Multiple myeloma in a patient with suspected hyperparathyroidism

Case Report

Alireza Emami-Ardekani[1], Sara Harsini[1,2], Armaghan Fard-Esfahani[1], Mohammad Eftekhari[1]

[1]Research Center for Nuclear Medicine, Tehran University of Medical Sciences, Tehran, Iran
[2]Association of Nuclear Medicine and Molecular Imaging (ANMMI), Universal Scientific Education and Research Network (USERN), Tehran, Iran

(Received 16 February 2019, Revised 16 April 2019, Accepted 22 April 2019)

ABSTRACT

Multiple myeloma (MM) is a clonal B-lymphocyte neoplasm of terminally differentiated plasma cells. Imaging modalities which allow the recognition of the effects of myeloma cells on the skeletal system have been utilized for a long time. Herein, we represent a patient with generalized osteoporosis and hypercalcemia, who was referred for parathyroid scan, in whom the widespread bone marrow technetium-99m-methoxy-2-isobutylisonitrile (^{99m}Tc-MIBI) uptake suggested the presence of a bone marrow involving pathology, which turned out to be multiple myeloma on bone marrow biopsy. The current case report highlights the importance of ^{99m}Tc-MIBI scintigraphy, with a relatively low cost and better accessibility compared with other high sensitivity modalities such as PET-CT, to be used to demonstrate multiple myeloma bone marrow involvement, which could incline physicians to consider ^{99m}Tc-MIBI scintigraphy as a complementary diagnostic tool for multiple myeloma.

Key words: Multiple myeloma; Hypercalcemia; Tc-99m-Methoxy-2-isobutylisonitrile

Iran J Nucl Med 2020;28(1):43-47
Published: January, 2020
http://irjnm.tums.ac.ir

Corresponding author: Dr. Sara Harsini, Research Center for Nuclear Medicine, Tehran University of Medical Sciences, Tehran, Iran. E-mail: sara.harsini@gmail.com

INTRODUCTION

Multiple myeloma (MM) is a clonal B-lymphocyte neoplasm of terminally differentiated plasma cells with the median age at diagnosis of 65 years, representing about 1% of all malignancies and accounting for approximately 10% of hematologic malignancies. It is known that about 3% of MM cases are diagnosed prior to the age of 40 years [1].

Imaging modalities which allow the recognition of the effects of myeloma cells on the skeletal system have been utilized for a long time. Such modalities include radiographic skeletal surveys, computed tomography (CT), and radionuclide imaging procedures [2]. Magnetic resonance imaging of bone marrow [3] and positron emission tomography (PET) with fluoro-deoxy-glucose (FDG) have been added more recently [4]. Among the nuclear medicine imaging modalities, radionuclide bone scan is known to be of limited value in uncomplicated multiple myeloma and hence not frequently carried out due to its low sensitivity compared with conventional radiography [5]. Besides, there have been reports on the use of technetium-99m-methoxy-2-isobutylisonitrile (^{99m}Tc-MIBI) in the diagnosis of MM since 1996 in the literature [6-8].

Here, we report a patient with generalized osteoporosis and hypercalcemia, who was referred for parathyroid scan with hyperparathyroidism suspicion, in whom the widespread bone marrow ^{99m}Tc-MIBI uptake suggested the presence of a bone marrow involving pathology, which turned out to be multiple myeloma on bone marrow biopsy. To the best of our knowledge, this is the first case of multiple myeloma presenting such a scenario.

