Minimally Invasive Radionuclide-Guided Parathyroidectomy Using ^{99m}Tc -Sestamibi in Patients with Primary Hyperparathyroidism: A Single-Institution Experience

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Key Words

Radio-guided parathyroidectomy • ^{99m}Tc -sestamibi • Parathyroid adenoma

Abstract

Objective: To evaluate the efficacy and usefulness of ^{99m}Tc -sestamibi scintigraphy and gamma probe localization of parathyroid glands in patients with primary hyperparathyroidism and establish radio-guided minimally invasive parathyroidectomy at Hussain Makki Al Jumma Center for Specialized Surgery, Kuwait. **Subjects and Methods:** Twelve patients with primary hyperparathyroidism (mean age: 48 ± 14 years; median age: 46 years; age range: 29–68 years) were evaluated. The diagnosis of hyperparathyroidism was established by elevated serum calcium and parathyroid hormone levels. All patients had a well-defined parathyroid lesion on previous standard ^{99m}Tc -sestamibi scintigraphy with or without ultrasound study. All had a normal thyroid gland, no history of familial hyperparathyroidism or multiple endocrine neoplasia nor any history of previous neck irradiation. On the day of surgery, patients were injected with 740 MBq (20 mCi) of ^{99m}Tc -sestamibi followed by a half-hour-delayed

single standard pinhole view of the neck. A skin marker was placed on the basis of maximum count intensity during gamma probe localization. Patients were then sent for radio-guided minimally invasive parathyroidectomy. **Results:** The preoperative localization of the affected gland was successful in all cases using a gamma probe and ^{99m}Tc -sestamibi scintigraphy. The pathological parathyroid tissue was localized and successfully removed with the gamma probe. The histopathological diagnosis was parathyroid adenoma in 11 cases and hyperplasia in the remaining one. All patients remained disease and symptom free at 12-month follow-up. **Conclusions:** Our initial experience with intraoperative use of a gamma probe to carry out minimally invasive parathyroidectomy was a useful, easy and safe procedure for treating patients with primary hyperparathyroidism.

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Introduction

Primary hyperparathyroidism, a disorder characterized by excessive secretion of parathyroid hormone by one or more enlarged parathyroid glands, is caused main-

Fig. 1. ^{99m}Tc -sestamibi dual-phase parathyroid scintigraphy. **a** Early images at 20 min. **b** Delayed images at 120 min.

ly by a single adenoma in 85–90% of the cases [1]. The classic operation for hyperparathyroidism involves identification of the pathological gland after exploration. Success depends on the surgeon's knowledge of normal anatomy and its variations. The use of new procedures such as unilateral exploration is becoming more common as they appear to reduce operative time, hospital stay and perioperative complications while improving cosmetic results [2, 3].

Localization of abnormal parathyroid glands is a challenging task. Ultrasound imaging has a localization accuracy of 40–80% [4]. The sensitivity of CT scans ranges from 45 to 75%, and is lower in previously operated patients [5]. MRI sensitivity (50–80%) is slightly better than that of CT scans [6, 7]. In 1989, Coakley et al. [8] reported that ^{99m}Tc -sestamibi was taken up and retained in abnormal parathyroid glands. A number of studies have reported successful utilization of ^{99m}Tc -sestamibi imaging for abnormal gland localization [9, 10]. The accuracy of the ^{99m}Tc -sestamibi scan in detecting single adenomas is 90% [11, 12]. The addition of SPECT imaging considerably improves the localization of ectopic sites which are difficult to explore, such as the retro-esophageal space or mediastinum [13, 14].

^{99m}Tc -sestamibi scintigraphy also has a role in preoperative localization of abnormal parathyroid tissue and minimally invasive parathyroidectomy (MIP). This technique of parathyroid imaging and localization with a gamma probe allows surgeons to plan localized exploration to remove a single focus of disease [15]. The aim of this study was to evaluate radio-guided MIP in patients with primary hyperparathyroidism and help establish this procedure as a primary method for localization and removal of pathological parathyroid tissue at our institute.

