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Role of Imagery in Preoperative Evaluation of Parathyroid Lesions in Hyperparathyroidism

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Abstract

Background: Hyperparathyroidism (HPT) is an endocrine disease characterized by a hypercalcemic state due to hyper secretion of parathyroid hormone. Imaging in parathyroid disease (hyperparathyroidism) is aimed at localizing enlarged parathyroid glands after a biochemical diagnosis of hyperparathyroidism has been made. By precisely identifying the number and location of abnormal parathyroid glands, surgical parathyroidectomy can be considered and planned.

Objective: This article discusses our experience with hyperparathyroidism, from a radiological point of view, the commonly used techniques for imaging the parathyroid glands and their role in the preoperative evaluation of patients with primary hyperparathyroidism in our tertiary hospital center. The commonly used noninvasive imaging techniques: songraphy, CT, and MRI- their advantages and limitations will be discussed.

Material and methods: We have carried out a retrospective study in patients admitted for surgical treatment between January 2009 to December 2013, preoperatively diagnosed with HPT. All patients were hospitalized and prepared for surgery in the Service of Endocrinology and Nephrology where they came from. The data on patient's histories, diagnostic procedures, treatment and complications were acquired from medical reports. In order to detect and locate abnormal parathyroid tissue for preoperative localization study of diseased gland, we have used neck ultrasonography (NUS), computed axial tomography (CT) and magnetic resonance imaging (MRI).

Conclusion: The treatment of parathyroid disease is primarily surgical. However, parathyroidectomy would not be successful without accurate preoperative localization of the abnormal gland. This requires skilled radiologists at performing ultrasonography, Ct and other imaging modalities to guide the surgeon in localizing the abnormal gland(s).

Keywords: Neck sonography; CT; IRM; Hyperparathyroidism

Introduction

Primary hyperparathyroidism, whether caused by an adenoma or hyperplasia, is surgically curable with a high rate of success [1]. When performed by experienced surgeons, traditional surgical therapy-bilateral four-gland exploration is successful in more than 90% of cases [2,3]. The development of unilateral and focused surgical approaches over the past decade, however, has made it even more imperative for imaging to accurately locate abnormal parathyroid glands before surgery. With optimized preoperative mapping, the success rate of these less invasive techniques equals that of the traditional bilateral approach [4]. Experts have advocated the use of routine preoperative localization, arguing that, not all surgeons have the full experience for accurate surgical exploration; it can result in a shorter operation time; avoid the need for bilateral neck exploration, and identify rare patients with ectopic parathyroid adenomas [1,5].

Even in specialist wards, 5-10% of operations for PHP are unsuccessful [6]. The main reasons seem to be ectopy of the parathyroid gland, numerous adenomas, multiglandular parathyroid hyperplasia, and intrathyroid location of the parathyroid [7,8]. The statement of the radiologist Doppman [9] is that "the only localization study needed by a patient undergoing initial parathyroid surgery is to locate an experienced parathyroid surgeon" was still valid in 1986 during the conference held by the National Institutes of Health on the diagnostics of parathyroid glands.

First of all it is very important to reduce the number of unsuccessful operations. In light of the above, imaging

examinations of parathyroid glands should be according Table 1 & 2:

Table 1: Examinations enabling identification of disease-transformed parathyroid glands examinations.

S. No.	Parathyroid Glands Examinations
1	USG
2	CT
3	MRI
4	Scintigraphy
a)	Subtraction (thallium technetium).
b)	'Washout' (SPECT)/Tc99m sestamibi.
5	PET

Table 2: Characteristics of non-invasive methods to localize disease-transformed parathyroid glands.

	USG	CT	IRM
Sensitivity	71-80%	46-80%	64-88%
Specificity	80-89%	80%	88-95%
Reoperation sensitivity	40%		50-88%
Falsely positive	15-20%	50%	18%
Dependent on Examiner skills	+++	+	++
Exposure to Radiation	No	++	No
Costs	+	+++	++++

a) Highly sensitive.

b) Highly specific.

c) As minimally invasive as possible.

d) Cost-effective.

e) Available [10].

