

Localization of pathological gland's site in primary hyperparathyroidism: ten years experience with MIBI scintigraphy

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SUMMARY: Localization of pathological gland's site in primary hyperparathyroidism: ten years experience with MIBI scintigraphy

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Background. Primary hyperparathyroidism (PHPT) is characterized by pathological hyperfunctioning of one or more of the parathyroid glands leading to excessive parathyroid hormone (PTH) secretion. The aim of this study was to assess the diagnostic capacity of scintigraphy with MIBI, considering the surgical findings and the level of agreement with the result of cervical ultrasonography.

Patients and methods. In the period January 1996 to January 2006, 84 cases with PHPT were included in the study, in which scintigraphy with MIBI was used in addition to cervical ultrasonography. All were hospitalised as "short stay surgery" patients and then seen as outpatients at follow-up visits (at 7, 14 and 30 days), during which calcium, phosphorus and PTH values were measured.

Results. In 55 cases (65.5%), the site of the pathology was suspected on the basis of the cervical ultrasonography. Scintigraphy with MIBI was positive in 76 cases (90.4%) and negative in the other eight (9.6%). In six of these eight cases the site had been detected by the cervical ultrasonography. In the remaining two cases (2.4%), neither of these examinations gave positive diagnostic findings. In 58 patients we proceeded with the removal of a single adenoma, in 19 cases with the removal of two out of the four glands, and in seven cases with the removal of three out of the four glands, the single formations removed not showing clearly-defined macroscopic characteristics; in two of the seven patients in whom three of the four glands were removed, the preoperative diagnostic examinations had not shown any evidence of gland pathology.

Conclusions. We regard scintigraphy with MIBI as a preoperative diagnostic examination that has modified the surgical approach to PHPT, inclining surgeons towards a mini-invasive surgical procedures. We consider CT, MRI and SPECT techniques to be indicated only in cases of relapse of PHPT, possibly associated with ectopic localisation of the parathyroid gland not identified in the course of previous surgical procedures.

RIASSUNTO: La scintigrafia con MIBI: esperienza decennale chirurgica nella diagnosi di sede.

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Background. L'iperparatiroidismo primitivo (IPP) è caratterizzato da una patologica iperfunzione di una o più ghiandole paratiroidi con conseguente eccessiva secrezione di paratormone (PTH). Lo scopo dello studio è stato di valutare la sensibilità della scintigrafia con MIBI in rapporto al riscontro chirurgico ed al livello di accordo con il risultato della ecografia cervicale.

Pazienti e metodi. Da gennaio 1996 a gennaio 2006, 84 casi di pazienti affetti da IPP sono stati inclusi nello studio nel quale la scintigrafia con MIBI era stata eseguita insieme all'ecografia cervicale. Tutti sono stati trattati in regime di short stay surgery e successivamente rivalutati a visita ambulatoriale di controllo a 7, 14 e 30 giorni dall'intervento chirurgico con valutazione di calcio sierico, fosforo e PTH.

Risultati. In 55 casi (65,5%) la sede della ghiandola patologica era stata sospettata sulla base dell'ecografia cervicale. La scintigrafia con MIBI era positiva in 76 casi (90,4%) e negativa in altri 8 (9,6%). In sei degli otto casi era stata evidenziata la sede dall'esame ecografico. Nei rimanenti due casi (2,4%) nessuna delle due indagini, ecografia, e scintigrafia avevano posto sospetto di sede. In 58 pazienti abbiamo proceduto con la rimozione del singolo adenoma, in 19 casi con la rimozione di due ghiandole su quattro ed in sette casi con la rimozione di tre ghiandole su quattro; in due dei sette pazienti nei quali abbiamo rimosso tre ghiandole su quattro, gli esami diagnostici preoperatori non avevano evidenziato alcuna evidenza di sede di ghiandola patologica.

Conclusioni. La scintigrafia con MIBI come esame diagnostico preoperatorio ha modificato l'approccio chirurgico all'IPP, permettendo l'introduzione di tecniche mini-invasive. Noi consideriamo la TC, la RMN e la SPECT indagini diagnostiche che devono essere indicate solo nei casi di recidiva di IPP e soprattutto nei casi di localizzazione ectopica della ghiandola paratiroide non identificata in corso di precedenti procedure chirurgiche.

KEY WORDS: PTH - Hyperparathyroidism - Ultrasonography - Scintigraphy - MIBI - Parathyroidectomy.
PTH - Iperparatiroidismo - Ecografia - Scintigrafia - MIBI - Paratiroidectomia.

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Introduction

Primary hyperparathyroidism (PHPT) is characterised by idiopathic, pathological hyperfunctioning of

one or more of the parathyroid glands leading to excessive parathyroid hormone (PTH) secretion. This excessive hormonal secretion determines a clinical picture correlated with elevated serum calcium levels (>10.5 mg/dl) and symptoms ascribable to the hormonal imbalance induced by the excessive PTH secretion.

