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Parathyroid adenoma imaging-preoperative localization

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ABSTRACT
Primary hyperparathyroidism (PHPT) is a frequent endocrine disorder that can only be cured by a surgical procedure that is parathyroidectomy. The main causes are usually solitary benign adenoma (80-85%), diffuse or nodular hyperplasia (10-15%), or parathyroid carcinoma (<1%). Out of the known localization techniques, ultrasonography, nuclear scintigraphy and computer tomography (CT scan) are most commonly used [1].
The aim of this study is to evaluate the sensibility of ultrasonography by comparison to scintigraphy and CT scan for the preoperative localization of parathyroid adenoma in patients with biochemically confirmed primary hyperparathyroidism. Localization studies were correlated with intraoperative findings, histopathological outcomes.
In a retrospective study we analyzed 60 patients out of 245 patients who had undergone parathyroidectomy for PHPT between 2012-2013 in the Surgery Department of the National Institute of Endocrinology, Bucharest.
Preoperative evaluation included imaging explorations (ultrasonography, scintigraphy and cervical CT scan) and therapeutic success was confirmed by histopathological result and the evolution of hormonal and biochemical tests.
Intraoperative exploration revealed a single adenoma in 59 patients and one double adenoma.
Thyroid disease was associated in 27 (45%) patients.

Keywords: parathyroid adenoma, ultrasonography.

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Introduction

Primary hyperparathyroidism is a common endocrine disorder , with rising incidence, that affects 1% of the adult population and for which surgical treatment remains the only curative method. The common causes are usualy solitary benign adenoma (80-85%), diffuse or nodular hyperplasia (10-15%), or parathyroid carcinoma (<1%).

PHPT is one of the main etiologies of secondary osteoporosis, its increasing incidence being diagnosed when assesing high-risk fracture osteoporosis causes [1, 2].

Even in 1982 it was demonstrated that minimally invasive approach after succesfully preoperative localization would significantly reduce operative time, hospitalization period and patient recovery time [3].

The aim of this study was to evaluate the sensibility of ultrasonography by comparison to scintigraphy and CT scan in the preoperative localization of parathyroid adenomas in patients with biochemically confirmed primary hyperparathyroidism. Localization studies were correlated with intraoperative findings, histopathological outcomes.

Material and methods

In a retrospective study we analyzed 60 patients who had undergone parathyroidectomy for PHPT between 2012-2013 in the Surgery Department of the National Institute of Endocrinology, Bucharest.

Preoperative evaluation included imaging explorations (ultrasonography, scintigraphy and cervical CT scan) and therapeutic success was confirmed by histopathological result and the evolution of hormonal and biochemical tests.

The diagnosis of PHPT was confirmed by elevated parathyroid hormone (PTH) in association with high serum and urinary calcium values.

Intraoperative exploration revealed a single adenoma in 59 patients and one double adenoma.

Thyroid disease was associated in 27 (45%) patients.

From patients charts we analyzed data referring to medical history, pre-and postoperative phosphocalcic metabolism as well as bone densitometric examination, PTH, 25 (OH) vitamin D, cervical ultrasound, PT scintigraphy, neck and upper thorax CT and histopathological result.

Imagistic evaluation

CT scans of the cervical and mediastinal region were performed with a SIEMENS SOMATOM EMOTION (16 slices) using 5mm slices and 2 mm sagital and coronoray reconstructions in native and intravenous contrast medium scanning.

Ultrasonographic evaluation was performed using a General Electric LOGIQ P5 ecoedition with anteroposterior, transverse and longitudinal sections.

Sestamibi scintigraphy (99m Tc-sestamibi) by substraction was performed using Siemens E.CAM Signature series scintigraph.

BMD evaluation of the forearm, lumbar spine and femur was performed by dual-energy X-ray absorptiometry DXA (GE Healthcare Lunar Prodigy).