Material and Methods

We have carried out a retrospective study in patients admitted for surgical treatment between January 2009 to December 2013, preoperatively diagnosed with HPT [1,2]. All patients were hospitalized and prepared for surgery in the Service of Endocrinology and Nephrology where they came from. The data on patient's histories, diagnostic procedures, treatment and complications were acquired from medical reports. All patients were symptomatic. The diagnosis was established biochemically by the measurement of the total calcium serum level, the serum ionized calcium level and PTH hormone level.

To support the diagnosis, radiologic examinations of the urinary system and osteo-articular system were necessary. In order to detect and locate abnormal parathyroid tissue for preoperative localization study of diseased gland, we have used neck ultrasonography (USG), computed axial tomography (CT) and magnetic resonance imaging (MRI). Scintigraphy and PET scan cannot be done at our hospitals. Calcium was measured before and after surgery, PTH hormone was monitored postoperatively.

Surgical cure was defined as the normalization of serum (ionized) calcium level and PTH levels for a period of at least 6 months after surgery. Persisting hypercalcemia or renewed of PTH within the first 6 months after surgery was considered surgery failure. A period of one year follow-up is necessary in these cases in collaboration with the endocrinology service. All patients were operated through a classical cervicotomy. Both inferior and superior parathyroid glands are identified by this approach. It continues to be the gold standard of surgical treatment. Neck ultrasonography and CT- scan were used in 100% of patients. For 4 cases with persistent HPT, neck MRI was utilized.

Correct localization or a true positive (TP) result was defined as identifying an abnormal parathyroid gland during surgery on the same location as reported by the imaging study. Abnormal parathyroid glands that were not identified by imaging technique were considered false negative (FN). Abnormalities reported by imaging that did not correspond to an abnormal parathyroid gland were considered false positive (FP). Sensitivity was calculated as TP/(TP+FN) and positive predictive value was calculated as TP/(TP+FP). In this analysis, the results were considered a TP if either studies correctly localized the abnormal gland. Abnormal parathyroid glands not imaged by either technique were recorded as FN, and all imaged abnormalities that did not correspond to abnormal parathyroid glands for both tests were recorded as FP.

Results

Demographics

In total, data from 14 patients were analyzed. They were 9(60%) females and 5(40%) males, with an age ranging from 34 to 68 years old. Patients belong to sporadic PHP (primary hyperparathyroidism) without any family history and SHP (secondary-renal hyperparathyroidism). Only one patient had MEN2a syndrome representing ectopic (and supernumerary) parathyroid carcinoma, medullar thyroid carcinoma and bilateral pheochromocytomas. In 8 cases there was co-existing thyroid pathology (nodular goiter) and one patient had thyroid medullar carcinoma.

Preoperative evaluation

Table 3: Symptoms in patients with HPT.

Symptoms	Nr	%
Uropoetic system	12	85.70%
Osteoarticular system	9	64.30%
Gastrointestinal system	5	35.70%
Neuropsychic	13	71.40%

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In our study group, the disease was manifested with symptoms from different systems (Table 3). Renal manifestations, especially urolithiasis, nefrolithiasis and their complications were present in 78.6% of cases. Patients also presented with symptoms of bone resorption, especially bone pain and fractures (64.3%) and digestive system symptoms (35.7%). Neuro-psychic symptoms were present in all patients. These data supported by positive imagery exams are shown in Table 4.

Table 4: Imaging in patients with HPT.

Imaging	Nr	%
Osteoarticular imaging	14	100%
Urinary tract imaging	12	85.70%
Bone scintigraphy	9	64.30%

All our patients resulted with high serum levels of calcium and PTH hormone. Neck ultrasonography and CT- scan were used for 100% of patients. For 4 cases with persistent HPT, neck MRI was utilized.

Histopathologic findings included 7 eutopic solitary parathyroid adenomas, 3 ectopic parathyroid adenomas found 2 mediastinal and one intrathyroid position. One case with 3 gland parathyroid hyperplasia, and one case with parathyroid carcinoma located mediastinaly in a supernumerary gland (fifth inferior parathyroid gland). Two other cases were secondary renal hyperparathyroidism, with four gland hyperplasia (Table 5).

Table 5: Histopathologic findings.

Histopathology	N	%
Adenoma	10	71.40%
Hyperplasia	3	21.40%
Carcinoma	1	7.20%

Table 6: Comparison between US and Ct in 14 patients with hyperparathyroidism.

