

Short Reports

Minimally invasive radioguided surgery for parathyroid adenomas (MIRP)

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ABSTRACT

Background. Parathyroid adenoma is the most common cause of primary hyperparathyroidism. Conventional surgical management includes bilateral neck exploration with removal of the adenoma(s) and biopsy of one of the other glands with visualization of all glands. It is associated with a risk of permanent hypoparathyroidism. Radioguided excision of parathyroid adenoma is a widely accepted technique which provides accurate localization and complete excision of the lesion with low morbidity. We report our experience with this technique.

Methods. We performed radioguided excision of parathyroid adenomas in 15 patients. All of them had preoperative localization of the adenoma using a dual tracer, dual phase ^{99m}Tc -Sestamibi scan. A dose of 8–10 mCi of ^{99m}Tc -Sestamibi was injected intravenously 2 hours before surgery. Under local anaesthesia, surgical excision of the lesion was done after localizing it using a hand-held gamma probe. Complete excision was confirmed by frozen section of the excised lesion and an intraoperative quick parathormone assay.

Results. The ^{99m}Tc -Sestamibi scan revealed an increased uptake by the adenoma in all patients and complete excision was possible in all the patients. Frozen section confirmed the diagnosis and the quick parathormone assay (within 15 minutes) revealed a drop in parathormone levels to < 50% after excision in all of them. Three patients developed hypocalcaemia postoperatively and were treated with intravenous calcium supplementation. At a follow up of 2–29 months, all the patients were normocalcaemic. The renal functions improved in 2 of 6 patients who had renal failure.

Conclusion. Minimally invasive radioguided excision of parathyroid adenomas is a simple, safe and effective technique associated with a low morbidity and can be done as a day-care procedure.

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INTRODUCTION

An increase in the use of screening techniques has resulted in increased detection of hyperparathyroidism.¹ In the West, most patients are detected when they are asymptomatic. However, in India most patients are diagnosed while being investigated for recurrent renal stones, renal failure, pancreatitis or severe osteoporosis. The conventional surgical management includes bilateral neck exploration with removal of the adenoma and biopsy of one of the other glands with visualization of all glands.² This procedure poses the risk of injury to the recurrent laryngeal nerves. This is also associated with a high incidence of permanent hypoparathyroidism.³ The incidence of iatrogenic hypoparathyroidism (severe permanent hypoparathyroidism lasting >1 year) is 2.5%–4% after primary surgery and 21% after re-exploration.³ However, with minimally invasive radioguided surgery, the incidence of iatrogenic hypoparathyroidism is practically nil.³

Radioguided excision of the parathyroid adenoma is a technique which helps in accurate localization and complete removal of the adenoma. It is gradually replacing the traditional 4-gland exploration as the procedure of choice in many institutions and has comparable cure rates.^{4,5} We report the results of 15 patients who had successful excision of the parathyroid adenoma using a gamma probe for guidance.

METHODS

Fifteen patients with a parathyroid adenoma were managed from May 2004 to October 2006. There were 10 women and 5 men with an age range of 24–57 years. Thirteen of these patients were symptomatic and were referred from the Nephrology and Endocrinology units. (Table I).

Biochemical confirmation of the diagnosis was done in all cases based on high serum calcium, low serum phosphate and high serum parathormone levels. Preoperative imaging included a high resolution ultrasound examination of the neck and a dual tracer dual phase ^{99m}Tc -pertechnetate/ ^{99m}Tc -Sestamibi scintigraphy. A dual tracer dual phase scan was preferred in view of the high incidence of thyroid nodules in the Indian population.⁶ In 14 patients with concordant ultrasound and scintigraphy findings, no further imaging was done whereas in 1 patient, ultrasound of the neck was normal and the Sestamibi scan revealed an adenoma in the superior mediastinum. A SPECT with CT superimposition was performed for accurate localization of the adenoma. The inclusion criteria included a distinct increased uptake of ^{99m}Tc -Sestamibi by the adenoma (positive scan) and absence of multiple endocrine neoplasia (MEN) syndromes or familial hyperparathyroidism.

After confirmation of a solitary adenoma on Sestamibi scan, the patients underwent an operative procedure (Figs 1–4). A dose of 8–10 mCi of ^{99m}Tc -Sestamibi was injected intravenously about 2 hours before surgery. The entire operative procedure was performed under local anaesthesia. Prior to the surgical incision, the patient's neck was scanned using a hand-held gamma probe to identify the maximum activity count area corresponding to the cutaneous projection of the parathyroid adenoma, which was marked. A 2–2.5 cm long transverse incision was made at the site under local anaesthesia and deepened. The gamma probe was introduced repeatedly into the incision to guide the surgeon to the

area of maximum count on the adenoma. After removal of the target tissue, radioactivity was measured on the *ex vivo* parathyroid adenoma and the surgical area to confirm successful removal of the adenoma.

