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Case Report

Incidentally detected cardiac amyloidosis on ^{99m}Tc-MDP bone scintigraphy ☆

Ahmed Fathala, MD

Department of Radiology, King Faisal Specialist Hospital & Research Center, MBC#28 P.O. Box 3354, Riyadh, Saudi Arabia

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ABSTRACT

Cardiac amyloidosis (CA) is an important cause of restrictive cardiomyopathy and heart failure with preserved ejection fraction (HFpEF). At present, 3 bone-seeking tracers, ^{99m}Tc-diphosphono-1,2-propanodicarboxylic acid (^{99m}Tc-DPD), ^{99m}Tc-pyrophosphate (^{99m}Tc-PYP), and ^{99m}Tc-hydroxymethylene diphosphonate (^{99m}Tc-HMDP), have been evaluated for detecting CA, but they are not widely available. In contrast, methylene diphosphate (MDP) is widely available. However, only sporadic case reports have shown that MDP can accumulate in patients with CA. We report an 86-year-old man with multiple medical problems, including hypertension, hyperlipidemia, HFpEF, and a history of treated prostate cancer, who was referred for a ^{99m}Tc-MDP bone scan to rule out bone metastasis. The bone scan was negative for bone metastasis, but there was mild tracer accumulation in the heart, suggestive of CA. Subsequently, CA was diagnosed on ^{99m}Tc-PYP imaging. MDP may play a role comparable to other bone-seeking tracers in the diagnosis of CA and may be used as a noninvasive adjunct in the diagnosis of CA. Future research should compare MDP with other bone-seeking tracers for the diagnosis of CA. In addition, mechanistic studies on tracer binding to amyloid fibrils may help understand the pathophysiology of CA and facilitate the development of better and more specific tracers for CA.

Introduction

The detection of cardiac amyloidosis (CA) is difficult because patients present with nonspecific symptoms and nonspecific electrocardiography (ECG) and echocardiography findings. It is important to identify patients with CA at an early stage to initiate appropriate therapy, and it is crucial to differentiate between immunoglobulin light chain (AL) and transthyretin (TTR) subtypes [1,2]. In the past, it was thought that there is no effective therapy for CA, however, this no longer the case. Patients with AL CA may have improved survival up to 12 years with appropriate chemotherapy [3] and there are novel pharmacological agents available and under development for TTR CA [4]. In recent years, radionuclide scintigraphy with bone-seeking tracers such as 99mTc-diphosphono-1,2- propanodicarboxylic acid (99mTc-DPD), 99mTc-pyrophosphate (99mTc-PYP), and 99mTc-hydroxymethylene diphosphonate (99mTc-HMDP) have emerged as a valuable tool in the diagnosis of CA subtypes. Recent multicenter studies have

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E-mail address: afathala@kfshrc.eud.sa

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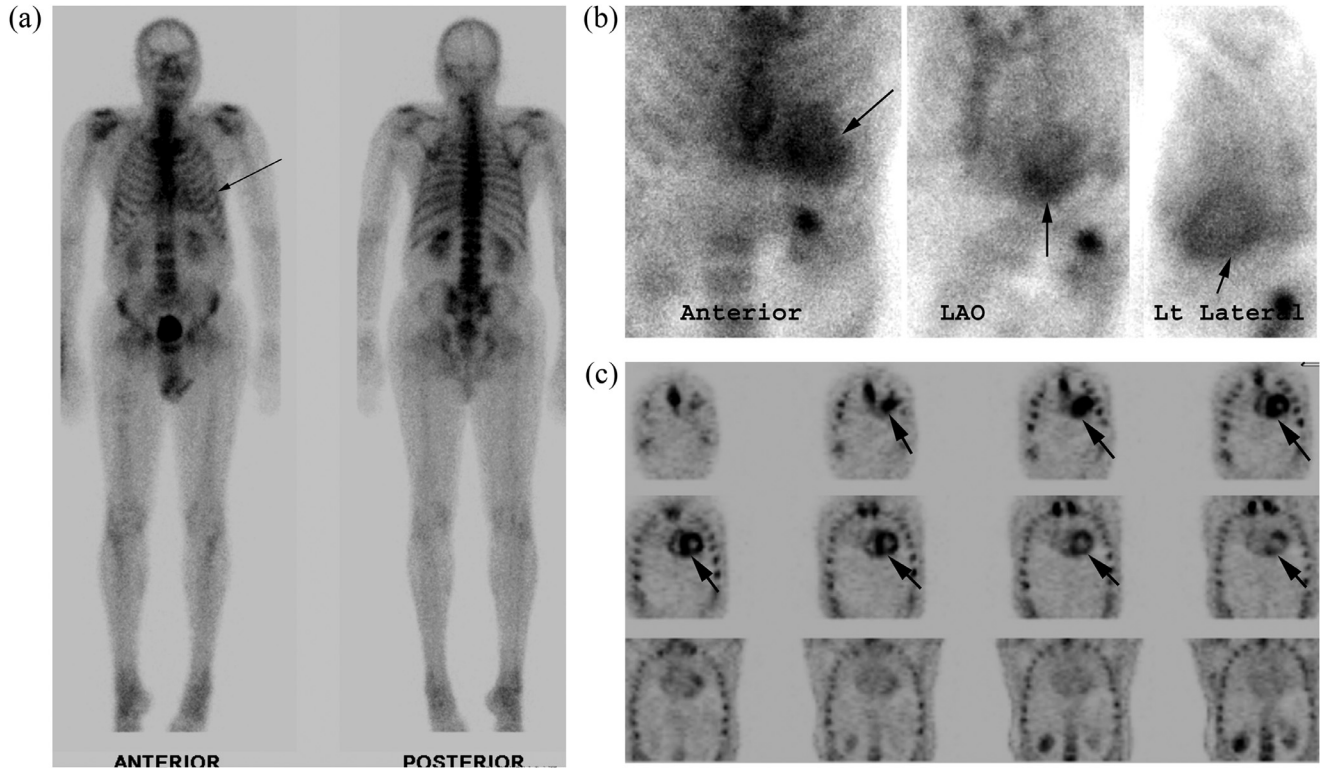