	Positive Results	TP	FP	FN	S (%)	PPV (%)
USG	11 78.50%	8 57.10%	3 21.40%	3 21.40%	72.80%	72.80%
CT	13 92.80%	10 71.40%	3 21.40%	1 7.10%	91%	77%

N: Number of parathyroid glands; TP: True Positive; FP: False Positive; FN: False Negative; S: Sensitivity; PPV: Positive Predictive Value

The diagnostic accuracy values for US, CT and IRM are shown in Table 6. USG was positive in 78.5% and accurately localized the pathology in 72.8%, according to surgery. It has a false positive rate of 21.4% and a false negative rate of 21.4%, sensitivity of 72.8% and positive predictive value of 72.8%. CT results in higher values of positive results, sensitivity and positive predictive values, in comparison to USG exam. At our hospitals we cannot do parathyroid glands scintigraphy and PET-scan, for this reason we have to depend on examiner skills for the above methods.

Discussion

Ultrasonography and 99mTc-sestamibi scintigraphy were the dominant imaging techniques for preoperative localization of parathyroid glands disease. Numerous studies comparing these techniques suggest similar sensitivities and specificities for solitary adenoma detection [11-13]. Localization accuracy is also improved when both studies are obtained preoperatively [12]. Reported sensitivities for the detection of solitary parathyroid adenomas with preoperative ultrasonography range from 72% to 89% in recent large series [10].

CT images through the neck show intense enhancement in the typical locations for parathyroid tissue in the setting of adenoma. Scanning from the skull base through the mediastinum has the additional advantage of detecting most ectopic glands. In cases of failed initial parathyroidectomy, artifacts from surgical clips placed in the neck often limit the diagnostic quality of CT. Reported sensitivities of CT range from 46% to 87% [14]. Combined studies of sonography and CT suggest that supplemental CT will detect few additional adenomas over sonography alone. Thus, CT is usually reserved for cases of failed parathyroidectomy or in cases of altered anatomy, in which CT may aid in operative planning [15,16].

Recent studies have combined 99mTc-sestamibi SPECT with co-registered CT in an attempt to improve sensitivity by combining anatomic and functional information, but results from these initial studies are conflicting in their conclusions about the added usefulness of CT.

Although less commonly used for preoperative localization than sonography and CT, MRI provides similar sensitivity to other techniques in the detection of abnormal parathyroid tissue [17,18]. More commonly, MRI is used in patients with persistent or recurrent hyperparathyroidism, in whom it has been shown to be effective in locating remaining abnormal parathyroid tissue [19].

The T1 and T2 characteristics of abnormal parathyroid tissue are variable. The most common tissue characteristics are intermediate- to low-intensity T1 signal and high-intensity T2 signal. Less commonly, fibrosis or old hemorrhage can cause low signal intensity on T1-and T2-weighted images. Subacute hemorrhage into adenomas can cause high signal intensity on both T1-and T2-weighted images [19]. Abnormal parathyroid tissue cannot be diagnosed on MRI by signal characteristics alone because cervical lymph nodes have similar signal characteristics. Therefore, accurate MRI diagnosis depends on knowledge of the typical morphology and location of the parathyroid glands and common sites of ectopic glands.

In the current study, we compared ultrasonography with CT and MRI images. The significant positive result reported by CT (92.8%) as well correctly predicting the surgical findings in 71.4% of patients with HPT, signifies the importance of utilizing Ct as well. The results were significantly higher than

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the corresponding value for US, (78.5% positive result, and predicting the surgical findings in 57.1% of patients). The sensitivity and positive predictive value were for US 72.8% and 72.8% and for CT were 91% and 77%. MRI images were used only in persistent/recurrent disease.

Among previous reports that have directly compared US and CT in patients undergoing initial parathyroid surgery, Mazzeo et al. [20] and De feo et al. [5] reported that the two methods were similar in their ability to correctly predict the surgical findings, while Casas et al. [21] and Lumachi et al. [22] found that the CT imaging was superior. In a large study encompassing US in 449 patients and SS in 700 of these patients, Cha Puis et al. [23] found that the US provides better results.

Conclusion

The treatment of parathyroid disease is primarily surgical. However, parathyroidectomy would not be successful without accurate preoperative localization of the abnormal gland. This requires skilled radiologists at performing ultrasonography, Ct, IRM and other imaging modalities to guide the surgeon in localizing the abnormal gland(s).

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