Subjects and Methods

Twelve patients (mean age: 48 ± 14 years; median age: 46 years; age range: 29–68 years) were evaluated for radioguided MIP for primary hyperparathyroidism in our department. The diagnosis of hyperparathyroidism was previously established by elevated serum calcium and parathyroid hormone levels. All patients had a normal thyroid gland (no nodular goiter), no history of familial hyperparathyroidism or multiple endocrine neoplasia, and no history of previous neck irradiation. All patients had undergone previous diagnostic ^{99m}Tc -sestamibi scintigraphy using a standard method as described by Norman et al. [16] with or without ultrasound examination. All patients had a well-circumscribed unifocal lesion in the neck on these diagnostic ^{99m}Tc -sestamibi scans. In 3 of the 12 patients parathyroidectomy (with preoperative scintigraphic localization) had been attempted before and had failed. In all 3 patients, a repeat diagnostic sestamibi study after the previous operation showed an intact parathyroid lesion.

Preoperative Localization

On the day of surgery, approximately 740 MBq (20 mCi) of ^{99m}Tc -sestamibi was administered intravenously. Half an hour after the injection, a static image of the parathyroid region was obtained using a pinhole collimator up to a total of 350,000 counts in a 128×128 matrix size. This was followed by gamma probe localization of the lesion visualized on the static image aided by the previous diagnostic ^{99m}Tc -sestamibi localization image (fig. 1).

Gamma Ray Detecting Probe

The gamma ray detecting probe was Scinti-Probe MR 100, from Pol.Tech. Carsoli (Italy). The radioactivity detected by the probe was transduced into digital readout and acoustic signals. The intensity and frequency of the acoustic signal were directly proportional to the level of radioactivity. The probe was used in the imaging room and a skin mark was placed at the site of maximum counts. The patient was taken to the operating room within 2.5 h of injection and thereafter the probe was used preoperatively to confirm the skin projection of the parathyroid tissue seen on the scintigraphic images.

Operation

The skin was incised directly over the marked point, and the gamma probe was then used to guide dissection. Following a cervical incision, skin flaps were elevated in craniocaudal direction. The strap muscles were divided at the midline and radioactive counts were repeated from both sides (fig. 2). In order to obtain a satisfactory surgical field, an incision measuring between 2 and 2.5 cm was found to be adequate. During surgery, radioactivity counts as measured with the probe coupled to its audible guidance system were used to localize the parathyroid gland. After removal of the parathyroid tissue, ex vivo counts were obtained and a count in excess of 20% of the residual background was considered to represent a satisfactory surgical removal.

Table 1. Patient characteristics and histopathological findings

Pa-tient	Age	Sex	Histo-pathology	Positive US	Weight mg	Localization
1	32	F	adenoma	yes	2,200	left lower
2	65	M	adenoma	yes	3,300	right lower
3 ¹	68	F	adenoma	yes	1,600	left upper
4	29	F	adenoma	yes	1,900	left lower
5	43	F	adenoma	yes	1,100	right upper
6 ¹	56	M	adenoma	no	900	right lower
7	30	M	hyperplasia	no	800	left lower
8	48	F	adenoma	yes	2,400	left upper
9	65	F	adenoma	yes	3,500	right lower
10	44	M	adenoma	yes	2,300	left lower
11	58	M	adenoma	yes	1,300	left upper
12 ¹	38	F	adenoma	no	1,200	left lower

US = Ultrasound.

¹ Patients with repeat probe-assisted parathyroidectomy. **Fig. 2.** Unilateral surgical exploration revealing parathyroid adenoma.**Table 2.** Serum calcium and parathyroid hormone (PTH) levels

Parameter	Serum calcium before surgery	Serum calcium 24 h after surgery	PTH before surgery	PTH after surgery	In vivo counts	Ex vivo counts
Mean	2.64	2.02	10.2	6.7	452.7 ± 118	498.5 ± 135
Range	2.1–2.9	1.8–2.12	7–13	2–7		
Normal levels: calcium 2.2–2.26 mmol/l; serum PTH: 1.0–7.2 pmol/l.						

