



Parathyroid imaging with [^{99m}Tc]Tc-MIBI SPECT/CT — unexpected findings of bone marrow involvement of non-Hodgkin's lymphoma

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Hyperparathyroidism is a condition caused by increased secretion of the parathormone (PTH), which plays an important role in calcium homeostasis. Parathormone raises the serum calcium level by the renal absorption of calcium, decreasing reabsorption of phosphate, and stimulating osteoclasts. The second important player in calcium homeostasis is vitamin D₃ (VitD₃). The main function of 1,25(OH)₂D₃, the active form of VitD₃, is to increase calcium absorption from the intestine. Low 1,25(OH)₂D₃ status leads to reduced efficiency in intestinal calcium absorption, which causes increased secretion of PTH.

Primary hyperparathyroidism is considered to be present when serum calcium is elevated and PTH is increased or inappropriately normal. From the literature review, it can be seen to be primarily the result of a parathyroid adenoma (80–85% of cases), hyperplasia (10–15% of cases), or (albeit rarely) parathyroid carcinoma (0.5–1% of cases).

Surgical removal of the hypersecreting gland is the primary treatment; hence, localisation of the hyperfunctional parathyroid before it is most important.

[^{99m}Tc]Tc-MIBI subtraction imaging or washout imaging is currently the method of choice for parathyroid localisation, with the reported sensitivity ranging from 80% to 90%. The addition of single-photon emission computed tomography (SPECT) and more recently SPECT/CT improves the anatomical localisation and helps in the differentiation of the parathyroid from the thyroid lesions.

A 72-year-old man, diagnosed previously with small B-cell lymphoma, underwent [^{99m}Tc]Tc-MIBI examination due to suspicion of hyperparathyroidism based on

endocrinology consultation (biochemical examination: hypercalcaemia Ca²⁺ 1.31 mmol/L n: 1.15–1.29 mmol/L, PTH 235 pg/mL n: < 65 pg/mL, and Vit D₃ 11.2 ng/mL n: > 30 ng/mL). Previously performed ultrasound (US) was described as unremarkable, with no typical sign of parathyroid, multiple enlarged lymph nodes were seen.

As a standard procedure subtraction [^{99m}Tc]NaTcO₄ (A)/[^{99m}Tc]Tc-MIBI (D — subtraction), [^{99m}Tc]Tc-MIBI dual phase (B — [^{99m}Tc]Tc-MIBI early, C — [^{99m}Tc]Tc-MIBI late image), and early SPECT/CT was performed (E-MIP).

The dual-phase (B, C) and subtraction examination (D) did not reveal typical uptake for hyperfunctional parathyroid. On early and late [^{99m}Tc]Tc-MIBI imaging surprisingly diffuse uptake in the locus of bone was seen (B, C).

SPECT/CT image showed increased uptake in two lesions below the left lobe of the thyroid (F, G). Also, enlarged neck and axillary lymph nodes were found, some with increased tracer uptake (H) and diffuse increased uptake in the bone in the field of examination (E, H).

Because of uptake not only in two lesions below the left lobe of thyroid, but also in some of the neck and axillary lymph nodes, the SPECT/CT examination was considered ambiguous. Fine needle biopsy of the suspected lesion confirmed involvement of the primary process lymph node. The bone marrow biopsy revealed only 10% bone marrow involvement.

In the PET era the young generation of physicians have forgotten about the possibility of using different tracers in oncological disease. [^{99m}Tc]Tc-MIBI, originally developed for scintigraphic evaluation of myocardial blood flow, has also been applied



