MAR Oncology and Hematology (2026) 6:3

Review Article

Unexpected Splenic Uptake of 99mTc-HMDP on Bone Scintigraphy in an Adult Patient with Sickle Cell Disease: A Diagnostic Pitfall and Pathophysiological Correlation

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Received: 25 March 2026

Published: 01 April 2026

DOI: https://doi.org/10.5281/zenodo.19355837

Abstract

Bone scintigraphy using 99mTc-hydroxymethylene diphosphonate (HMDP) is routinely employed to assess bone metabolism, usually without visualization of extraosseous soft tissues apart from the urinary tract. Splenic uptake of this tracer is unusual, particularly in adult patients with sickle cell disease, because functional or anatomical asplenia is commonly observed as a consequence of repeated splenic infarctions.

We report the case of a 57-year-old woman with long-standing sickle cell disease, a history of multiple blood transfusions, and a spleen not visualized on recent ultrasound. During bone scintigraphy performed for right hip pain, faint but definite splenic uptake of 99mTc-HMDP was observed, together with nonspecific visceral opacifications and bone changes consistent with sickle-related infarctions. The absence of recent contrast-enhanced cross-sectional imaging limited the direct assessment of calcifications. This splenic uptake was interpreted as secondary to dystrophic fibro-calcific remodeling after infarction, promoted by chronic iron overload and chelation therapy. Splenic visualization of 99mTc-HMDP in an adult patient with sickle cell disease must be interpreted with caution and should not be equated with residual splenic function. Clinical correlation and multimodality imaging are essential. This finding represents a diagnostic pitfall and should not be misinterpreted as residual splenic function. Careful clinical correlation and multimodal imaging assessment are essential.

Keywords: *Sickle cell disease, Splenic uptake, Bone scintigraphy, 99mTc-HMDP.*

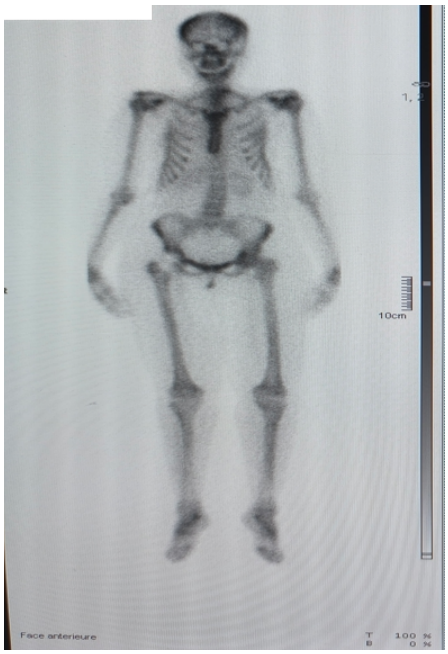
Introduction

Sickle cell disease is a severe genetic disorder caused by abnormal hemoglobin S (HbS). It is a truly systemic disease whose morbidity is driven by painful vaso-occlusive crises, aplastic and hemolytic episodes, and splenic sequestration, frequently associated with osteoarticular complications such as bone infarctions, acute and chronic osteomyelitis, and osteonecrosis (1,2). In patients with sickle cell disease, functional or anatomical asplenia is almost universal in adulthood because of repeated splenic infarctions and autosplenectomy. In the setting of bone scintigraphy performed to investigate osteoarticular involvement of the disease, the presence of splenic uptake of 99mTc-HMDP, a bone-seeking tracer, represents an unusual phenomenon that may be misleading if misinterpreted (3).

We report a case illustrating this uncommon finding and discuss its potential pathophysiological mechanisms.

Observation

A 57-year-old woman was followed for sickle cell disease complicated by vaso-occlusive crises since the age of 5 years, the most recent crisis having occurred 8 years earlier, with a history of multiple blood transfusions. She was receiving folic acid supplementation and oral iron chelation therapy with deferasirox. Abdominopelvic ultrasound performed two years earlier for surveillance of hepato-biliary and renal complications showed no significant abnormalities, apart from a few simple left renal cysts and an atrophic, non-visualized spleen. No recent contrast-enhanced CT scan was available. Bone scintigraphy was indicated for etiological assessment of right hip pain evolving over two months in a patient with a right total hip replacement implanted 7 years earlier for femoral head osteonecrosis secondary to vaso-occlusive events. The examination showed no evidence of prosthetic loosening but revealed non-fixing degenerative sclerotic-geodic changes around both acetabula. It also demonstrated diffuse heterogeneous remodeling of the bone trabeculae with lacunar lesions of the humeral heads, consistent with bone infarctions on the hybrid CT images, in a context of diffuse bone demineralization. In addition, faint splenic uptake was observed, together with visceral opacifications that could be related to a side effect of deferasirox, and multiple visceral opacities mimicking contrast enhancement, particularly in the stomach and large bowel.



