The role of combined techniques of scintigraphy and SPECT/CT in the diagnosis of primary hyperparathyroidism

A case report

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Abstract

Rationale: Primary hyperparathyroidism, usually as a result of a hyperfunctioning parathyroid gland, represents more than 90% cases of patients evaluated for hypercalcemia. Combined techniques of preoperative scintigraphy and SPECT/CT serve as a successful minimally-invasive parathyroidectomy. This recent imaging method provides four-dimensional functional images with advanced contrast resolution which greatly facilitates preoperative localization of parathyroid adenomas.

Patient concerns: We presented the case of a male Caucasian patient, aged 67 years, who was investigated for hypercalcemia. Increased levels of parathormone, cervical ultrasonography without pathological changes, and negative planar parathyroid scintigraphy have led to the performance of a parathyroid scintigraphy combined with SPECT/CT.

Diagnoses: The diagnosis of right inferior parathyroid adenoma was confirmed by the 99mTc-MIBI-SPECT/CT that revealed on early phase increased radiotracer uptake in the area of projection of the lower third of the right thyroid lobe. The SPECT/CT scan localized this area behind the lower pole of the right thyroid lobe, in the right side of the trachea, with CT correspondent of hypodense lesion, with a maximum diameter of 20 mm.

Interventions: During hospitalization, the decision to undergo surgical intervention was taken. The patient underwent surgical intervention, and minimally-invasive right inferior parathyroidectomy was performed.

Outcomes: The histopathological examination confirmed the diagnosis and the patient’s recovery was complete, with the normalization of parathormone, calcium levels, and metabolic parameters.

Lessons: Modern combined techniques of scintigraphy and SPECT/CT proved to be of excellent clinical utility in the preoperative diagnosis of primary hyperparathyroidism, localizing a parathyroid tumor undetected by planar scintigraphy alone.

Abbreviations: 99mTc-MIBI = Technetium-99 metastable sestamibi, CT = computed tomography, HDL = high-density lipoprotein, LDL = low-density lipoprotein, SPECT = single photon emission computed tomography.

Keywords: primary hyperparathyroidism, scintigraphy, SPECT/CT

1. Introduction

Primary hyperparathyroidism is the third most common endocrine disease, as a result of solitary parathyroid adenomas in 75%–85% of cases and diffuse hyperplasia in most of the remaining cases, with increased production of parathormone, which mobilizes calcium to the blood stream.\textsuperscript{[1]} The treatment of choice is surgical removal.\textsuperscript{[2]} A large number of cases of parathyroid adenomas which are not visualized by ultrasonography and neither by classic planar scintigraphy are reported in literature. Technetium-99 metastable sestamibi (99mTc-MIBI) scintigraphy has more than 80% sensitivity for the detection of parathyroid lesions, which can be increased by adding single photon emission computed tomography (SPECT) and computed tomography (CT), offering important preoperative functional evaluation and precise anatomic localization for a minimally-invasive surgical approach.\textsuperscript{[1,3]}

We presented the case of a male patient, diagnosed with primary hyperparathyroidism secondary to a parathyroid adenoma due to modern combined imaging techniques, to emphasize the importance of combined 99mTc-MIBI scintigraphy and SPECT/CT evaluation (99mTc-MIBI-SPECT/CT) in
patients with increased levels of parathormone and calcium, specific metabolic disorders, and negative planar scintigraphy.

2. Case report

We report the case of a male Caucasian patient, aged 67 years, with repetitive episodes of acute pancreatitis, stage II hypertension poorly controlled with two antihypertensive agents, biliary and renal lithiasis in his personal medical history. Due to investigations for acute pancreatitis, hypercalcemia was revealed, with multiple determinations of total serum calcium levels, with values from 11.87 to 13.64mg/dl (with normal reference range between 8.8 and 10mg/dl) and ionized serum calcium levels from 7.02 to 8.16 mg/dl (with normal reference range between 4.6 and 5.4mg/dl), the patient being guided to the Endocrinology Department for extensive evaluation regarding the etiology of hypercalcaemia, presenting symptoms as fatigue, dizziness, and weight loss. Physical examination at the time of admission revealed pale skin, pain at lumbar spine, and blood pressure values of 190/110 mm Hg.