Fig. 1 – Whole-body planar images of ^{99m}Tc-methylene diphosphonate (^{99m}Tc-MDP) 3 hours following intravenous injection of 20 mCi of ^{99m}Tc-MDP demonstrated a mild, diffuse, circular pattern in the region of the heart, suggesting cardiac amyloidosis (CA), arrow. The pattern of bone metastasis was not identified.

demonstrated greater than 90% sensitivity and specificity of bone scintigraphy in distinguishing between TTR CA and AL CA [5,6]. The exact mechanism by which bone-seeking tracers visualize CA and the reason why certain bone-seeking tracers such as ^{99m}Tc-PYP and ^{99m}Tc-DPD consistently visualize CA but ^{99m}Tc-methylene diphosphate (^{99m}Tc-MDP) does not remain unknown [7]. We report a case of CA that was incidentally suspected on 99mTc-MDP bone imaging and was subsequently confirmed with 99mTc-PYP.

Case report

A 86-year-old man with known multiple medical problems, including hypertension, hyperlipidemia, heart failure with preserved ejection fraction (HFpEF), and a history of prostate cancer treated several years ago, presented with elevated prostate specific antigen and back pain. A ^{99m}Tc-MDP scan was performed to rule out bone metastasis. The scan was negative for bone metastasis and revealed mild age-related degenerative changes in multiple joints. Incidentally noted was mild, abnormal, diffuse myocardial uptake of the tracer that raised the suspicion of cardiac CA (Fig. 1). ^{99m}Tc-PYP was performed and demonstrated intense myocardial uptake consistent with CA in both planar and single-photon emission computed tomography images (Figs. 2 A and B). Serum immunofixation and free light chain assay were negative for AL. TTR CA was diagnosed, and the patient was referred to the cardiology department for further treatment.

Discussion

Radionuclide bone scintigraphy with 99mTc-labeled bisphosphonates has been reported to localize cardiac amyloid deposits, however, the molecular basis of this mechanism remains unknown. A high calcium level in the amyloid deposit has been proposed to play a role, as it is associated with increased bone tracer accumulation [8]. However, some questions remain to be answered: (1) why do bone tracers bind more strongly to TTR amyloids and not to AL amyloids and (2) why do certain tracers such as ^{99m}Tc-DPD and ^{99m}Tc-PYP but not ^{99m}Tc-MDP consistently visualize TTR CA, although all 3 tracers share the same mechanism. Several single-center studies have confirmed a high diagnostic accuracy (sensitivity and specificity more than 90%) of ^{99m}Tc-PYP [9], DPD [10], ^{99m}Tc-HMDP [11], and ^{99m}Tc-hydroxydiphosphonate (HDP) [12] for TTR CA.