Laboratory variables

Blood samples were collected under fasting conditions (between 8:00 and 10:00 AM). The serum PTH, 25 (OH) vitamin D, osteocalcin and crosslaps were measured by electrocheminiscence (ECLIA, Cobas e601, Roche). The intra- and interassay variation coefficients in our laboratory were 1,08% and 4,75% , respectively for PTH, 3,27% and 9,1%, respectively for 25 (OH) vitamin D, 0,63% and 3,9%, respectively for osteocalcin and 1,28% and 4,22%, respectively for crosslaps. PTH reference variations were 15-65 pg/ml. Lower detection limit was 4,2 ng/ml for 25 (OH) vitamin D, 0,5 ng/ml for osteocalcin and 0,01 ng/ml for crosslaps.

Blood samples were also collected for total calcium and phosphorus and measured using VITROS FS5.1. Urinary 24h calcium was measured by VITROS FS5.1.

Statistical analyses

For statystical interpretation we used Microsoft Office Excel 2010 version.

Results

In the time mentioned (2012-2013) 245 parathyroidectomies were

performed, of which 225 representing 91,8% for primary hyperparathyroidism (196 women and 29 men). We selected 60 patients whose preoperative evaluation included ultrasonography, scintigraphy as well as cervical and mediastinal CT.

Gender distribution reveals a 4:1 ratio (F:M) with 12 male patients (20,12%) and 48 females (80,48%) .

The age group of 60-69 years including 23 patients (38,33%) showed maximum incidence of

PHPT, followed by 50-59 years age category which included 19 patients (31,67%) . The youngest patient was 30 years old (Fig. 1).

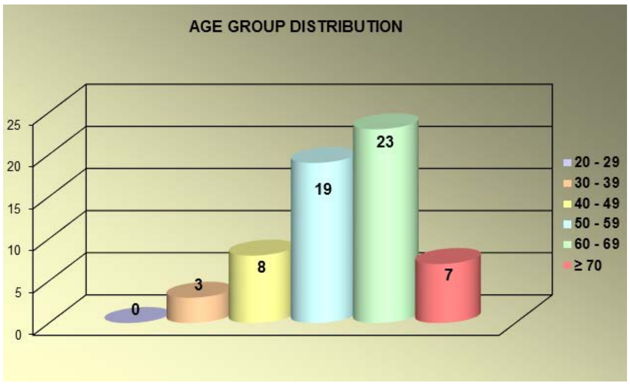

Fig 1– Age distribution

PTH serum levels were measured for all the patients in the study. Preoperative findings revealed high levels of PTH (between 82.25 pg/ml and 829 pg/ml) thus supporting the diagnosis. Immediate postoperative PTH assay showed decreased values in all patients except 2 of them in which PTH was lower but remained above the upper limit of normal. In 16 patients PTH fell temporary below the normal reference (Fig 2.).

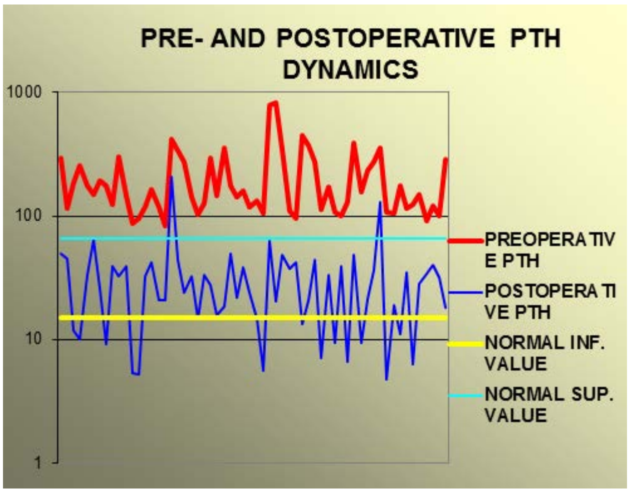

Fig 2 – PTH dynamics

Concerning the certainty of the diagnosis, besides elevated PTH levels, the biological tests also revealed hypercalcemia in 52 patients (86.67%) one hour before surgery. Calcium normalization was found in 46 of them (76.67%) the day after surgery, while hypocalcemia occured in 14 cases (23.33%) (Fig. 3).