Laboratory data showed increased total serum calcium levels of 12.6 mg/dl and increased ionized serum calcium levels of 6.89 mg/dl, increased urinary calcium levels of 738.9 mg in 24 h, low phosphate levels of 2.5 mg/dl and increased parathormone levels of 104.9 pg/ml. Metabolic evaluation revealed modified lipogram with dyslipidemia based on slightly increased levels of cholesterol, with normal levels of high-density lipoprotein (HDL)-cholesterol and slightly increased levels of low-density lipoprotein (LDL)-cholesterol, and high levels of triglycerides, mild hyperuricemia, and impaired glucose tolerance. All these parameters are presented in Table 1. Osteodensitometry was performed, revealing a T-score at lumbar spine of −2.9. The patient has normal thyroid function, thyroid ultrasonography without pathological changes, and electrocardiography revealed signs of ischemic heart disease.

Parathyroid ultrasonography and parathyroid Technetium sestamibi scintigraphy with “subtraction” method were performed, both showing no signs of pathologically modified parathyroid glands. The preoperative parathyroid scintigraphy images realized by “subtraction” method are presented in Figure 1.

A Technetium sestamibi planar scintigraphy with “washout” method combined with SPECT/CT was done, which revealed on early phase inhomogeneous radiotracer uptake in the right thyroid lobe, with increased uptake in the area of projection of the lower third of the right thyroid lobe. The preoperative parathyroid scintigraphy images accomplished with “washout” method are presented in Figure 2 and early images of SPECT/CT scan are presented in Figures 3 and 4.

The SPECT/CT scan localized increased uptake in the area behind the lower pole of the right thyroid lobe, in the right side of the trachea, with CT correspondent of hypodense lesion compared with thyroid parenchyma, inhomogeneous, with the anteroposterior diameter of 15 mm, the laterolateral diameter of 19 mm, and the craniocaudal diameter of 10 mm, with the long shaft of approximately 20 mm, which pleads for pathological modified right inferior parathyroid gland.

In delayed phase, late static images at 1.5h postinjection revealed removal of the radiopharmaceutical from the thyroid parenchyma, with remnant activity in the right inferior parathyroid gland. Late static images at 1.5h postinjection are presented in Figure 5.

The diagnosis of right inferior parathyroid adenoma was established on the base of the 99mTc-MIBI-SPECT/CT scan evaluation, with complications such as hypertension, dyslipidemia, hyperuricemia, and impaired glucose tolerance. Other causes of hypercalcemia were excluded based on the absence of suggestive clinical and biological data of malignancy, secondary hyperparathyroidism, thyrotoxicosis, primary adrenal

| Parameters        | Values | References value |
|-------------------|--------|------------------|
| Total serum calcium | 12.6   | 8.8–10mg/dl      |
| Ionized serum calcium | 6.89   | 4.6–5.4mg/dl     |
| Urinary calcium on 24 h | 738.9 | 100–320mg on 24 h |
| Phosphate         | 2.5    | 2.7–4.5mg/dl     |
| Parathormone      | 104.9  | 15–65pg/ml       |
| Cholesterol       | 208    | 109–202mg/dl     |
| Triglycerides     | 232    | 50–160mg/dl      |
| Uric acid         | 6.2    | 3–6.7mg/dl       |
| Glucose           | 130    | 80–115mg/dl      |

Figure 1. Preoperative parathyroid planar scintigraphy images by the subtraction method showing no signs of pathologically modified parathyroid glands.
insufficiency, or renal disease and the lack of use of medication associated with hypercalcemia. The decision to undergo surgical intervention was taken and minimally-invasive right inferior parathyroidectomy was performed. The histopathological examination confirmed the diagnosis and the patient’s recovery was complete, with the normalization of parathormone and calcium levels. Postoperatively, the metabolic profile of the patient has improved significantly, with normalization of
Figure 4. Preoperative hybrid molecular images of 99mTc-MIBI-SPECT/CT scan on early phase.

Figure 5. Preoperative parathyroid scintigraphy with late static images revealing remnant activity in the right inferior parathyroid gland.
cholesterol and triglycerides levels, decreased levels of uric acid, and better control of hypertension.

3. Discussion

The etiology of hypercalcemia is strongly related by the clinical setting, mostly in patients who present no significant symptoms and in cases where hypercalcemia is detected incidentally. Primary hyperparathyroidism is the most common cause of hypercalcemia, usually secondary to a hyperfunctioning parathyroid gland.

Preoperative localization of hyperfunctioning parathyroid glands can be highly challenging and it is required for the establishment of surgical approach, for the identification of the cases that are suitable for minimally-invasive intervention, and for reducing operating times and decreasing complications and rate of surgical failure.