CASE PRESENTATION

A 33-year-old man with previous history of generalized osteoporosis (lumbar spine Z-score: -2.83, left femoral neck Z-score: -2.60) and multiple compression fractures extending from L1 to L5 vertebrae as a consequence of falling from a height of 30 cm two years ago, presented with a 3-month history of neck, chest and back pain as well as fatigue. He had lost 15 kg of weight in 3 months. The patient had been on alendronate (Ostomod), vitamin D3 and calcium supplement therapy for the previous year, after he was diagnosed with osteoporosis. He was admitted to the internal medicine department because of suspected malignancy. Physical examination was non-contributory. Initial laboratory results were as follows: blood routine examinations showed hemoglobin 12.2 g/dL (normal range: 14-17) with a normal mean cell volume and mean cell hemoglobin; and normal counts for white blood cells (WBC 10800/mm3) and platelets (222,000/mm3). Further analysis showed blood urea nitrogen 22 mg/dL (normal range: 5-21), creatinine 1.18 mg/dL (normal range: 0.3-1.4), erythrocyte sedimentation rate 17 mm/h (normal range: 0-22), blood calcium 14.9 mg/dL (normal range: 8.8-10.2), phosphorus 3.5 mg/dL (normal range: 2.6-4.5), β2 microglobulin 4.7 µg/mL (normal value up to 3), intact parathyroid hormone 103 pg/mL (normal range: 15-68) and normal values of serum albumin, ferritin, serum iron, total iron binding capacity, thyroid stimulating hormone, prostate specific antigen, carcinoembryonic antigen, and cancer antigen 19-9. The patient underwent neck and abdominopelvic ultrasound as well as the ileocolonoscopy, all of which failed to reveal any abnormal findings. Further detailed diagnostic imaging procedures including spiral neck, chest, and abdominopelvic computerized tomography (CT) and bone scintigraphy were carried out. Severe generalized osteoporotic changes and decreased height of vertebral bodies (specially the T9, L1, and L5) were detected on CT scan (not included). Radionuclide bone scan was performed subsequently in order to assess the whole skeleton. After intravenous administration of 20 mCi technetium-99m methylene diphosphonate (^{99m}Tc-MDP), whole body imaging was carried out after an interval of 3 hours. Images showed a multitude of focally increased uptake within the ribs, sternum, and along the cervical, thoracic, and lumbar vertebrae (Figure 1).

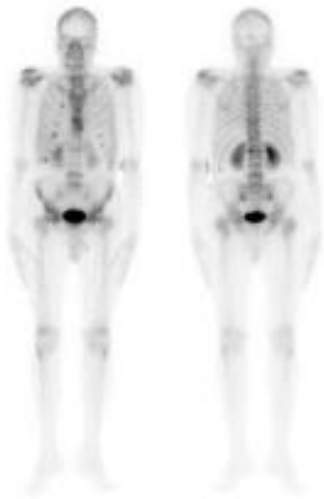

Fig 1. Whole body bone scan with ^{99m}Tc-MDP showing a multitude of focally increased uptake within the ribs, sternum, and along the cervical, thoracic, and lumbar vertebrae.

Differential diagnosis included either osteoporotic or pathologic fractures with possible underlying malignancy.

The patient was then referred to the endocrinology department with suspected diagnosis of hyperparathyroidism and received intravenously administered pamidronate and furosemide, since when, both the calcium and iPTH levels have been normalized. Parathyroid ^{99m}Tc-MIBI scintigraphy was

performed to assess the presence of parathyroid adenomas. Following intravenous injection of 20 mCi ^{99m}Tc-MIBI, sequential imaging from neck and mediastinum was performed in anterior projection, 15, 120 and 180 minutes after radionuclide administration. Normal radiotracer uptake throughout the thyroid lobes (after 15 min) and subsequent washout from thyroid gland on delayed images (after 120 and 180 min) were seen, with no evidence of persistent focus of activity either in neck or mediastinum (Figure 2).

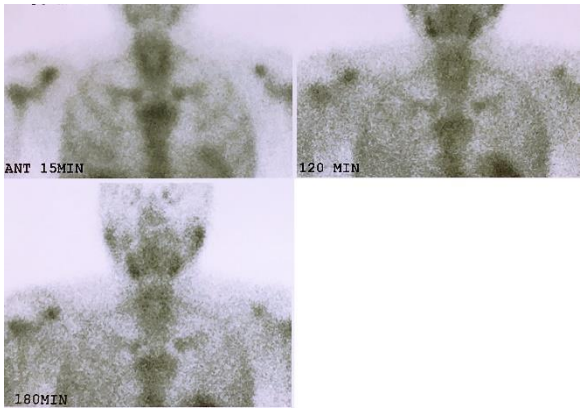

Fig 2. Parathyroid scan with ^{99m}Tc-MIBI depicting tracer distribution throughout the thyroid lobes (15 min after radiotracer injection) and subsequent washout from thyroid gland on the delayed images (120 and 180 min after radiotracer injection) with no evidence of persistent focus of increased uptake in the thyroid bed and mediastinum. Diffuse radiotracer uptake was also noted in the part of the skeleton visualized in both the cervical and mediastinal regions.

