Original Article

BONE MARROW UPTAKE IN PARATHYROID SCINTIGRAPHY IS A CONSEQUENCE OF EXTREMELY HIGH PARATHYROID HORMONE LEVELS*

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ABSTRACT

Objective: We retrospectively evaluated patients with end-stage renal disease (ESRD) who were referred to our department for parathyroid scintigraphy. The aim of this study was to investigate the causes of bone marrow uptake observed on parathyroid scintigraphy.

Methods: We included 18 ESRD patients (10 F, 8 M; mean, 52 ± 13 years old; range, 45-59) in the study. The follow up period was 7.7 ± 4.7 years. The patients' mean plasma calcium and parathormone (PTH) levels were 9.7 ± 1.4 mg/dL and 1553.3 ± 691.7 pg/mL, respectively. Dual-phase technetium-99m 2-methoxyisobutyl-isonitrile (Tc-99m MIBI) parathyroid imaging and, if necessary, additional Tc-99m pertechnetate scintigraphy were performed. Quantification of the planar early phase parathyroid images was performed for various regions (sternum, humerus, ribs) with the same size rectangular region of interest (ROI, 176 × 176 pixels). Average counts were compared with paired samples Student's *t* tests, and $P<.05$ was considered statistically significant.

Results: Tc-99m MIBI parathyroid imaging revealed parathyroid hyperplasia, adenoma, and ectopic adenoma in 7, 3, and 2 patients, respectively. The other 7 patients had normally scintigraphy results with regard to parathyroid pathologies. Bone marrow uptake in the sternum, ribs, and humerus was observed in 6 patients. The difference between the average quantitative value obtained from the ROIs drawn on the sternum and humerus was also statistically significant compared to patients without bone marrow uptake ($P<.05$). All 6 patients' exhibited extremely high PTH levels (>2000 pg/mL; mean, 2413.7 ± 150 pg/mL) compared to the other 12 patients (mean, 1342.8 ± 249 pg/mL).

Conclusion: Our results show that bone marrow uptake on parathyroid scintigraphy is a consequence of extremely high PTH levels in ESRD patients; no further analysis is required. **(Endocr Pract. 2013;19:000-000)**

Abbreviations:
ESRD = end-stage renal disease; **PTH** = parathormone; **ROI** = region of interest; **Tc-99m MIBI** = technetium-99m 2-methoxyisobutyl-isonitrile; **Tl-201** = thallium 201

INTRODUCTION

Hyperparathyroidism is a consequence of increased production of parathormone (PTH). Increased PTH plasma levels trigger a series of events that exert unwanted effects on bone metabolism. Increased osteoclast and osteoblast activities damage healthy bone and cause accompanying hypercalcemia and hypophosphatemia in plasma, as well as hypercalciuria.

The treatment of primary hyperparathyroidism (parathyroid adenoma) depends on which surgical approach is used. The success rate of an appropriate surgical intervention is approximately 90% (1). Localization procedures have gained importance since minimal invasive procedures were introduced in the parathyroid surgery (2).

Parathyroid scintigraphy is performed by either thallium 201-technetium 99m subtraction (Tl-201-Tc-99m) or dual-phase technetium-99m 2-methoxyisobutyl-isonitrile

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(Tc-99m MIBI) imaging, with or without additional Tc-99m pertechnetate thyroid scintigraphy. Both Tl-201 and Tc-99m MIBI are tumor-specific agents. We are sometimes faced with unexpected accumulation of both tracers in soft tissues in routine parathyroid scintigraphy or myocardial perfusion scintigraphy. Bone marrow uptake of Tc-99m MIBI has been evaluated in some malignant disease contexts, but systematic evaluation of incidental Tc-99m MIBI bone marrow uptake in patients with end-stage renal disease (ESRD) has not been performed. The aim of this study was to evaluate possible reasons for faint bone marrow uptake during parathyroid scintigraphy in ESRD patients.

METHODS

Patients

Eighteen ESRD patients (10 F, 8 M; mean, 52 ± 13 years old; range, 45-59) with were included in the study. All underwent parathyroid scintigraphy because of clinical suspicion of parathyroid adenoma between March 2010 and April 2011. The mean follow up period was 7.7 ± 4.7 years. The mean calcium and PTH levels of patients were 9.7 ± 1.4 mg/dL and 1553.3 ± 691.7 pg/mL, respectively. The study was conducted in accordance with the Helsinki Declaration.