It depends on symptoms, laboratory findings, and imaging. The preoperative and postoperative evaluation of phosphocalcic, lipid, and purine metabolism is of major interest.

Classically, the preoperative imaging techniques for parathyroid evaluation are Technetium sestamibi scintigraphy and cervical ultrasonography. Technetium sestamibi scintigraphy is performed using the dual-phase protocol, with early and late phase acquisitions. The sensitivity of this method for the diagnosis of parathyroid adenoma is between 50% and 86%. The principle consists of the distinct kinetics that Technetium sestamibi has in thyroid and parathyroid glands, revealing hyperfunctioning parathyroid glands in delayed phase. This method is appreciated for simplicity of the technique and low cost. It also has some disadvantages, which make this technique having its limits. These disadvantages consist of the fast clearance of Technetium sestamibi and low sensitivity for localizing parathyroid lesions or differentiating thyroid nodules from parathyroid lesions. A negative parathyroid scan does not exclude the diagnosis of hyperparathyroidism.

In the case reported, it was impossible to detect a parathyroid adenoma by classic scintigraphy and ultrasonography. Increased parathyroid and calcium levels together with poor blood pressure control and impaired lipid and purine metabolism have led us to extensive investigations. Combined methods of parathyroid scintigraphy and SPECT/CT led to a concrete diagnosis of parathyroid adenoma, as similar data is reported in literature.

In recent years, 99mTc-MIBI-SPECT/CT has been used to detect parathyroid adenomas. Case reports of combined imaging techniques were first reported in the early 2000s, localization ectopic mediastinal parathyroid adenomas, leading to a minimally-invasive surgical approach.

SPECT alone has a high sensitivity and specificity in finding parathyroid lesions, but it has its limits because of the inability to provide anatomical data. The addition of CT to SPECT allows precise topographic detection of the lesions, including the relations to the thyroid, trachea, esophagus, muscles, and blood vessels. SPECT/CT provides fusion images of high quality and precision, offering anatomical details due to CT, and functional data due to SPECT acquisitions. Compared to SPECT alone, SPECT/CT has increased sensitivity in the detection of parathyroid lesions not visualized by Technetium sestamibi dual-phase scintigraphy.

CT and SPECT acquisitions can be obtained with two separate devices, with the fusion of the images using a specific software or, acquisitions can be realized in a single examination, using a hybrid molecular imaging SPECT/CT device which integrates a SPECT camera with a CT scanner.

Planar images are obtained first. In the Technetium-99 metastable sestamibi dual-phase protocol, SPECT/CT may be acquired in early or in delayed phase, or in both, with carefully monitoring radiation exposure of the patient. Attenuation corrected acquisitions, with better image contrast, may be used especially for detecting and localizing mediastinal ectopic parathyroid adenomas.

In a large cohort study of patients diagnosed with sporadic primary hyperparathyroidism, preoperative SPECT/CT acquisitions provided more reliable data compared to SPECT alone. 99mTc-MIBI-SPECT/CT, although of great clinical utility, is not commonly performed to avoid extra radiation exposure from computed tomography CT.

Primary hyperparathyroidism is usually an asymptomatic disorder, as seen in this case report, the patient presenting unspecific symptoms. Modern imaging techniques offer genuine details to facilitate the detection of pathologically modified parathyroid glands, avoiding the attempts of intraoperative localization and surgical failure.

The particularity of this case is the misleading conclusion of a negative planar scintigraphy, not visualizing a 20 mm adenoma, temporarily blocking the diagnosis.

Regarding the evolution of the case reported, we refer the postoperative metabolic parameters, which improved rapidly, with normalization of calcium, phosphate, and parathormone levels, decreasing levels of cholesterol, triglycerides, uric acid, and lower values for blood pressure.

4. Conclusions

Modern imaging acquisitions of 99mTc-MIBI-SPECT/CT represent a highly sensitive and specific diagnostic tool, of great clinical utility in the diagnosis of primary hyperparathyroidism. This technique offered a precise anatomical localization of a parathyroid tumor undetected by planar scintigraphy alone, leading to a minimally-invasive parathyroidectomy and a significant improvement in the postoperative metabolic parameters.

Author contributions

All authors contributed equally to this manuscript in terms of acquisition, analysis and interpretation of data, conception and design, drafting the manuscript. All authors read and approved the final manuscript.

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