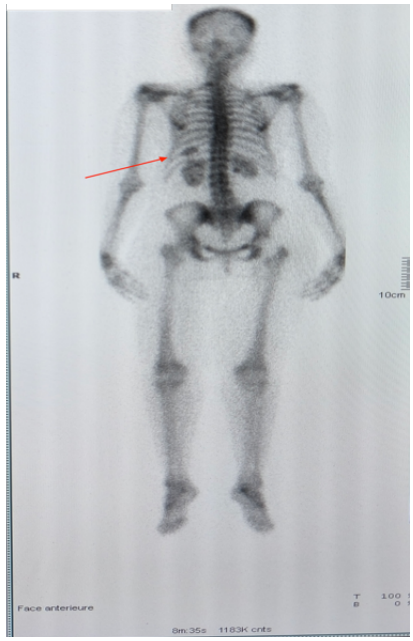


Figure 1a: Anterior whole-body view **Figure 1b:** Posterior whole-body view.

Figure 1: Whole-body bone scintigraphy images showing faint uptake of the osteotropic tracer projected over the left suprarenal region.

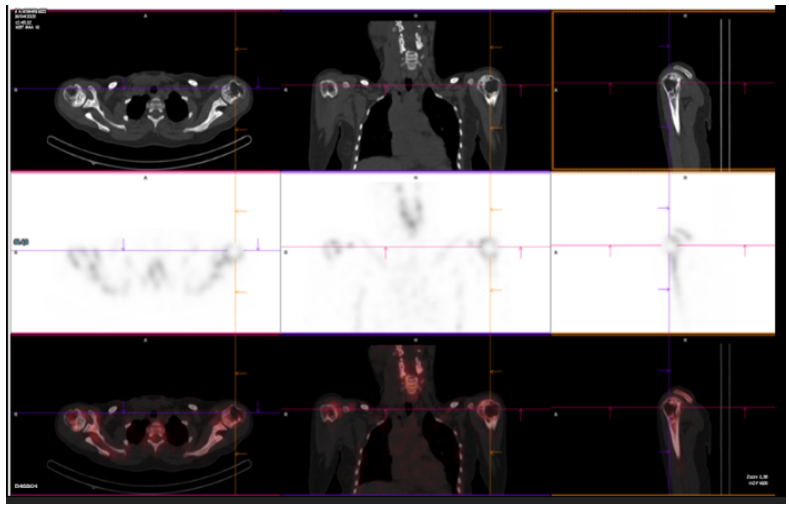


Figure 2: Heterogeneous remodeling of the bone trabeculae with lacunar lesions of the humeral heads, compatible with infarctions.

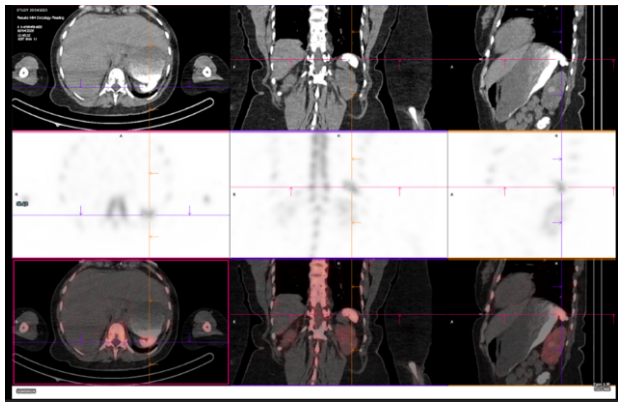


Figure 3a

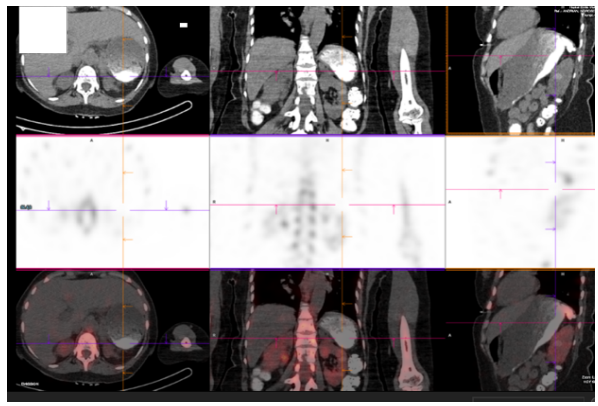


Figure 3b

Figure 3a&b: Faint splenic uptake associated with visceral digestive opacifications.

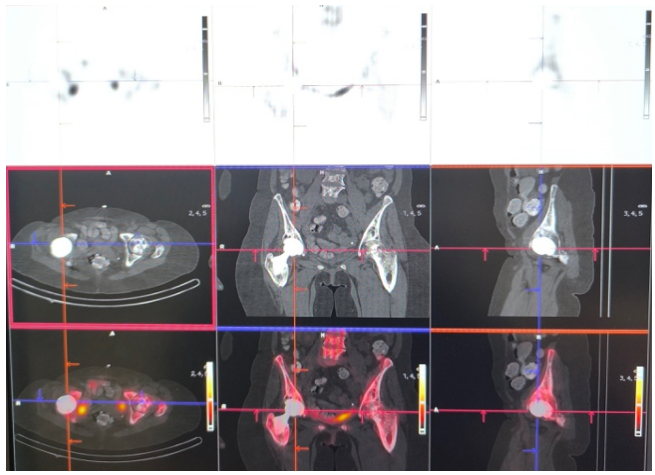


Figure 4: No abnormal uptake suggestive of prosthetic conflict or bi-compartmental peri-prosthetic loosening of the right hip