In 1996, we introduced scintigraphy with ^{99m}Tc-sestaMIBI into our protocol of preoperative evaluation of the parathyroid glands.

Thanks both to preoperative localisation of the site of the pathology and intra-operative measurement of PTH, it has been found that the cause of PHPT, in a high percentage of cases (85-90%), is a single parathyroid adenoma, and this has led to an increase in mini-invasive surgical procedures (unilateral exploration of the neck, radioguided excision, video-assisted parathyroidectomy) (1-5).

The aim of this study was to assess the diagnostic capacity of scintigraphy with MIBI, considering both the surgical findings and the level of agreement with the result of cervical ultrasonography. It is, in fact, on these diagnostic considerations that the choice of the mini-invasive surgical strategy is based.

Patients and methods

In the period January 1996 to January 2006, 84 cases with PHPT were included in this study, in which scintigraphy with MIBI, in addition to cervical ultrasonography, was used (after blood chemistry including PTH, calcium and phosphorous levels) as a II-level diagnostic examination on which to base the diagnosis of PHPT. The results of these diagnostic investigations were correlated with the results (presence of pathological parathyroid glands) of surgical cervical exploration which was performed bilaterally even in the event of ultrasonography and scintigraphy with MIBI suggesting the same pathological localisation. To ensure homogeneity of the sample, patients treated using mini-invasive video-assisted parathyroidectomy (mivap) were excluded.

We removed parathyroid glands that were deemed pathological on the basis of their dimensions, and in some cases also the contralateral gland, performing an extemporaneous histological examination in frozen sections in order to obtain intra-operative diagnostic confirmation of the homogeneity of these cases with those treated at the end of the 1990s.

All the patients were hospitalised as "short stay surgery" patients and then seen as outpatients at follow-up visits (at 7, 14 and 30 days after surgery), during which calcium, phosphorus and PTH values were measured. Thirty days after surgery, they were referred back to other specialists (endocrinologists and nephrologists) for complementary therapies.

Results

Of the 84 patients treated in our clinic, 53 were women and 31 were men. Their mean age was 51.4 years (range: 21-82). The main symptoms at onset were renal

TABLE 1 - SYMPTOMS IN 84 CASES OF PHPT.

Renal colic	64.3%
Bone pain	29.8%
Asthenia	10.7%
Depression	5.9%

colic in 54 patients (64.3%), diffuse bone pain in 25 (29.8%), asthenia in 9 (10.7%), and depression in 5 (5.9%) (Table 1).

In 55 cases (65.5%) the site of the pathology was suspected on the basis of cervical ultrasonography. Scintigraphy with MIBI was positive in 76 cases (90.4%) and unremarkable (negative) in the other 8 (9.6%). In six of these eight cases the possible site of the pathology had been detected by ultrasonography (Table 2). In the remaining two cases (2.4%) neither of these examinations were diagnostic.

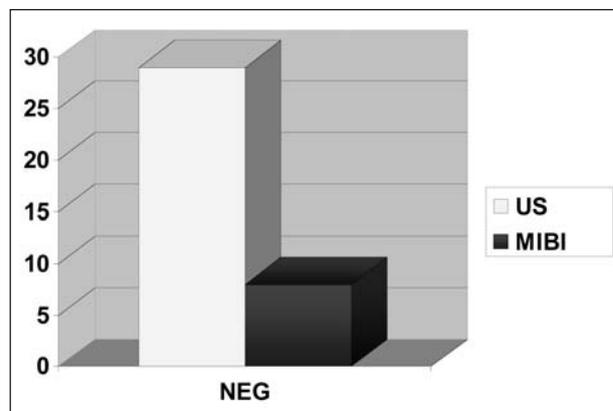
All the patients underwent exploratory cervicotomy. In 58 patients we proceeded with the removal of a single adenoma, in 19 cases with the removal of two of the four glands, and in seven cases with the removal of three of the four glands, the single formations removed not showing clearly-defined macroscopic characteristics; in two of the seven patients, in whom three of the four glands were removed, the preoperative diagnostic examinations had not shown any evidence of gland pathology.

The definitive histological examination showed:

- 67 cases (79.8%) of parathyroid adenoma;
- 14 cases (16.6%) of hyperplasia of the parathyroid glands;
- 1 case (1.2%) of double adenoma;
- 2 cases (2.4%) of parathyroid carcinoma (associated thyroid lobectomy).

We recorded a relapse of PHPT in one patient who had presented preoperative PTH and calcium levels oscillating just above the upper limits of normal.

TABLE 2 - CERVICAL ULTRASONOGRAPHY (US) WAS NEGATIVE (NEG) IN 29 CASES AND MIBI IN 8 CASES. SIX OF THESE EIGHT HAD POSITIVE ULTRASONOGRAPHY.