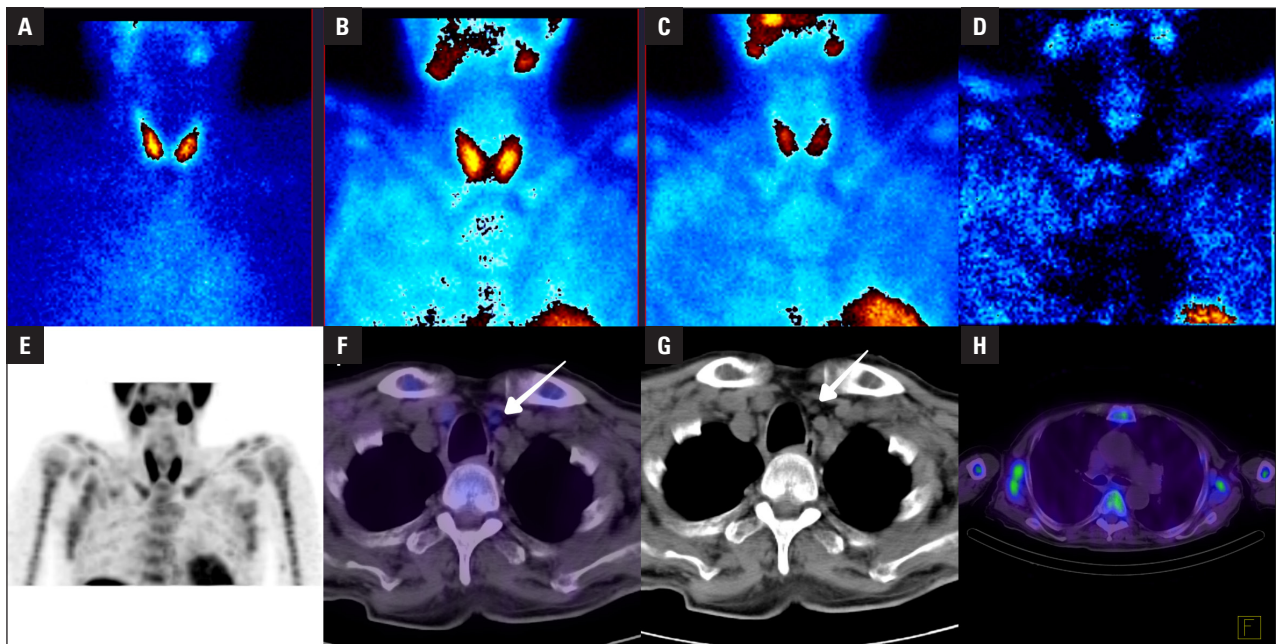


Figure 1. Parathyroid scintigraphy. A. $[^{99m}\text{Tc}]\text{NaTcO}_4$; B. $[^{99m}\text{Tc}]\text{Tc-MIBI}$ early phase; C. $[^{99m}\text{Tc}]\text{Tc-MIBI}$ late image; D. Subtraction $[^{99m}\text{Tc}]\text{Tc-MIBI}/[^{99m}\text{Tc}]\text{NaTcO}_4$; E. MIP SPECT; F. Fusion SPECT/CT; G. CT; H. Fusion SPECT/CT

to detect functional P-gp expression and used for imaging several types of malignant cells including non-Hodgkin's lymphoma, with high diagnostic accuracy up to 94% [1]. Moreover, the uptake, washout rate, and retention of $[^{99m}\text{Tc}]\text{Tc-MIBI}$ could be helpful in the identification of drug resistance; patients with negative or decreased radiotracer activity tend to have unfavourable responses to chemotherapy compared to those with prominent radiotracer accumulation, irrespective of lymphoma type [2]. Also, a later scan (180 min after injection) could provide a more accurate prediction of chemoresistance than an early scan (30 min after injection) [3]. The involvement of bone marrow in multiple myeloma and correlation with in vitro and in vivo uptake was described by Fonti et al. [4, 5].

In the presented case $[^{99m}\text{Tc}]\text{Tc-MIBI}$ showed much greater bone marrow involvement than was shown by the biopsy, which resulted in the change of treatment scheme. The patient underwent chemotherapy (R-CHOP) with partial response. Visible uptake in the late phase of $[^{99m}\text{Tc}]\text{Tc-MIBI}$ examination performed during standard procedure examination predicted the chemosensitivity. In follow-up, normalisation of Ca^{2+} level and decrease of PTH was observed; hence, the increased level of PTH was probably associated with low VitD_3 .

Nowadays, this is a surprising image of small B-cell lymphoma in the $[^{99m}\text{Tc}]\text{Tc-MIBI}$ examination.

Compliance with ethical standards

All authors declare that they have no conflict of interest in relation to this article. This article does not contain any studies with animals performed by any of the authors. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Conflict of interest

None.

References

- Ohta M, Isobe K, Kuyama J, et al. Clinical role of Tc-99m-MIBI scintigraphy in non-Hodgkin's lymphoma. *Oncol Rep.* 2001; 8(4): 841–845, doi: [10.3892/or.8.4.841](https://doi.org/10.3892/or.8.4.841), indexed in Pubmed: [11410795](https://pubmed.ncbi.nlm.nih.gov/11410795/).
- Fujii H, Nakamura K, Kubo A, et al. $^{99m}\text{Tc-MIBI}$ scintigraphy as an indicator of the chemosensitivity of anthracyclines in patients with breast cancer. *Anticancer Res.* 1998; 18(6B): 4601–4605, indexed in Pubmed: [9891525](https://pubmed.ncbi.nlm.nih.gov/9891525/).
- Lazarowski A, Dupont J, Fernández J, et al. $^{99m}\text{Tc-MIBI}$ uptake in malignant lymphomas. Correlation with chemotherapy response. *Lymphat Res Biol.* 2006; 4(1): 23–28, doi: [10.1089/lrb.2006.4.23](https://doi.org/10.1089/lrb.2006.4.23), indexed in Pubmed: [16569203](https://pubmed.ncbi.nlm.nih.gov/16569203/).
- Fonti R, Del Vecchio S, Zannetti A, et al. Bone marrow uptake of $^{99m}\text{Tc-MIBI}$ in patients with multiple myeloma. *Eur J Nucl Med.* 2001; 28(2): 214–220, doi: [10.1007/s002590000434](https://doi.org/10.1007/s002590000434), indexed in Pubmed: [11303893](https://pubmed.ncbi.nlm.nih.gov/11303893/).
- Fonti R, Pace L, Cerchione C, et al. $^{18}\text{F-FDG}$ PET/CT, $^{99m}\text{Tc-MIBI}$, and MRI in the prediction of outcome of patients with multiple myeloma: a comparative study. *Clin Nucl Med.* 2015; 40(4): 303–308, doi: [10.1097/RLU.0000000000000696](https://doi.org/10.1097/RLU.0000000000000696), indexed in Pubmed: [25608167](https://pubmed.ncbi.nlm.nih.gov/25608167/).