All the aforementioned data were consistent with a normal parathyroid scan negative for parathyroid adenoma. However, the study depicted diffuse abnormal radiotracer uptake in the skeleton. While keeping in mind the previously published reports emphasizing the use of ^{99m}Tc-MIBI in the diagnostic work-up of bone marrow involvement in hematological malignancies [7-10], whole body ^{99m}Tc-MIBI scintigraphy was also performed after the first image. Noticeably diffusely increased bone marrow uptake was detected throughout the skeleton with possible bone marrow expansion (Figure 3).

Serum protein electrophoresis was then performed, which revealed hypogammaglobulinemia. Although biochemical analysis demonstrated negativity for Bence Jones' protein in the urine, bone marrow aspiration biopsy found plasma cell infiltration of 50%, which led to a final diagnosis of multiple myeloma. The patient refused to undergo further evaluation and therefore, we were unable to perform serum immunofixation electrophoresis and to evaluate the free light chains (FLC). The patient was then transferred to the hematology department for treatment with bortezomib and autologous hematopoietic cell transplantation.

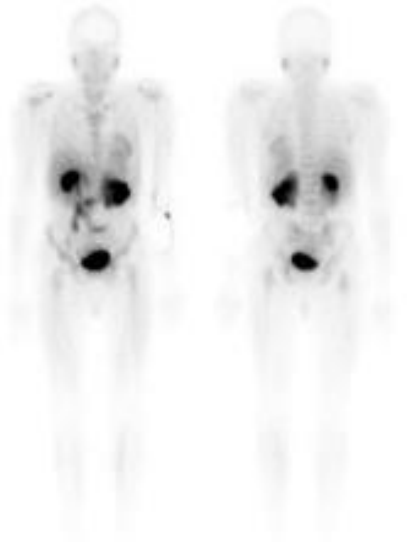

Fig 3. Whole body ^{99m}Tc-MIBI scintigraphy showing abnormal diffusely increased bone marrow uptake throughout the skeleton. Bowel activity noted here could be attributed to either the underlying disease (multiple myeloma) or radiotracer impurity. Normal radiotracer distribution is noted in the urinary system.

DISCUSSION

Multiple Myeloma, a neoplastic disorder of plasma cells, primarily involves the bone marrow [11], and is known as an incurable relapsing disease which warrants constant monitoring. Parameters including β2 microglobulin level, urinary Bence Jones protein, serum protein electrophoresis, serum globulin level, free light chains, as well as the bone marrow aspiration and biopsy findings as well as cytogenetics and fluorescent in situ hybridization (FISH) for chromosomal defects are routinely explored for precise diagnosis and follow-up of multiple myeloma cases [12]. As plain X-rays could depict osteolytic bone lesions, which are present in up to 90% of patients with multiple myeloma [11], they have conventionally been used to evaluate the extent of bone lesions; however, these have limited sensitivity of 80% [13]. In comparison with plain X-rays, CT scan provides superior sensitivity for detection of lytic lesions [14]. MRI is the other imaging modality that currently has a major role in the detection of marrow disease, although having some inherent limitations in follow-up evaluations [15]. With regard to the nuclear medicine imaging modalities, poor sensitivity of ^{99m}Tc-MDP bone scans have been reported for detection of osteolytic myeloma bone disease [16] since these lesions do not produce a significant concomitant osteoblastic reaction (sensitivity of 40-60%). On the other hand, PET-CT scanning with fluoro-deoxy-glucose (FDG) has emerged as an