Parathyroid Scintigraphy

Approximately 20 mCi (740 MBq) Tc-99m MIBI was intravenously injected. After a 10 minutes, a planar image with 1.33 zoom that included the neck region and a sequential planar image with no zoom that included the neck and mediastinal region were obtained with a double-head gamma camera (Infinia, GE Healthcare, Little Chalfont, UK) equipped with a high-resolution, low-energy collimator. Imaging was repeated approximately 2 to 3 hours after Tc-99m MIBI injection. Single-photon emission computed tomography imaging was also performed in patients suspected to have early-phase ectopic parathyroid adenoma, and Tc-99m pertechnetate thyroid scintigraphy was performed if considered necessary for interpretation. The images were assessed by an experienced nuclear medicine physician using anatomic correlation obtained by ultrasonography.

Quantification

Quantification of the planar early-phase parathyroid images was performed for various rectangular regions of interest (ROIs; sternum, humerus, ribs) of the same size (176 × 176 pixels) (Fig.1). We obtained average counts from these regions and background counts from the liver.

Statistical Analysis

The ratio of average counts was compared by paired samples Student's *t* tests, and $P<.05$ was considered statistically significant.

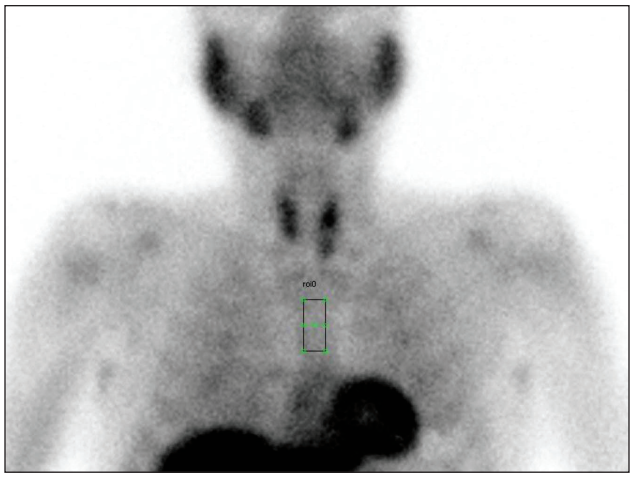

Fig. 1. Regions of interests in an early-phase Tc-99m MIBI planar image of a patient with increased bone marrow uptake.

RESULTS

Parathyroid scintigraphy with Tc-99m MIBI revealed parathyroid hyperplasia in 7 patients, adenoma in 3 patients, and ectopic adenoma in 2 patients. The scintigraphy of the other 6 patients showed no parathyroid pathologies. Bone marrow uptake in the sternum, ribs, and humerus was observed in 6 patients. The difference between quantitative values obtained from the sternum and humerus ROIs in these 6 patients was statistically significant compared to those in the patients without bone marrow uptake ($P<.05$) (Table 1). All 6 of these patients exhibited extremely high PTH levels (>2000 pg/mL; mean, 2413.7 ± 150 pg/mL) compared to the other 12 patients (mean, 1342.8 ± 249 pg/mL). Detailed clinical information for these 6 patients is summarized in Table 2.

DISCUSSION

Parathyroid scintigraphy is usually the method of choice for diagnosing parathyroid adenoma. The other diagnostic methods are ultrasonography, which is highly specific but not sensitive, especially in the lower neck, and computed tomography and magnetic resonance imaging, both of which have sensitivities around 70% (3, 4). A conclusive review of parathyroid disease diagnosis assessed all these methods and determined that the best method for localizing parathyroid adenoma is parathyroid scintigraphy (5).

Whole body scintigraphy (WBS) with Tc-99m MIBI is an accurate method for the demonstrating the presence, severity, and prognosis of bone marrow disease (6). The most important application of this method is in multiple myeloma patients (7). Tc-99m MIBI WBS shows multiple myeloma, and uptake intensity correlates with disease stage and clinical status (8).

Table 1
Comparison of the average counts in early-phase images from patients with and without bone marrow uptake.