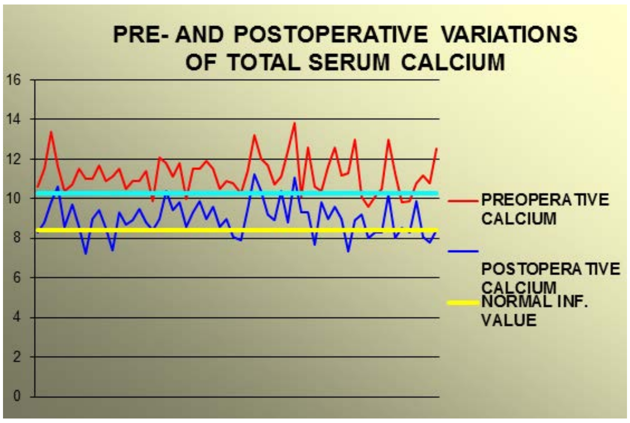

Fig 3 – Serum calcium variations

Preoperative serum phosphate dynamics showed normal values in 35 cases (58.33%), hypophosphatemia in 24 of them (40%) and hyperphosphatemia in one single patient. After surgery, seric levels of phosphate became normal in 85% of the patients with exception of 6 cases (10%) which had hypophosphatemia and 3 (5%) with hyperphosphatemia. (Fig. 4).

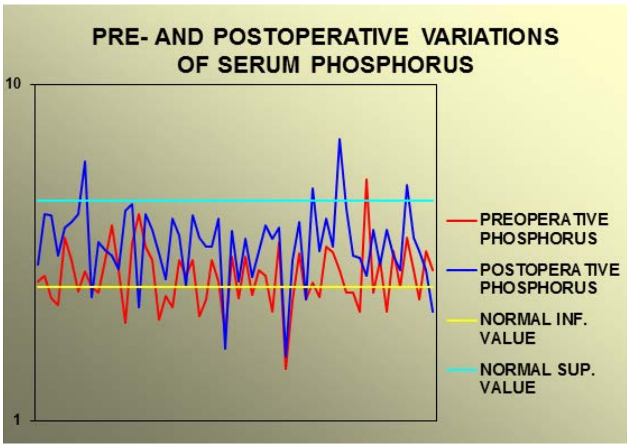

Fig 4 – Serum phosphorus variations

Measuring preoperative calcium excretion revealed hypercalciuria in 15 patients representing 39.47% and normal values in 16 of them (42.10%). Seven patients had below normal limits calciuria

(18.43%) (Fig 5).

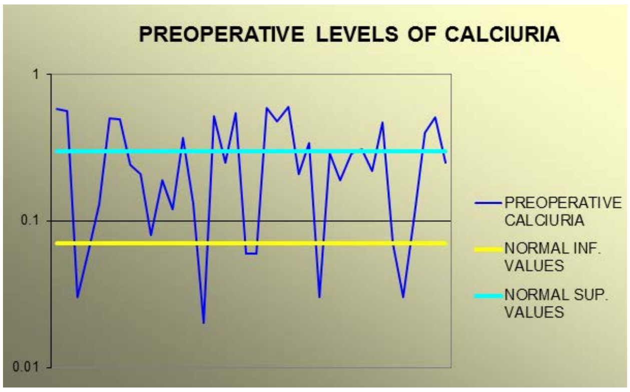

Fig 5 – Preoperative levels of calciuria

All patients included in the study had serum preoperative 25OHvitamin D below normal (between 5.19 ng/ml and 27.05 ng/ml). After surgery, all patients started vitamin D supplementation treatment (Fig. 6)

