SIGNIFICANCE OF ⁹⁹ᵐTc-MIBI SCINTIGRAPHY AS PREOPERATIVE DIAGNOSTIC METHOD IN PARATHYROID GLAND DISORDERS: CASE REPORT

Jovan Pesović¹, Ivana Paunović², Stanko Mrvić³, Dolores Srbovan⁴, Aleksandar Đukić⁵, Ljubisa Acimović⁶, Dejan Lazić¹ and Dragan Canović¹
¹Surgical Clinic, Clinical Center, Krusevac, ²Endocrine Surgery Center, Institute of Endocrinology, Diabetes and Metabolic Disorders, Clinical Center of Serbia, Belgrade, ³Institute of Pathological Physiology, School of Medicine, Krusevac, ⁴Institute of Oncology, Institute of Nuclear Medicine, Sremska Kamenica

INTRODUCTION

PHPT is a disorder that is characterized by an enormous increase of parathyroid hormone secretion that directly affects the metabolism of calcium in that way that it goes out of physiological limits (1). In PHPT there is an increase of mass of functional parathyroid glands and their disturbed function. PHPT can occur as a hereditary or sporadic disorder. In hereditary forms, its manifestation as the cause of HPT is rare and it is found in 0.5–5% of cases of HPT (4, 5). Diagnosis of primary HPT is established solely by laboratory analyses (4, 6). The basic parameters are: hypercalcemia, increased parathyroid hormone (PTH) and calcuria. Symptomatic primary HPT is treated surgically and it falls into the most successful treatments in surgery. But, unsuccessful surgery with persistent hyperparathyroidism, due to inadequate preoperative or intraoperative localization, may be observed in about 10% patients. The conventional surgical approach is bilateral neck exploration, whereas minimally invasive parathyroidectomy has been made possible by the introduction of ⁹⁹ᵐTc-MIBI scintigraphy for preoperative localization of parathyroid gland (9).

