Methods of imaging of primary hyperparathyroidism

***Marcin Gierach[1,2], Agnieszka Skowrońska[2], Cyprian Świętaszczyk[3], Stanisław Pilecki[3], Roman Junik[1]**

[1]Department of Endocrinology and Diabetology with Laboratory of Nuclear Medicine, Nicolaus Copernicus University in Toruń, Collegium Medicum in Bydgoszcz
Head of Department: prof. Roman Junik, MD, PhD
[2]Internal Ward, Hospital in Wąbrzeźno
Head of Internal Ward: Marcin Gierach, MD
[3]Regional Specialist Hospital in Grudziądz
Head of Nuclear Medicine Institute: Stanisław Pilecki, MD

METODY OBRAZOWANIA PIERWOTNEJ NADCZYNNOŚCI PRZYTARCZYC

S t r e s z c z e n i e

Pierwotna nadczynność przytarczyc to stan wzmożonego wydzielania parathormonu, którego przyczyną jest pierwotny defekt komórek przytarczyc, wyrażający się nadprodukcją PTH, nieadekwatną do potrzeb ustrojowych i niewrażliwą lub mało wrażliwą na supresyjne działanie hiperkalcemii. P-HTP jest trzecią co do częstości występowania chorobą endokrynologiczną (zaraz po cukrzycy i chorobach tarczycy) występującą z częstością 4-6/100 0000 rocznie, najczęściej u kobiet w okresie pomenopauzalnym. Najczęstszą przyczyną P-HTP jest pojedyńczy gruczolak (75-85%), rzadziej występują mnogie gruczolaki (dwie zmiany: 2-12%; trzy: 1-2%; cztery i więcej: <1%) oraz rak przytarczyc <1%.

Słowa kluczowe: pierwotna nadczynność przytarczyc, gruczolak, parathormon

INTRODUCTION

Primary hyperparathyroidism (P-HTP) is characterized by an increased parathyroid hormone (PTH) secretion caused by a primary defect of parathyroid cells, PTH overproduction, which exceeds the needs of the organism and remains resistant to or poorly controlled by the suppressive effect of hypercalcaemia. P-HTP is the third most prevalent endocrine disorder (after diabetes and thyroid disorders), occurring in 4-6/100,000 people per year, most frequently in women in their postmenopausal stage.

The most common cause of P-HTP is a single gland adenoma (75-85%), less frequent are multigland adenomas (two lesions: 2-12%; three: 1-2%; four and more: <1%) and parathyroid cancer <1%. Few cases of primary hyperthyroidism may be due to the paraneoplastic production of parathyroid hormone by tumours not related with parathyroids (1).

IMAGING TECHNIQUES

In patients with clinical and biochemical signs indicative of hyperparathyroidism, medical imaging techniques should be used to enable the final diagnosis. The first essential examination employing such a technique is ultrasonography (US) of the thyroid. It should be conducted using a high-frequency linear probe; a 12-15 MHz probe may be used if other frequency ranges are unavailable. During the examination, the patient's arms should be supported by a pillow. The assessment should cover the area between the carotid artery and the median line, and between the hyoid bone and the manubrium sterni. Lower parathyroids may be examined during the swallowing reflex. Usually the glands are not visible in routine examinations, since they are isoechoic to the thyroid tissue. During the US assessment, the tumour is described as homoechoic or hypoechoic, limited by tissue. It is oval- to bean-shaped. The sensitivity of tumour detection depends on the size of parathyroids; a normal gland has a size of 5 x 3 x 1 mm. The diameter of altered glands usually exceeds 5 mm. Among the correctly assessed glands weighing above 4,000 mg, 95% are detected as altered, while among those weighing below 1,500 mg, only 40% are detected as altered (2). Gland hyperplasia is rarely visualized and diagnosed, as the tumour size is smaller than in adenomas. The reactivity of inflamed lymph nodes may be confused with that of enlarged parathyroids and lead to the misidentification of the former as parathyroid adenomas or hyperplasias (1). US examinations are immediately available and relatively cheap. The sensitivity of this method reported in the literature can be as high as 91%. The parameter is highly dependent on the experience and the skills of the ultrasonographer. However, due to the ease, availability and noninvasiveness of the US technique, it may be a useful tool for the location of lesions in preoperative diagnostics (2). Additionally, the use of Color Doppler Ultrasonography (CDU) or Power Doppler Ultrasonography (PDU) has been reported in the assessment of blood flow through parathyroids. This permits the differentiation between adenomas and pathologies of the surrounding tissues (3). By using these techniques, pathology may be identified in the case of a lack of vascular blood flow in either central or peripheral parts of parathyroids, but also in the case of a uniformly increased vascular flow called the “spot of fire”. Blood vessels occurring in pathological lesions usually originate from the inferior thyroid artery. The sensitivity of the method is estimated at 97% (4).

