imaging: the Requisites, 5th Ed. Philadelphia, PA: Elsevier, Inc; 2021.
7. Giurato L, Meloni M, Izzo V, Uccioli L. Osteomyelitis in diabetic foot: A comprehensive overview. World J Diabetes 2017;8(4):135-142.
8. Vanderhave KL, Perkins CA, Scannel B, et al. Orthopaedic Manifestations of Sickle Cell Disease. J Am Acad Orthop Surg 2018;26(3):94-101.

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