Discussion

The incidence of PHPT has increased in recent years as a result of the increase in the number of patients in whom calcium values above normal have been found incidentally in the course of multiphasic examinations that included calcium measurements. The symptomatology is linked to the direct action of PTH on bone (bone pain, spontaneous fractures, subperiosteal resorption), on the kidneys (polyuria, nocturia, dehydration, tubular acidosis, nephrolithiasis), on the gastrointestinal tract (anorexia, polydipsia, nausea, vomiting, dehydration, biliary colic, gastric ulcers), on the nervous system (ideation disorders, amnesia, mental confusion, depression and headache), and on the cardiovascular apparatus (atherosclerotic lesions, conduction disorders, arrhythmia and hypertension) (6-11).

The use of imaging techniques to study the parathyroid glands plays a key role in the surgeon's preoperative appraisal and planning of the surgical procedures required; it must be remembered that diagnostic techniques help us to diagnose the site of the pathology, not the disease itself. The diagnostic techniques currently available are ultrasonography, scintigraphy with ^{99m}Tc-sestaMIBI, and in a few cases SPECT, CT and MRI (12). SPECT can be used for three-dimensional imaging of the pathological gland and is, like CT and MRI, particularly useful in the detection of unusual or abnormal sites mediastinal localisations. In this study, we set out to establish, in the light of the intraoperative findings, the reliability of cervical ultrasonography and scintigraphy with ^{99m}Tc-sestaMIBI in diagnosing the site of the pathological parathyroid glands.

Ultrasonography has shown, in our experience, a diagnostic sensitivity, for site, of 65%, as well as the capacity, in some borderline cases, to detect possible pathological sites missed by scintigraphy. In the not uncommon cases of thyroid in association with parathyroid disease, it is a fundamental examination (13-15).

The introduction in recent years of scintigraphy with ^{99m}Tc-sestaMIBI has modified considerably the preoperative localisation of pathological parathyroid glands, inclining surgeons towards mini-invasive procedures and introducing, as part of the intra-operative management of PHPT, unilateral exploration of the neck in combination with measurement of the intra-operative PTH value (a drop of at least 50% compared to the preoperative level, 10 minutes after removal of the gland). This correct pre- and intra-operative diagnostic protocol nevertheless needs to be supported by adequate post-surgical follow up in order to appraise the real incidence of relapse of PHPT. The high sensi-

tivity of scintigraphy with MIBI, moreover, has led to a reduction in the duration of the surgical procedures undertaken, and reduced both surgical manipulation of the cervical region and the incidence (already low) of post-operative complications (paralysis of the recurrent nerve, haemorrhage). These findings still need to be validated through more extensive follow-up studies.

Today, however, we are seeing increasingly early, and often incidental, diagnoses of PHPT in patients presenting with oligosymptomatic clinical pictures and serological parameters compatible with PHPT, or at the upper limits of normal. Recent published reports have shown that the result of scintigraphy with MIBI can be correlated with the functional stage of the glands, and with the serum calcium and PTH levels (low values are correlated with reduced sensitivity of MIBI).

In the light of such data, it seems that it could be potentially dangerous, in these cases, to rely exclusively on unilateral surgical exploration or on parathyroidectomy dictated exclusively by tracer captation (radio-guided surgery). Moreover, PHPT is a pathology in which the detection of subclinical forms is on the increase and in which surgery constitutes the definitive therapeutic step; other methods, such as alcoholisation of the parathyroid glands, which are reserved for patients who are not suitable candidates for surgery (because of increased risks associated with surgery and anaesthesia), have a lower success rate. In certain cases, other therapies are emerging based on second generation calcimimetics, currently used for the treatment of the hypercalcaemia caused by parathyroid carcinoma and in patients with secondary hyperparathyroidism (16, 17).

We maintain that scintigraphy with ^{99m}Tc-sestaMIBI is the most appropriate method for the preoperative localisation of the site of the pathology, due to its high sensitivity compared to other non-invasive imaging techniques; its combination with cervical ultrasonography remains indicated, the latter being a sensitive and economical examination that is able, in an acceptable percentage of patients, to provide responses to the diagnostic questions concerning site and volume. Its combination with scintigraphy is indicated in those cases in which there is doubt over the localisation.

On the other hand, on account of their high costs, we regard the CT, MRI and SPECT techniques to be indicated only in cases of relapse of PHPT, possibly associated with ectopic localisation of the parathyroid gland not identified in the course of previous surgical procedures.

Today, in cases presenting with negative preoperative imaging but serological parameters suggestive of PHPT, we perform a bilateral exploration using a clas-

sis or video-assisted technique. Through cervical exploration conducted by expert surgeons has always produced 95% success rates, identifying parathyroid glands with dimensions of just a few millimetres, thus smaller than those detectable using more sophisticated

and expensive imaging techniques. We nevertheless regard scintigraphy with MIBI as a preoperative diagnostic examination that has modified the surgical approach to PHPT, inclining surgeons towards mini-invasive surgical approaches.

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