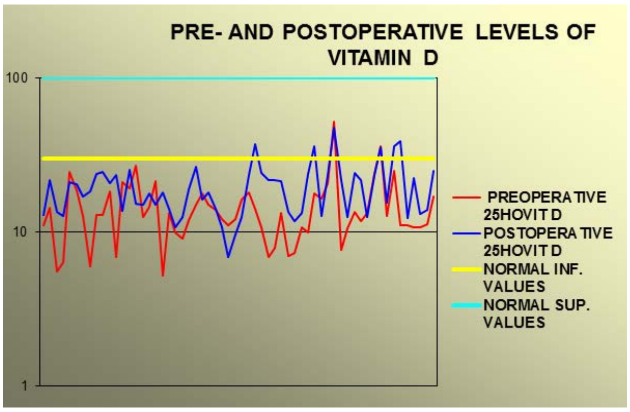

Fig. 6 – Vitamin D variations

Increased bone resorbtion was revealed by high preoperative levels of cross-laps in 14 of the 20 patients in which bone turnover was studied. Values dropped significantly 6 months after the surgery (Fig. 7). Osteocalcin levels were surprisingly high in only 9 patients, highlighting poor coupling between bone formation and resorbtion , one explanation being vitamin D deficiency in these patients (Fig. 8).

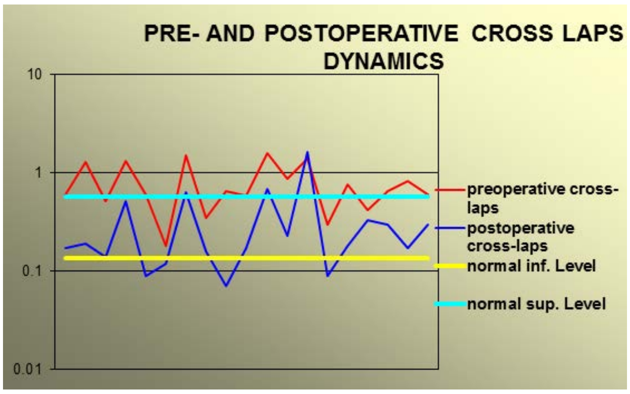

Fig. 7 – Cross laps variations

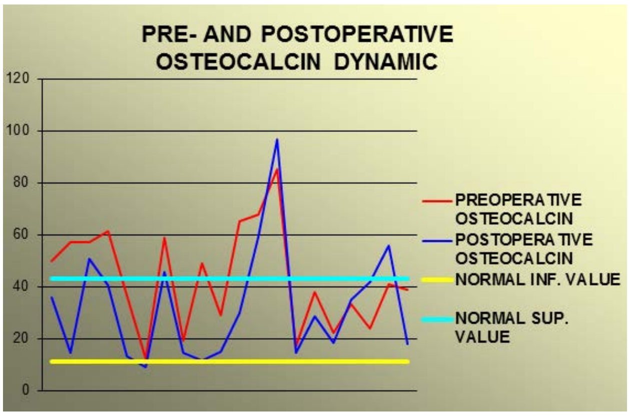

Fig. 8 – Osteocalcin variations

The most common HPTH complication encountered in our study was bone loss affecting 40 patients (66.67%) followed by cardiovascular disease found in 33 patients (55%). Renal impairment was discovered in 25 cases (41.67%) (Fig. 9).

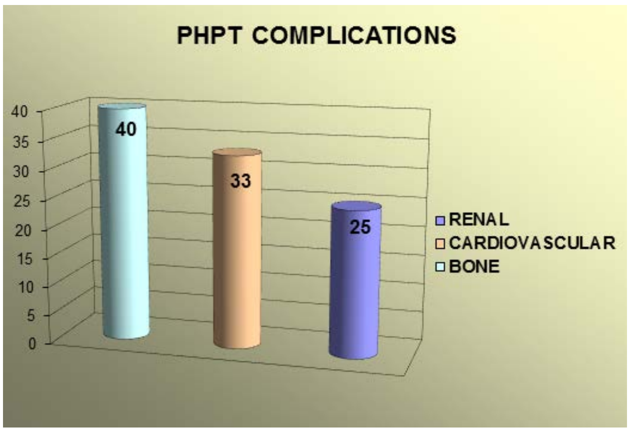

Fig. 9 – PHPT complications

Osteoporosis was most commonly found in radius in 22 patients (36.67%) followed by lumbar spine, 11 patients (18.33%) and less frequent at the hip level, 9 patients (15%)(Fig.10)