CASE REPORT

The patient, male, age 54, had many complaints in the last few years such as: exhaustion, polyuria, renal colic, hypertension, depression, pains in muscles and bones as well as pathologic fractures of bones of the left lower leg and left forearm. His complaints gradually inten-
sified and after several hospitalizations, the diagnosis of primary hyperparathyroidism was established by laboratory examinations (serum calcium, PTH, calcu-
ria). Nodular disorder of the left lobe of thyroid gland (cold solitary nodule) was established by standard diag-
nostic procedures (US, scintigraphy, hormonal status). Increased values of serum calcium, low values of inor-
ganic phosphates, calcuria (Table 1), high values of PTH (Table 2) were noted in the laboratory. After adequate endocrinologic preoperative preparation that consisted of the application of calcium antagonists (30 mg of pamidronat-Aredia), biphosphonates, corticosteroids (the last value of serum calcium was 2.86 mmol/L) as well as infusions of crystalloid solutions, the patient underwent a surgical intervention. Left lobectomy and resection of isthmus of the thyroid gland were performed, as well as subtotal parathyreoidectomy on the right and parathyreoidec
tomy on the left with resection of the cervical thymus. Hyperplasia of the removed parathyroid glands was confirmed by PH findings. Pathohistologic findings (no. 326 from 31.01.2005): Primary, nodular hyperplasia of PT, with domination of major cells and follicular histologic organization occurring here and there. Immediately after the surgical intervention, a slight decrease of calcium value occurs (2.87 mmol/L). The patient is discharged from hospital. During the control examination, symptoms of PHPT are still present Labo-
atory analyses show increased values of serum calcium (3.16 mmol/L), low values of inorganic phosphate (0.36 
mmol/L) and increased values of PTH (1150 pg/mL), which points out the existence of ectopic parathyroid 
gland. Localization examinations are indicated as well as 99mTc-MIBI scintigraphy and computerized tomo-
graphy (CT). Pathologic accumulation of radiopharmacs in the upper right half of the posterior mediastinum was registered by performed MIBI scintigraphy. Two-phase scintigraphy of the area of neck and the mediastinum was done 10 minutes after initiating 555 MBq 99mTc-MIBI and then after 2 hours. On the obtained scintigrams (thyroid phase), the accumulation of radiopharmacs is perceived in operative remains of the thyroid gland (the right lobe) with notable accumulation of radiopharmacs in the region of the upper mediastinum, directly next to pulmonary apices, (Figure 1). On the late scintigram (parathyroid phase) after washing, slight accumulation of radiopharmac can be seen in the position of the thy-
roid gland remains, and the area of accumulation of radiopharmacs can also be detected in the upper medi-
astinum (next to pulmonary apices, more to the right side), which corresponds scintigraphically to the ectopic 
tissue of the parathyroid gland (Figure 2). Computerized tomography of the mediastinum in the middle posterior 
mediastinum retro and paratracheal on the right shows multiocular septal tumor shadow with peripheral cal-
cificates and calcification of septa, attenuation of soft tissues, of size 45x55x65 mm. The change dislocates the esophagus and trachea to the opposite side and it is in close contact with the ascending aorta. After the ap-
lication of contrast, marginal coloration of the tumor 
occurs with clear demarcation of cysticly degenerated parts (Figure 3). Existence of the ectopic parathyroid 
gland, the cause of PHPT was established by localization examinations. The second surgical intervention 
consisted of partial sternotomy and extirpation of the tumor size about 6x10 cm (Figure 4). PH findings of the extirpated tumor change (no.1225 from 01.04.2005): Carcinoma glandulae parathyreoideae (middle differentiated his-
tologic type). The tumor consists of irregular major and light cells with moderate number of mitoses. Acel-
ular hyalinated bands are present between the groups of malignant cells. There are clear calcifications in the 
connective tissue. Postoperative course went without surgical complications. Values of serum calcium (1,93 
mmol/L) and parathormone (15.6 pg/mL) immediately after the surgical intervention decreased. Postoperative substitution therapy is performed (Ca-sandos, CaCl2, Alfa
calcidol, Mg). Six days after the surgical intervention, the patient is taken to the Metabolic unit of the Internal Medicine Clinic where the treatment is continued with 
pharmaceutical preparations of calcium, magnesium, active form of vitamin D, ACE inhibitors, calcium an-
tagonsits, antibiotics, low-molecular heparin, with a constant monitoring of electrolytic, acido-basic, and 
hemodynamic status, with necessary corrections. The period of parenteral substitution lasted for a long time 
(about 3 months) which showed the intensity and dura-
tion of PHPT. After the administered therapy, subjective and objective improvement occurs (Table 3,4), so that 
the patient is discharged as recovered and examined to continue further treatment at the outpatient department 
with therapy: Calcium gluconate, ascorbic acid 500 tabl. 
2+2+2, Alfa
calcidol 0.25 tabl. 2+2+2, Magnesium hydroxide 150 tabl. 1+0+1, Quinapril 20 tabl. 1+0+1, 
Amlodipine 5 tabl. 1+0+0.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>value 1</th>
<th>value 2</th>
<th>value 3</th>
<th>Reference scope</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>3.41</td>
<td>3.21</td>
<td>3.45</td>
<td>2.1–2.6 mmol/L</td>
</tr>
<tr>
<td>Magnesium</td>
<td>0.38</td>
<td>0.38</td>
<td>0.38</td>
<td>0.8–1 mmol/L</td>
</tr>
<tr>
<td>Calcium clearance</td>
<td>1.51</td>
<td>2.94</td>
<td>0.031</td>
<td></td>
</tr>
<tr>
<td>Inorganic phosphate</td>
<td>0.50</td>
<td>0.74</td>
<td>0.63</td>
<td>0.8–1.6 mmol/L</td>
</tr>
<tr>
<td>Phosphorus clearance</td>
<td>21.0</td>
<td>19.8</td>
<td>15.6</td>
<td>6.0–15.0 ml/min</td>
</tr>
<tr>
<td>Calcuria</td>
<td>7.41</td>
<td>13.5</td>
<td>9.25</td>
<td>2.5–7.5 mmol/dU</td>
</tr>
<tr>
<td>Phosphaturia</td>
<td>14.82</td>
<td>21.06</td>
<td>14.0</td>
<td>12.9–42.0 mmol/dU</td>
</tr>
<tr>
<td>TRPO4 (%)</td>
<td>74.7%</td>
<td>74.8%</td>
<td>82.3%</td>
<td>82–95 %</td>
</tr>
<tr>
<td>Ionized calcium</td>
<td>2.00</td>
<td>1.12</td>
<td>1.23</td>
<td>1.12–1.23 mmol/L</td>
</tr>
<tr>
<td>Ratio of Cca/Ccr</td>
<td>0.0182</td>
<td>0.0374</td>
<td>0.0211</td>
<td></td>
</tr>
<tr>
<td>Creatinine clearance</td>
<td>83.0 ml/min</td>
<td>78.6 ml/min</td>
<td>88.2 ml/min</td>
<td>97–137 ml/min</td>
</tr>
</tbody>
</table>