excellent technique for imaging myeloma lesions [17], but at a higher expense. This modality combines metabolic imaging with high resolution CT scanning and has the advantages of better body coverage, and more specificity in post treatment evaluation than what is achieved with MRI. The benefit of FDG PET-CT scanning for assessment of myeloma extent has been proven by multiple studies [18, 19]. Where FDG PET-CT is not available, ^{99m}Tc-MIBI imaging is regarded as a useful surrogate with similar patterns of disease extent to the FDG PET-CT scans and reported sensitivity and specificity of 82-100% and 75-88%, respectively [20]. ^{99m}Tc-MIBI is easily available in all nuclear medicine departments, far more cheaper than ^{18}F-FDG, which was first used for myeloma imaging in 1996 [20]. Despite the presence of reports of its usefulness in imaging multiple myeloma [7, 8, 10, 21-23], it never became popular in clinical practice. The physiological uptake of ^{99m}Tc-MIBI by multiple organs results in significant background activity of tracer and this makes it difficult to detect lesions on planar Gamma camera scanning. Although the lower resolution of ^{99m}Tc-MIBI imaging, when compared to PET-CT, could be improved by performing single photon emission computed tomography (SPECT), this time-consuming and costly acquisition technique, would take away some of the positive characteristics of ^{99m}Tc-MIBI imaging, namely, technical ease, rapidity of execution and low costs. These could stand as the main reasons ^{99m}Tc-MIBI never became popular as a whole body tumor-imaging agent. It has been speculated that FDG PET-CT and ^{99m}Tc-MIBI could provide complementary information in the diagnostic evaluation of MM patients by detecting focal and diffuse disease, respectively [18]. In spite of the limited capacity of ^{99m}Tc-MIBI imaging in detecting focal lesions, this mode of imaging still remains the most rapid and inexpensive technique for whole-body evaluation and may be an alternative option when a PET facility is not available. In addition, ^{99m}Tc-MIBI is a substrate for p-Glycoprotein in cells, and in this way, it acts as a unique tracer predicting tumor cells resistance to chemotherapy [7]. Therefore, uptake patterns of ^{99m}Tc-MIBI in myeloma are known to have significant prognostic value apart from the ability of this tracer to detect active disease [24, 25].

Multiple myeloma and hyperparathyroidism, both of which can lead to hypercalcemia, are frequently observed in the adult population. Nonetheless, the concurrence of these two relatively common conditions in the same patient is rare and has been reported only in 18 instances in the literature [26]. Herein, we presented a case of generalized osteoporosis and hypercalcemia, suspected to have hyperparathyroidism and referred for ^{99m}Tc-MIBI at the outset; however, in spite of negative study for evidence of primary hyperparathyroidism, diffuse bone marrow ^{99m}Tc-MIBI accumulation suggested the presence of a bone marrow involving pathology, finally proved as multiple myeloma by bone marrow aspiration biopsy. Although the patient refused to undergo serum immunofixation electrophoresis and further work-up to evaluate FLC, a non-secretory or oligo-secretory multiple myeloma could be suspected, diagnosis of which is made based on the depiction of clonal/atypical plasma cells in bone marrow aspiration, bone marrow biopsy, or biopsy of the osteolytic lesion. Since no data are available directly on non-secretory or oligo-secretory myeloma regarding the imaging preferences, data is extrapolated from investigations on secretory MM, which is stated above. Magnetic resonance imaging is known as a useful tool for weighing disease burden for patients with newly diagnosed non-secretory or oligo-secretory myeloma. In addition, FDG PET/CT could be considered in patients diagnosed with non-secretory or oligo-secretory myeloma. Currently, serial monitoring of disease burden of patients with non-secretory or oligo-secretory myeloma are mostly carried out using whole body MRI/diffusion weighted MRI or FDG–PET/CT. The present case could notify the possible role of ^{99m}Tc-MIBI scintigraphy in non-secretory or oligo-secretory myeloma [27].

Such case signifies the examination and interpretation of any available information other than the main objective of the study (e.g, bone marrow uptake in parathyroid scan, in addition to main data regarding parathyroid gland). Whenever one is evaluating Tc-^{99m}Tc-MIBI studies, including parathyroid scan as in the current case and myocardial perfusion scan (MPS), review of all available data should be regarded as an essential part of the interpreting process, helping to identify both quality-control problems and incidental findings. Multiple causes of ^{99m}Tc-MIBI uptake, including breast cancer, lymphoma, thyroid abnormalities, and parathyroid adenomas have been reported in MPSs thus far. In patients referred for any type of ^{99m}Tc-MIBI imaging, detection of unusual findings in areas other than the fields of interest requires systematic and careful inspection of all images. Detecting and reporting these findings may occasionally lead to disease detection in a timely manner. In addition, the information provided in the current paper together with the advantages of ^{99m}Tc-MIBI scintigraphy, including a relatively low cost and better accessibility compared with other high sensitivity modalities such as PET-CT, should incline physicians to consider ^{99m}Tc-MIBI scintigraphy as a complementary diagnostic tool for multiple myeloma.