Results

Of the 12 patients, 7 were females and 5 males. The median age of patients was 46 years (range 29–68 years). Preoperative scintigraphy localized the diseased gland successfully in all patients while preoperative ultrasonography localized 9 diseased glands (fig. 1, table 1). Mean serum calcium level was 2.64 mmol/l (range: 2.1–2.9 mmol/l) and mean serum parathyroid hormone level was 10.2 pmol/l (range: 7–13 pmol/l) (table 2).

The mean operation time was 40 min (range 25–60 min). In most cases, the adenoma was easily indentified as a pale yellow, often multilobular structure with significantly higher counts than the surrounding tissue. Frozen-section diagnosis was parathyroid adenoma in 11 cases and hyperplasia in 1. All parathyroid lesions were >0.8 cm and weighed >800 mg (table 1). In 2 patients, although gross appearance resembled an adenoma, the fro-

zen sections only revealed parathyroid tissue. As diagnosis cannot always be established from frozen sections, gross appearance of parathyroid adenoma together with histological diagnosis of parathyroid tissue were thought to be sufficient for diagnosing the parathyroid adenoma. All patients remained disease- and symptom-free at the 12-month follow up.

Discussion

The traditional operative strategy in patients with primary hyperparathyroidism is bilateral exploration of the neck. Radioguided MIP offers an alternative with the advantages of less morbidity, shorter duration of hospital stay (thereby reducing costs), shorter operative time, and better cosmetic results. ^{99m}Tc-sestamibi is the only radiopharmaceutical currently used to identify the site of para-

thyroid adenomas by radioguidance [17]. We adapted an imaging strategy similar to Norman and Cheda [16], who performed scintigraphy on the day of surgery.

In a series of 35 patients, Sullivan et al. [18] localized 34 adenomas using preoperative scintigraphy and 33 adenomas with an intraoperative gamma probe. Similarly, Kumar et al. [19] successfully localized parathyroid adenomas in all 29 patients in their series. Similar to these results, our study demonstrated excellent postoperative results using a strategy involving routine preoperative scintigraphy or ultrasonography for primary hyperparathyroidism. There are 2 potential caveats in the radioguided MIP procedure. Firstly, solid thyroid nodules can concentrate ^{99m}Tc -sestamibi quite avidly, giving rise to false-positive results [20]. This problem is partly overcome by double-tracer subtraction protocols ($^{123}\text{I}/^{99m}\text{Tc}$ -sestamibi or ^{99m}Tc -pertechnetate/ ^{99m}Tc -sestamibi) or bilateral neck exploration [21]. The second caveat is absence of an abnormal uptake on delayed images due to rapid ^{99m}Tc -sestamibi washout in some parathyroid adenomas (false-negative results) [22].

In our series, the 3 cases that underwent repeat surgery (which was successful) were a stark reminder that an operative strategy solely based on a preoperative diagnostic ^{99m}Tc -sestamibi scan for localizing the lesion without the use of an intraoperative probe could be potentially flawed. The lesions in these 3 cases were located deep in the neck and the surgical team went for deeper exploration only on the basis of probe findings of persistent high counts in that region. These adenomas were by no means

small, and once identified could be seen as multilobulated yellow structures which were then dissected out.

Radioguided MIP seems to be an appropriate approach in patients who have a high probability of a solitary parathyroid adenoma established on the basis of ^{99m}Tc -sestamibi scintigraphy (and ultrasound imaging), provided there is significant ^{99m}Tc -sestamibi uptake in the parathyroid adenoma with no coexisting ^{99m}Tc -sestamibi-avid thyroid nodules. Applying this criterion to patients with primary hyperparathyroidism, about 60–70% of all cases will possibly be candidates for radioguided MIP [23]. Additional settings in which radioguided MIP is indicated include reoperation for persistent or recurrent hyperparathyroidism and ectopic adenomas (especially major ectopy). The >95% success rate reported by most authors (as assessed by postoperative normalization of serum calcium and parathyroid hormone levels) was replicated in our study and thus constitutes a sound basis for the regular use of this procedure along with the conventional surgery.

Conclusions

Our initial experience confirmed that radioguided MIP is a very attractive surgical approach to treat patients with primary hyperparathyroidism, and a high probability of solitary parathyroid adenoma and a normal thyroid gland.

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