Table 1. Laboratory analyses before the first operation.
Table 2, Hormonal analyses before the first operation.

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Value</th>
<th>Reference scope</th>
</tr>
</thead>
<tbody>
<tr>
<td>fT4</td>
<td>9.2</td>
<td>(7–18) pmol/L</td>
</tr>
<tr>
<td>TSH</td>
<td>1.3</td>
<td>(0.25–4) μIU/mL</td>
</tr>
<tr>
<td>PTH</td>
<td>1270.0</td>
<td>(15–65) pg/mL</td>
</tr>
<tr>
<td>Calcitonin</td>
<td>5.6</td>
<td>(&lt;8.4) pg/mL</td>
</tr>
</tbody>
</table>

Table 3, Values of ionized calcium on discharge.

<table>
<thead>
<tr>
<th>Date (2005)</th>
<th>30.03</th>
<th>01.04</th>
<th>05.04</th>
<th>12.04</th>
<th>20.04</th>
<th>24.06</th>
<th>26.06</th>
</tr>
</thead>
<tbody>
<tr>
<td>ion Ca mmol/L</td>
<td>1.30</td>
<td>1.05</td>
<td>1.03</td>
<td>1.10</td>
<td>1.01</td>
<td>1.18</td>
<td>1.05</td>
</tr>
</tbody>
</table>

DISCUSSION

Laboratory diagnostic methods (values of serum calcium, calcuria and PTH) are the basis for establishing the diagnosis of parathyroid gland disorders (4,6–8). Operative treatment of the parathyroid gland disorders requires clear localization of the same ones, which emphasizes the significance of localization examinations in the preoperative procedure (10–17).

Localization examinations can be non-invasive and invasive. Non-invasive methods are: ultrasound diagnostics (US), scintigraphy (primarily 99mTc-MIBI scintigraphy is used), computerized tomography (CT) and magnetic resonance imaging (MRI) (18–24). In invasive localization examinations, the fine needle biopsy under the con-
trol of ultrasound, selective arteriography and selective venous catheterization is used (21).

In 1983, Ferlin applied first the double radioisotopic scintigraphy with 201TI - chloride and 99mTc pertech-
netate in order to visualize the parathyroid glands (25).

There are many controversial opinions concerning the application of localization examinations before the first operation. In most cases, preoperative localization ex-
aminations are not applied in the first operation due to the attitude that some experienced surgeon will always
discover the diseased parathyroid gland during the first operation. This attitude is confirmed by the fact that
localization examinations are without great value in hyperplasias of the parathyroid glands (4,26–29). Dopp-
man is of the same opinion because he considers that the
only thing needed for the localization of pathologically
changed parathyroid gland is an experienced surgeon.
(6). However, frequent need for the second operation in treatment of PHPT has imposed the necessity for
localization examinations (27, 30–32). Localization ex-
aminations should be critically applied due to relatively
high percentage of false negative and false positive results,
which was shown by Clarck (16) (Table 5). Because of
the disadvantages of localization methods Clarck sug-
gests the algorithm of application of these methods in
diagnostics of pathological conditions of the parathyroid
glands. (Figure 5).