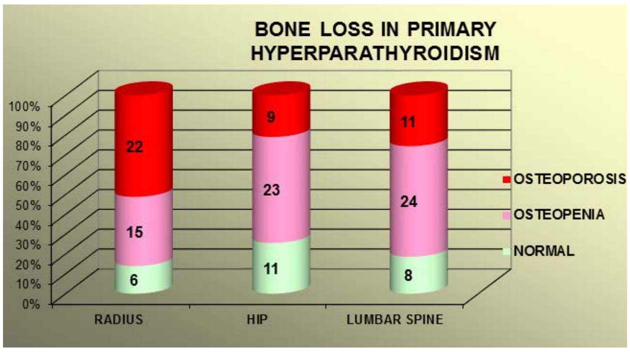

Fig. 10 – Bone loss

The most frequent associated thyroid pathology was multinodular goiter, diagnosed in 27 patients (45%) followed by chronic autoimmune thyroiditis – 7 patients (11.67%) and hyperthyroidism 4 patients (6.67%).

According to the intraoperative findings the most common localization of adenoma was inferior right (23 patients-38.33%) and the less frequent was the superior left in 6 cases (10%) (Fig. 11).

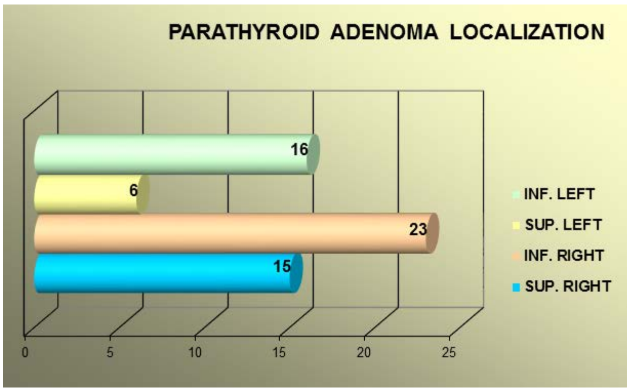

Fig. 11– Parathyroid localization

The imaging method with the highest sensitivity in PT adenoma localization proved to

be the cervical ultrasound which succesfully identified and localized the adenomas in 49 patients (81.67%). Ultrasonography was followed by CT scan positive in 80% of the cases. The scintigraphy was positive in 68.33% of the patients (Fig. 12).

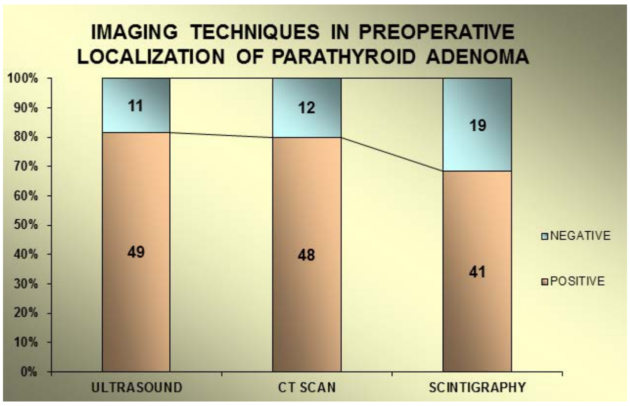

Fig. 12 – Imaging techniques in preoperative localization of parathyroid adenoma

Among the 49 patients in which ultrasound visualised and localised the parathyroid adenoma CT scan was positive in 45 (91,83%) and the PT scintigraphy was positive in 35 (71,43%) patients.

In 11 patients in which PT adenoma was not visualized by ultrasound the CT scan was helpful in only 3 cases (27,27%) and scintigraphy in 7 (63,63%).

Discussions

Out of the many methods of localization, ultrasonography (USG), nuclear scintigraphy (Tc-99m) and in selective cases CT scan, are the most commonly used in medical practice.

USG is a noninvasive, widely available, cheap technique and even reproducible in the operating room. However, the accuracy of ultrasound is operator dependent and its sensitivithy ranges from 64-91% [4, 5]. Also, the sensitivity of ultrasound is reduced in patients with concurrent thyroid disease which is present in up to 40% of cases. This common problem can be an advantage providing additional anatomical data and giving the possibility to develop a proper surgical plan [6]. Disadvantages of USG include reduced accuracy in patients with small, ectopic or intrathyroidal parathyroids, obesity, mediastinal glands located behind the clavicles [7]. Sonographic characteristics of parathyroid adenomas include: well-defined, homogeneous, hypoechoic mass and peripheral vascularity seen on Doppler imaging (Fig. 13) [8].