Ultrasonography permits a precise assessment of the anatomical localization of parathyroid lesions, however, the assessment of ectopic glands or those located deeper using this technique is impossible. To properly assess those regions, a transoesophageal US examination may be conducted. Still, techniques such as computed tomography, magnetic resonance imaging or scintigraphy are more useful (5).

Scintigraphy, based on the emission of a single photon, is the method of choice in parathyroid diagnostic imaging. Its sensitivity is approx. 80% (6). The first nuclear medicine technique in parathyroid diagnostics was introduced by Ferlin et al. and involved a simultaneous administration of two radioactive markers: thallium (^{201}Tl) i pertechnetate-^{99m}Tc (^{99m}Tc-technetium-pertechnetate). Both markers were absorbed by the thyroid. Parathyroid lesions, such as adenomas, hyperplasias and carcinomas, absorbed ^{201}Tl but did not absorb ^{99m}Tc, which permitted their identification. Since 1990, ^{99m}Tc-sestamibi (7) has been used, while ^{99m}Tc-tetrofosmin was introduced in 1995 (8). Both markers are lipophilic and can bind to a cell. ^{99m}Tc-tetrofosmin may correlate with the cell membrane and mitochondrial potential, whereas ^{99m}Tc-sestamibi correlates only with the mitochondrial potential. These properties allow ^{99m}Tc-tetrofosmin to be eliminated more slowly from the thyroid tissue and from parathyroid adenomas. A two-phase protocol employing ^{123}I and ^{99mc}Tc-sestamibi has also been used for some time (9). Initially, ^{123}I is administered and imaging is conducted after 4 hours, followed by the administration of ^{99mc}Tc-sestamibi and the second imaging exposure after another 10 min (10). The use of ^{123}I in parathyroid imaging has been dropped due to the high examination costs, poor availability and lengthy procedure. In 1992 Taillefer et al. introduced a procedure based on a two-phase administration of one isotope of ^{99mc}Tc-sestamibi (fig. 1). By using this technique, the images are obtained 20-30 minutes after radioactive marker administration, while the second scan is performed 120-180 minutes after the injection (7, 8, 11). The isotope accumulates in the thyroid and parathyroid tissue, and its elimination from healthy tissue occurs more quickly than in pathological tissues. However, in hyperplastic lesions, the radioactive marker is eliminated relatively rapidly, which prevents the detection of possible pathologies (9).

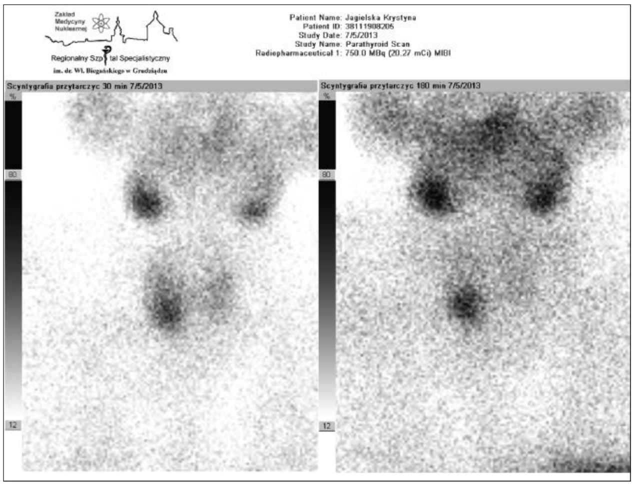

Fig. 1. A two-phase scintigraphy with the use of 99mTc-sestamibi (30 and 180 minutes after radioactive marker administration).

SPECT/CT is another important examination method used in patients with primary hyperparathyroidism. SPECT/CT enables a precise assessment of the anatomical localization of adenomas, especially those with ectopic localization. Thanks to the possibility of joining the analyses of tissue anatomy and function, SPECT/CT permits a precise assessment of the lesion before planned surgery. This examination method is usually conducted using the two-phase system of ^{99mc}Tc-sestamibi. The first SPECT/CT scan should be performed 15 minutes after isotope administration, while the second scan should be performed 120 minutes after the i.v. injection. It is the best method of preoperative determination of adenoma localization with a sensitivity of 85-100% (10, 12) (fig. 2).