REFERENCES

1. Bladé J, Kyle RA, Greipp PR. Multiple myeloma in patients younger than 30 years. Report of 10 cases and review of the literature. Arch Intern Med. 1996 Jul 8;156(13):1463-8.

2. Kyle RA. Diagnostic criteria of multiple myeloma. Hematol Oncol Clin North Am. 1992 Apr;6(2):347-58.

3. Walker R, Barlogie B, Haessler J, Tricot G, Anaissie E, Shaughnessy JD Jr, Epstein J, van Hemert R, Erdem E, Hoering A, Crowley J, Ferris E, Hollmig K, van Rhee F, Zangari M, Pineda-Roman M, Mohiuddin A, Yaccoby S, Sawyer J, Angtuaco EJ. Magnetic resonance imaging in multiple myeloma: diagnostic and clinical implications. J Clin Oncol. 2007 Mar 20;25(9):1121-8.

4. Schirrmeister H, Bommer M, Buck AK, Müller S, Messer P, Bunjes D, Döhner H, Bergmann L, Reske SN. Initial results in the assessment of multiple myeloma using 18F-FDG PET. Eur J Nucl Med Mol Imaging. 2002 Mar;29(3):361-6.

5. Nilsson-Ehle H, Holmdahl C, Suurküla M, Westin J. Bone scintigraphy in the diagnosis of skeletal involvement and metastatic calcification in multiple myeloma. Acta Med Scand. 1982;211(6):427-32.

6. Mele A, Offidani M, Visani G, Marconi M, Cambioli F, Nonni M, Catarini M, Brianzoni E, Berbellini A, Ascoli G, Brunori M, Agostini V, Corvatta L, Isidori A, Spinelli A, Gradari M, Leoni P. Technetium-99m sestamibi scintigraphy is sensitive and specific for the staging and the follow-up of patients with multiple myeloma: a multicentre study on 397 scans. Br J Haematol. 2007 Mar;136(5):729-35.

7. Fallahi B, Beiki D, Mousavi SA, Gholamrezanezhad A, Eftekhari M, Fard-Esfahani A, Alimoghaddam K, Mirpour S, Eskandarian A, Saghari M. 99mTc-MIBI whole body scintigraphy and P-glycoprotein for the prediction of multiple drug resistance in multiple myeloma patients. Hell J Nucl Med. 2009 Sep-Dec;12(3):255-9.

8. Fallahi B, Saghari M, Fard Esfahani A, Eftekhari M, Iravani M, Beiki D, Dabbagh Kakhki VR, Sadeghi R. The value of 99mTc-MIBI whole body scintigraphy in active and in remission multiple myeloma. Hell J Nucl Med. 2005 Sep-Dec;8(3):165-8.

9. Fonti R, Del Vecchio S, Zannetti A, De Renzo A, Di Gennaro F, Catalano L, Califano C, Pace L, Rotoli B, Salvatore M. Bone marrow uptake of 99mTc-MIBI in patients with multiple myeloma. Eur J Nucl Med. 2001 Feb;28(2):214-20.

10. Pace L, Catalano L, Pinto A, De Renzo A, Di Gennaro F, Califano C, Del Vecchio S, Rotoli B, Salvatore M. Different patterns of technetium-99m sestamibi uptake in multiple myeloma. Eur J Nucl Med. 1998 Jul;25(7):714-20.

11. Terpos E, Dimopoulos MA. Myeloma bone disease: pathophysiology and management. Ann Oncol. 2005 Aug;16(8):1223-31.

12. Angtuaco EJ, Fassas AB, Walker R, Sethi R, Barlogie B. Multiple myeloma: clinical review and diagnostic imaging. Radiology. 2004 Apr;231(1):11-23.