Fig. 13 – Right parathyroid adenoma

Sestamibi scintigraphy (99m Tc-sestamibi) clearly has an advantage in detecting parathyroid adenomas, as it is able to locate ectopic glands that are inaccessible by USG (Fig. 14). It has a high sensitivity (68-95%) and specificity (90%). However, the small size of hyperfunctioning parathyroid, oxyphil cell content and various degrees of apoptosis or necrosis may reduce MIBI uptake causing false-negative results [9, 10]. Combined scintigraphy and sonography for preoperative localization has been shown to predict the location of solitary adenomas more accurately than either technique alone [8]. A negative Tc 99m sestamibi scan does not preclude the diagnosis of primary hyperparathyroidism, since it occurs in 12-25% of patients [11, 12].

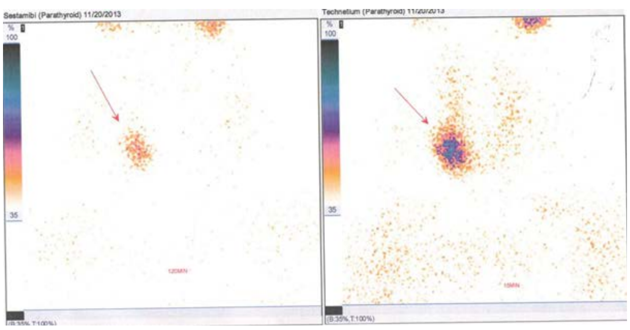

Fig. 14. Inferior-right parathyroid adenoma

SPECT – sestamibi single photon emission CT (MIBI-SPECT) leads to the identification of adenomas in 95% of cases and hyperplasia in 60-70% of cases, but the method is not widely available [13].

In difficult cases with ectopies or recurrent disease, computer tomography or magnetic resonance imaging can be useful. The sensitivity of the two methods is 81.3% for CT [14] with better results for 4D-CT (83-95%) or 40-85% for MRI [15, 16, 17].

Positron emission tomography (PET-CT) is one of the leading imaging techniques that performs both morphological and functional investigation, being used especially for postoperative recurrence. By using another radiotracer, C11-methionine (MET-PET-CT), the sensitivity of the methon can be increased, including in the parathyroid hyperplasia diagnosis (79-90%) [15].

Selective venous catheterization is the most common invasive modality used for parathyroid localization. It can identify hyperfunctioning parathyroid tissue when all other imaging modalities are negative [18]. Angiographic techniques are reserved for cases with persistent or recurrent PHPT, when other methods fail to highlight parathyroid lesions, with a sensitivity of 82%. Digital subtraction arteriography increased sensitivity to 90%.

The final differential diagnosis between a parathyroid adenoma and thyroid disease is made by fine needle biopsy (USG or CT guided) [1].

Preoperative HPTH evaluation should be made according to approved guidelines including diagnostic test, imaging techniques as well as correct evaluation of complications status concerning especially renal impairment, cardiovascular disease and bone loss.

Comparing the sensibility of cervical sonography, neck and mediastinal CT and PT scintigraphy, our study showed sonography superiority for succesfully preoperative PT adenoma localization. The main purpose of preoperative localization of parathyroid adenomas is minimally invasive parathyroidectomy, surgical technique that reduces not only the operative time and costs, postoperative pain, hospitalization period but also patient recovery time.

Conclusions

Compliance with preoperative diagnostic protocol is absolutely necessary for the establishment of clinical and laboratory features of hyperparathyroidism and monitoring the evolution of postoperative complications with efficient correction.

Cervical ultrasonography is a noninvasive, safe, widely avalilable and cheap technique. An experienced sonographer and a performing ultrasound machine ensure the premises of preoperative parathyroid adenoma localization and allowing minimally invasive parathyroidectomy.

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