Computed tomography is most frequently used for the assessment of ectopic lesions and becomes the conclusive method if the results of a SPECT/CT scan are dubious. The majority of adenomas are hyperechoic, as opposed to lymph nodes. A well-conducted CT examination requires the assessment of the area spanning from the base of the skull to the carina of the trachea, and the scans should be performed shortly after contrast administration. The sensitivity of adenoma detection using CT is 92-93% (13, 14). Since 2006, a four-phase CT imaging technique is used, constituting an alternative for the traditional contrast administration. The examination involves a quadruple scan of the region of interest. In the first phase of the study, images are taken without previous contrast administration. Twenty-five seconds before the initiation of the second phase, iodine-based contrast is given to the patient. Thirty seconds after the conclusion of the second phase, a scan is performed, and 45 seconds later the last phase of the examination begins. During phase I, the tissues are visualized without any contrast. In phase II, the early image after contrast administration is assessed, while in phases III

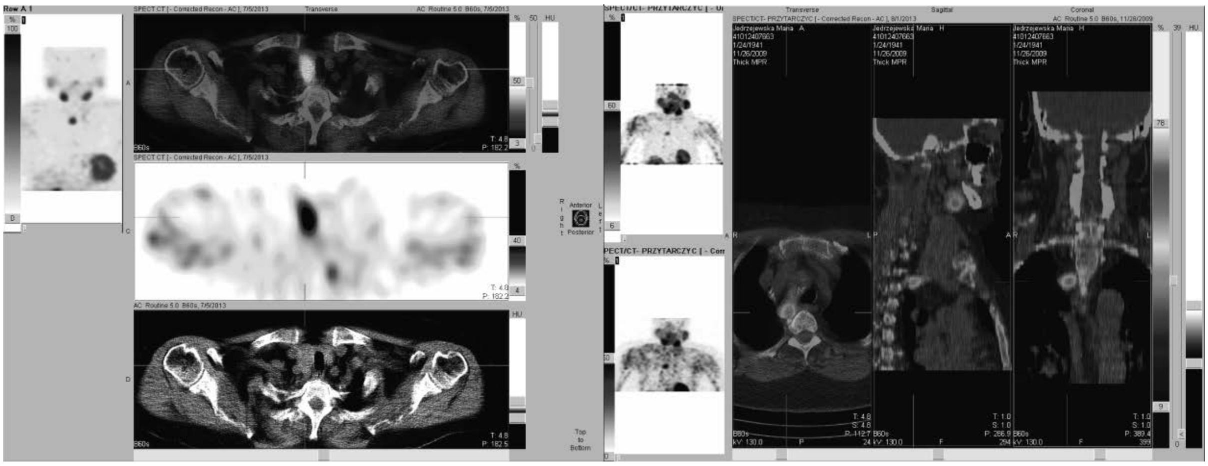

Fig. 2. SPECT/CT of parathyroid glands.

and IV, the late image after contrast administration is generated. The first three vascular phases of the study enable the differentiation between the capturing and elimination of the contrast in highly vascularized tissues (such as adenomas) and in the thyroid and lymph nodes (13).

Magnetic resonance imaging (MRI) is used less frequently in the preoperative diagnostics of parathyroid adenomas. The examination sensitivity is similar to that obtained using other techniques of imaging of pathological parathyroid tissues. MRI is indicated for use in patients with relapsing hyperparathyroidism, because this method may help to locate the altered parathyroid tissue. The visualized area spans from the hyoid bone to the manubrium sterni. The examination involves the use of T1 and T2 fat-suppressed sequences. The MRI image of adenomas is variable, but it is most frequently described as hypodense on the T1 sequence and hyperdense on the T2 sequence. Image enhancement on the T1 sequence may be obtained by adding gadolinium. This, however, will inevitably cause false negatives to appear. These false negatives are most often related with adenomas that are isodense on the T1 and T2 sequences. In such cases, administering contrast and performing the examination using fat suppression leads to increased lesion detection (15).

In the last decade, the technique of positron emission tomography (PET) has emerged. In parathyroid examination, the amino acid ^{11}C-methionine is used. The compound is absorbed by the parathyroid tissue and binds with proteins involved in protein synthesis and transmembrane amino acid transport. Thanks to this binding, the biochemical activity of the overactive parathyroids is visualized. The examination is characterized by a high sensitivity of approx. 85% (16). However, high costs and poor availability are the main disadvantages of the method. Therefore the US and SPECT examinations should be performed in the first place, while PET/CT may be used in patients with negative imaging results (12) but with a clinical image indicative of primary hyperthyroidism.

CONCLUSIONS

In patients in whom primary hyperthyroidism is suspected based on the clinical image, apart from the laboratory tests, a US examination of the neck and a SPECT examination using ^{99mc}Tc-sestamibi should be performed. Both methods dramatically increase the chance of a precise determination of the anatomical localization of the lesions and enable an accurate surgical intervention. □

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Address to corespondence:
*Marcin Gierach
Department of Endocrinology and Diabetology
of Ludwik Rydygier
Collegium Medicum in Bydgoszcz
University of Nicolaus Copernicus in Toruń
ul. M. Skłodowskiej-Curie 9, 85-094 Bydgoszcz
tel./fax: +48 (52) 585-42-40
e-mail: marcin_gierach@wp.pl