^{99m}Tc-MDP is more widely available than ^{99m}Tc-DPD or ^{99m}Tc-PYP and is regularly utilized in daily bone scans for many clinical indications. It would be a feasible and convenient option for the diagnosis of CA. Several case reports have shown that MDP radiotracers can accumulate in the heart in patients with CA [13–15]; however, there are no correspond-

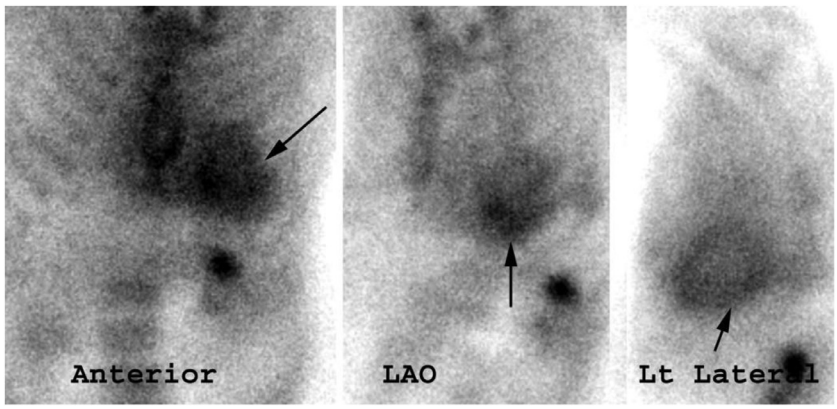

Fig. 2A – Multiple planar views of ^{99m}Tc-pyrophosphate (^{99m}Tc-PYP) in the chest demonstrated intense PYP accumulation in the heart, corresponding to grade 3 myocardial uptake (arrows). LAO, left anterior oblique; Lt lateral, left lateral.

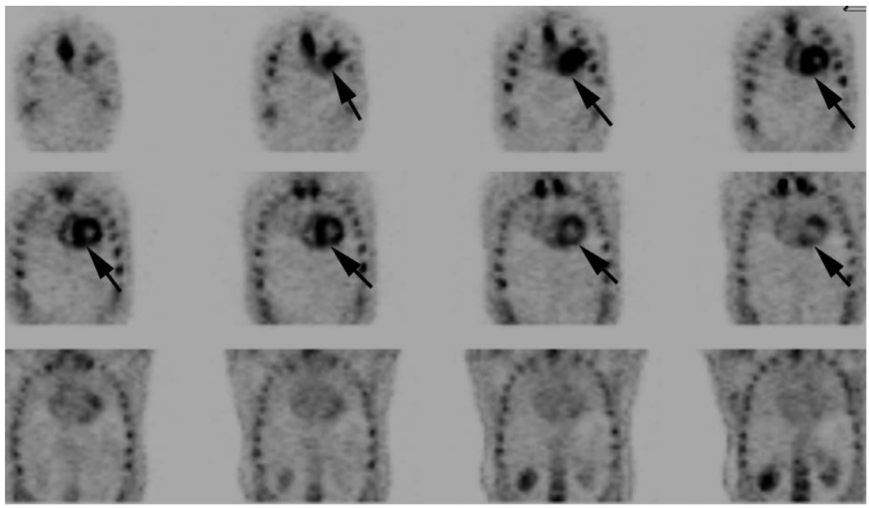

Fig. 2B – Selected coronal images corresponding to ^{99m}Tc-PYP single-photon emission computed tomography images confirmed the planar image findings of intense tracer uptake in the myocardium (arrows).

ing myocardial tissue biopsy results. Currently, there are no data comparing ^{99m}Tc-DPD and ^{99m}Tc-PYP. A recent study reported a similar diagnostic accuracy of 3 different radiotracers, DPD, PYP, and HMDP, but it did not include MDP. There is only case report comparing PYP and MDP that has suggested that MDP is less sensitive than PYP in the diagnosis of CA [7].

Our case demonstrated that albeit mild, the cardiac uptake of MDP correlates with that of PYP and could be a potential tracer for the diagnosis of CA. We believe that the binding of MDP is similar to that of PYP and DPD because transthyretin amyloid fibrils have a higher calcium content. Future research should compare MDP with other bone-seeking tracers for the diagnosis of CA. In addition, mechanistic studies on tracer binding to amyloid fibrils may help understand the pathophysiology of CA and facilitate the development of better and more specific tracers for both TTR CA and AL CA. Until then, MDP may serve as a bone-seeking tracer in the differential diagnosis of CA. More importantly, in routine ^{99m}Tc-MDP bone scintigraphy, any abnormal or suspicious accumulation in the heart should be reported and further CA investigation must be considered.

Conclusion

^{99m}Tc-MDP bone scans may play a role comparable to other bone-seeking tracers in the diagnosis of CA. MDP may serve as a bone-seeking tracer in the differential diagnosis of CA; any incidental MDP uptake in the routine bone scan should be reported and further investigation of CA must be considered.

Informed consent

There is identifiable patient information in this manuscript. It is a case report. Based on our institutional policy, neither IRB

approval nor informed patient consent is needed for such a publication.

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