Area	Average Counts Patients	Average Counts Controls	*P*
Humerus	62,335	55,427	**.032**
Ribs	103,246	81,793	.065
Sternum	111,279	75,294	**.015**
Liver	374,012	268,287	.213

There are several case reports regarding the incidental bone marrow uptake of Tc-99m MIBI. In a previous case report, increased Tc-99m sestamibi uptake in the axial and appendicular skeleton was observed in myocardial perfusion scintigraphy, and subsequent bone marrow biopsy revealed multiple myeloma (9). Diffuse bone marrow activity of another patient was determined to be secondary myelofibrosis by bone marrow biopsy (10). In another case report, sternal tumoral Tc-99m MIBI uptake was incidentally detected during myocardial perfusion scintigrapy (11). However, not all patients with incidental Tc-99m MIBI uptake in unexpected sites have undiagnosed malignancies. An example of this is a patient with primary hyperthyroidism. Unusual bone accumulation of the radiopharmaceutical was initially thought to be metastatic disease but was determined to be brown tumor uptake due to a parathyroid adenoma (12). The only study on incidental Tc-99m MIBI accumulation in bone marrow included 21 patients with bone marrow uptake among 44 parathyroid scintigraphy examinations, and the authors concluded that diffuse faint skeletal activity does not indicate malignancy (13). However Wakasugi et al. compared Tc-99m MIBI uptake in the femoral region of patients with and without malignancy and reported that patients with malignancy show intramedullary Tc-99m MIBI accumulation and control patients do not (14). In our opinion, there might be patients with malignant diseases that are incidentally identified by parathyroid or myocardial perfusion scintigraphy. The risks and benefits of screening all the patients with this uptake pattern should be evaluated.

Another radiopharmaceutical employed in parathyroid imaging is Tl-201, which is also a tumor marker. Incidental uptake of Tl-201 was described in a patient with nonsecretory myeloma (15). Tl-201 uptake of the bone marrow is explained by increased vascularity, cellularity, glucose consumption, and metabolism (16, 17).

Conversely, we determined that bone marrow uptake in ESRD patients is a consequence of extremely high PTH levels. The only exceptional case in our series was a man with ectopic mediastinal parathyroid adenoma, which may mask surrounding uptake (Fig. 2). Extremely high PTH levels probably cause increased bone metabolism, which might explain increased Tc-99m MIBI bone marrow uptake. The early-phase images were acquired for

Table 2
Clinical information of patients with bone marrow uptake by the time of parathyroid scintigraphy.

Patient No.	PTH (-65 pg/mL)	Creatinine (0.6 to 1.2 mg/dL)	Urea (10 to 50 mg/dL)	Potassium (3.5 to 5.5 meq/L)	Calcium (2.6 to 4.5 mg/dL)	Phosphorus (2.6 to 4.5 mg/dL)	Alkaline phosphatase (30 to 120 U/L)
1	2143	11.9	186	3.7	9.9	8.2	199
2	2500	6.1	76	6.1	11.4	5.5	–
3	2327	1.3	33	3.8	13	2.4	853
4	2500	9.7	206	6.7	10.8	6.7	–
5	2500	8.4	118	6	8.4	6.9	353
6	2327	6.6	127	4.5	9.3	4.5	93

quantification because the early phase more prominently reflects bone marrow uptake changes (13). Quantification of the images confirmed increased bone marrow uptake, except in ribs, which was probably influenced by the uptake of lung or other surrounding tissues. In addition, the ROI size was not appropriate to evaluate the ribs.

The limitations of this study are its retrospective nature and the lack of patient follow up or bone marrow biopsy results.

Collectively, our results indicate that bone marrow uptake in parathyroid scintigraphy in ESRD patients is a consequence of extremely high PTH levels.

DISCLOSURE

The authors have no multiplicity of interest to disclose.

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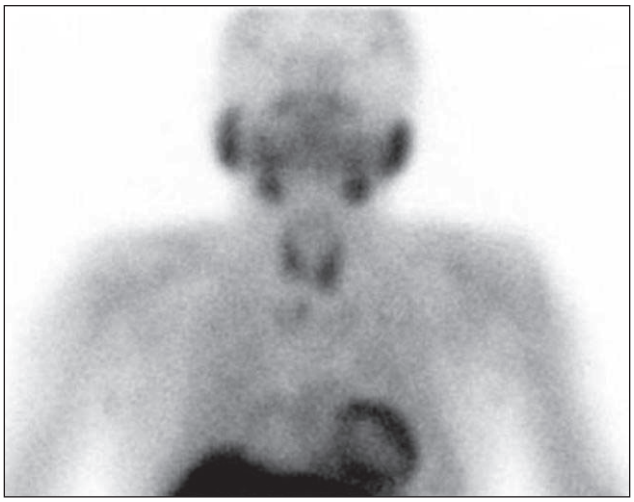

Fig. 2. Early-phase Tc-99m MIBI planar image of a unique patient with a PTH level >2000 pg/mL and an ectopic parathyroid adenoma without bone marrow uptake.

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