Discussion

During the course of sickle cell disease, the spleen is one of the first organs to be affected. Repeated vaso-occlusive crises lead to successive splenic infarctions, resulting in progressive fibrosis and most often functional, then anatomical asplenia by adolescence or adulthood (4,5). In adult patients with sickle cell disease, the spleen is usually atrophic and not visible on morphological imaging, and it is generally not identifiable on scintigraphy, regardless of the tracer used (6). This was also confirmed in our patient, whose abdominopelvic ultrasound did not visualize the atrophic spleen. Bone scintigraphy with 99mTc-HMDP is a standard nuclear medicine examination to evaluate bone metabolism and detect active osteoblastic processes, such as fractures, metastases, or osteonecrosis. Extraosseous uptake, such as visualization of visceral structures, is rare and unusual; it should raise diagnostic attention when it occurs in general, and particularly

in an adult with sickle cell disease, in whom the spleen is usually nonfunctional or absent (3,7,8). The identification of faint but definite splenic uptake of the technetium-labeled bone tracer in our patient was atypical and raised concern about the possibility of persistent splenic activity or function.

A focused analysis allowed us to exclude the hypothesis of persistent splenic function. First, the long disease duration, the patient's age, and a clinical history of numerous vaso-occlusive crises made this diagnosis unlikely (4,5). Second, recent abdominal ultrasound failed to visualize the atrophic spleen. It should be emphasized that bone scintigraphy is not an optimal examination for assessing splenic function. In the absence of specific imaging, such as 99mTc-colloid or labeled red blood cell scintigraphy, the uptake observed cannot be regarded as proof of residual splenic function (9). From a pathophysiological standpoint, the most likely hypothesis is nonspecific dystrophic uptake of 99mTc-HMDP in chronic post-ischemic splenic remodeling. Labeled diphosphonates are known to accumulate not only in bone but also in extraosseous tissues with dystrophic calcifications, chronic necrosis, or fibrosis (8,10). In addition, repeated splenic infarctions in sickle cell disease promote the formation of microscopic calcific deposits within residual fibrous tissue. These deposits, even if undetectable on conventional morphological imaging, may explain faint and heterogeneous 99mTc-HMDP uptake, as reported in a few cases in the literature (7,11). Our patient also had a history of multiple transfusions from a young age, exposing her to chronic iron overload. Although iron itself has no direct affinity for 99mTc-HMDP, iron overload can induce chronic tissue remodeling, including fibrosis, oxidative stress, and secondary dystrophic deposition (12). This specific metabolic background could therefore act as an indirect promoting factor for extraosseous uptake of the tracer in the atrophic spleen, as suggested in some series of chronically transfused patients (13).

An additional point of interest in this case is the scintigraphic appearance potentially related to deferasirox therapy. SPECT/CT performed in conjunction with bone scintigraphy demonstrated, in addition to splenic uptake, diffuse visceral opacifications in the stomach and colon on CT, mimicking contrast administration. Chelation therapy may alter tracer biodistribution, and some interactions between chelating agents and radiopharmaceuticals may favor nonspecific visceral uptake (10,14,15). Cases of nonspecific hepatic and splenic uptake of 99mTc-HMDP after concomitant or recent administration of interfering compounds have been reported, although the precise mechanism remains poorly understood (10,14,15). Larger studies would be useful to explore a potential causal relationship. Elsewhere on scintigraphy, our patient presented diffuse bone changes with lacunar lesions of the humeral heads consistent with bone infarctions on hybrid CT. These abnormalities fall within the well-known spectrum of osteoarticular involvement in sickle cell disease and reflect a generalized pattern of chronic ischemic injury (16,17). The association of diffuse bone remodeling with splenic uptake supports the hypothesis of a common mechanism involving chronic ischemic phenomena and multisystem dystrophic remodeling. In the absence of recent contrast-enhanced CT to confirm

macroscopic splenic calcifications, multimodality scintigraphic imaging, particularly SPECT/CT, can provide complementary morphological information and strengthen diagnostic interpretation, as recommended in the evaluation of unusual extraosseous uptake (8,10). Furthermore, concordance between clinical, ultrasound, and scintigraphic data can support a coherent pathophysiological approach, as in our case.

Conclusion

In contemporary bone scintigraphy practice, it is important to recognize unexpected extraosseous uptake of 99mTc-HMDP and to interpret such findings in light of the clinical context. In adult patients with sickle cell disease, splenic visualization on bone scintigraphy should not be considered evidence of residual splenic function but should instead primarily suggest nonspecific dystrophic uptake. Awareness of this diagnostic pitfall may help avoid misinterpretation and highlights the need for systematic correlation with clinical and morphological data.

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