Table 5. Efficacy of localization diagnostics according to Clarck et
al. (16).

<table>
<thead>
<tr>
<th></th>
<th>US</th>
<th>201TI/207TI</th>
<th>CT</th>
<th>MRI</th>
<th>SVC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>58%</td>
<td>49%</td>
<td>46%</td>
<td>66%</td>
<td>74%</td>
</tr>
<tr>
<td>Negative</td>
<td>31%</td>
<td>28%</td>
<td>39%</td>
<td>18%</td>
<td>29%</td>
</tr>
<tr>
<td>False positive</td>
<td>13%</td>
<td>2%</td>
<td>15%</td>
<td>18%</td>
<td>-</td>
</tr>
</tbody>
</table>

CONCLUSION

Localization methods, especially 99mTc-MIBI scinti-
graphy, US, CT and MRI are significant in preoperative
diagnostics of pathological conditions of the parathyroid
glands. The case presented shows that performed MIBI
procedure in combination with CT has localized the
etiologic cause of PHPT and that application of locali-
zation diagnostic procedures will significantly decrease
the need for secondary operative intervention and all the
risks that it may have.

REFERENCES

1. Bismar HA, El-Bakry AA. Primary hyperparathyroidism. Saudi
2. Kramps JL, Barber J. Familial parathyroidism in multiple en-
docrine neoplasia syndromes. In: Clark OH, Duh QY, eds. Text-
381–3.
without multiple endocrine neoplasia. World J Surg 1997; 21:
22–9.
4. Janković R. Primarni hiperparatiroidizam. U: Janković R. Hiru-
gija tiroidne i paratiroidnih žležda. 2-го izd. Beograd: Zavod za
5. Kebabev E, Arici C, Duh QY, Clark OH. Localization and reop-
eration results for persistent and recurrent parathyroid carcinoma.
6. Dopman JL. Reoperative parathyroid surgery: localization pro-
7. Rothmund H, Diethelm J, Brunner C, et al. Diagnosis and surgi-
183: 139–45.
8. Đurić i sar. Tumori endokrinskim sustavom. U: Janković R. Hiru-
gija paratiroidnih žležda. 1-vo izd. Beograd: Zavod za izdavanje
udžbenika, 1998: 491–500. (in Serbian)
9. Mariani G, Guicci A, Rubello D. Preoperative localization and ra-
10. Mimura Y, Kanachi H, Ogawa T, Kammori M, Kaminishi M. Re-
view of 41 patients operated on for primary hyperparathyroidism.
11. Shih WJ, Rastogi A, Stipp V, Gross KK, Couplal JJ, Magoun S.
99mTc MIBI SPECT for the detection of intrathoracic tumor masses.
12. Maxon HR. Detection of residual and recurrent thyroid cancer
SPECT: a highly sensitive diagnostic tool for localization of par-
207–16.
15. Kang YS, Rosen K, Clark OH, Higgins CB. Localization of ab-
normal parathyroid glands of the mediastinum with MR imaging.
16. Clark F, Woolridge T, Kleinpet K, Perrier N, Lovo J, Mor-
ton K. Providing optimal preoperative localization for recurrent
parathyroid carcinoma: a combined parathyroid scintigraphy and
computed tomography approach. Clin Nucl Med 2004; 29:
681–4.
17. Clark PB, Case D, Watson NE Jr, Perrier ND, Morton KA. En-
hanced scintigraphic protocol required for optimal preoperative
localization before targeted minimally invasive parathyroidectomy.
18. Hedman J, Hansson G, Lindberg LM, Tissel L. A clinical evalu-
ation of radiation-induced hyperparathyroidism based on 148
of the parathyroid glands with 201TI: experience with 250 oper-
20. Wünzelberg GG, Hydovitz JD. Radionuclide imaging of parathy-
roid tumors: historical perspectives and newer techniques. Semin