13. Mulligan ME. Skeletal abnormalities in multiple myeloma. Radiology. 2005 Jan;234(1):313-4.

14. Gleeson TG, Moriarty J, Shortt CP, Gleeson JP, Fitzpatrick P, Byrne B, McHugh J, O'Connell M, O'Gorman P, Eustace SJ. Accuracy of whole-body low-dose multidetector CT (WBLDCT) versus skeletal survey in the detection of myelomatous lesions, and correlation of disease distribution with whole-body MRI (WBMRI). Skeletal Radiol. 2009 Mar;38(3):225-36.

15. Healy C, Murray J, Eustace S, Madewell J, O'Gorman P, O'Sullivan P. Multiple myeloma: a review of imaging features and radiological techniques. Bone Marrow Res. 2011;2011:583439.

16. Ludwig H, Kumpan W, Sinzinger H. Radiography and bone scintigraphy in multiple myeloma: a comparative analysis. Br J Radiol. 1982 Mar;55(651):173-81.

17. Durie BG, Waxman AD, D'Agnolo A, Williams CM. Whole-body (18)F-FDG PET identifies high-risk myeloma. J Nucl Med. 2002 Nov;43(11):1457-63.

18. Fonti R, Salvatore B, Quarantelli M, Sirignano C, Segreto S, Petruzziello F, Catalano L, Liuzzi R, Rotoli B, Del Vecchio S, Pace L, Salvatore M. 18F-FDG PET/CT, 99mTc-MIBI, and MRI in evaluation of patients with multiple myeloma. J Nucl Med. 2008 Feb;49(2):195-200.

19. Hanrahan CJ, Christensen CR, Crim JR. Current concepts in the evaluation of multiple myeloma with MR imaging and FDG PET/CT. Radiographics. 2010 Jan;30(1):127-42.

20. Tirovola EB, Biassoni L, Britton KE, Kaleva N, Kouykin V, Malpas JS. The use of 99mTc-MIBI scanning in multiple myeloma. Br J Cancer. 1996 Dec;74(11):1815-20.

21. Balleari E, Villa G, Garrè S, Ghirlanda P, Agnese G, Carletto M, Clavio M, Ferrando F, Gobbi M, Mariani G, Ghio R. Technetium-99m-sestamibi scintigraphy in multiple myeloma and related gammopathies: a useful tool for the identification and follow-up of myeloma bone disease. Haematologica. 2001 Jan;86(1):78-84.

22. Nandurkar D, Kalff V, Turlakow A, Spencer A, Bailey MJ, Kelly MJ. Focal MIBI uptake is a better indicator of active myeloma than diffuse uptake. Eur J Haematol. 2006 Feb;76(2):141-6.

23. Luthra K, Bhave A, Lele RD. Tc 99m Sestamibi Scanning in Multiple Myeloma--a New look with SPECT-CT. J Assoc Physicians India. 2014 Sep;62(9):801-12.

24. Martín MG, Romero Colás MS, Dourdil Sahún MV, Olave P, Alba PR, Banzo JB. BaselinTc99-MIBI scanning predicts survival in multiple myeloma and helps to differentiate this disease from monoclonal gammopathy of unknown significance. Haematologica. 2005 Aug;90(8):1141-3.

25. Pace L, Catalano L, Del Vecchio S, De Renzo A, Fonti R, Salvatore B, Andretta C, Di Nuzzo C, Rotoli B, Salvatore M. Washout of [99mTc] sestamibi in predicting response to chemotherapy in patients with multiple myeloma. Q J Nucl Med Mol Imaging. 2005 Sep;49(3):281-5.

26. Fanari Z, Kadikoy H, Haque W, Pacha O, Abdellatif A. Medical management of primary hyperparathyroidism with concomitant multiple myeloma. Intern Med. 2010;49(6):581-4.

27. Chantry A, Kazmi M, Barrington S, Goh V, Mulholland N, Streetly M, Lai M, Pratt G; British Society for Haematology Guidelines. Guidelines for the use of imaging in the management of patients with myeloma. Br J Haematol. 2017 Aug;178(3):380-393.