Histological diagnosis was confirmed with the help of frozen section. A blood sample was drawn at 15 minutes after removal of the adenoma for quick parathormone (QPTH) assay. A fall in parathormone level to <50% of the preoperative value suggested adequate removal of all hyperfunctioning parathyroid tissue. The operative time ranged from 25 to 35 minutes.

Postoperative serum calcium levels were monitored in all patients to detect any hypocalcaemia occurring as a result of hungry bone syndrome.

RESULTS

Fourteen patients had an adenoma in the neck while in 1 it was in the superior mediastinum and was missed by an ultrasound of the neck. A SPECT with CT superimposition was done to localize this adenoma in relation to the subclavian vessels.

Intraoperative guidance with a hand-held gamma probe and adequate removal of hyperfunctioning parathyroid tissue was possible in all the patients. QPTH levels reduced to <50% of preoperative values in all the patients. There were no postoperative complications. Postoperative transient hypocalcaemia was seen in 3 patients and was treated with parenteral calcium supplementation.

The patients were followed up with serum calcium levels at monthly intervals after excision of the parathyroid adenoma. The follow up ranged from 2 to 29 months; 11 patients had a follow up of >6 months. All the patients were normocalcaemic.

DISCUSSION

Minimally invasive parathyroid surgery (MIP) is now the standard of care for the treatment of primary hyperparathyroidism.^{5,7} Two main factors have contributed to its development: (i) improvement in preoperative localization with the use of ^{99m}Tc-Sestamibi imaging and (ii) the availability of intraoperative QPTH assay that obviates the need for doing frozen sections on macroscopically normal-looking parathyroid glands.^{8,9}

Preoperative localization of the parathyroid adenoma is crucial for radioguided surgery.^{10,11} Localization of parathyroid adenoma and their precise excision has always remained a challenge because of inconsistent location of the normal parathyroid glands and the possibility of supernumerary ectopic glands. ^{99m}Tc-Sestamibi imaging and high resolution ultrasound of the neck provide the most accurate localization for solitary parathyroid adenomas. Localization of ^{99m}Tc-Sestamibi in parathyroid tissue is a function of the metabolic activity. When injected intravenously ^{99m}Tc-Sestamibi accumulates in both the thyroid gland as well as parathyroid adenoma. However, it is

washed out from the thyroid gland much faster and is retained by the parathyroid adenoma for longer. Hence, a scan done 2 hours after injection of the tracer delineates the adenoma precisely. We used double tracer, dual phase, ^{99m}Tc-Sestamibi scintigraphy for preoperative localization, which revealed the adenoma as a hot spot in 14 patients.

Two principal protocols have been proposed for radioguided surgery. Norman and Cheda described their single-day (imaging and surgery) approach.¹² This protocol is attractive as imaging and surgery are performed on the same day with a single full diagnostic dose of ^{99m}Tc-Sestamibi. However, it has disadvantages. The choice of radioguided surgery or bilateral neck exploration is based on scintigraphic findings and has to be made ‘on the spot’. Also, the time gap between tracer injection and beginning of surgery may be over 2–3 hours in which case wash out of ^{99m}Tc-Sestamibi may occur even from the adenoma.

We used a double tracer ^{99m}Tc-pertechnetate/^{99m}Tc-Sestamibi subtraction scan combined with an ultrasound of the neck to select patients suitable for radioguided surgery. On the day of surgery, we used a low dose of ^{99m}Tc-Sestamibi (8–10 mCi) about 2 hours before surgery. This has the advantage of negligible radiation exposure to operation theatre personnel.

In our experience, the availability of frozen section and intraoperative QPTH assay was crucial for confirmation of the

TABLE I. Primary diagnosis and laboratory parameters of patients

Age/ Sex	Diagnosis	Serum calcium (mg/dl)*	Serum parathyroid hormone (pg/ml)†	Quick parathyroid hormone (pg/ml)‡
25/F	Renal calculi	11.9	280	39.1
32/M	Renal failure	13.1	1404	192
52/F	Renal calculi	12.1	193	26
57/F	Renal failure	15.0	760	130
48/M	Renal failure, pancreatitis, psychosis	18.2	2776	800
53/F	Asymptomatic, detected on routine health check-up	12.1	461	25
24/F	Multiple fractures	13.7	796	37.8
35/M	Psychosis, renal calculi	13.5	945	122
45/F	Renal failure	13.8	645	98
40/M	Pancreatitis	13.8	763	20
50/F	Multiple renal calculi	14.0	382	31.4
28/F	Ureteric calculi, psychosis	13.0	238	58.3
48/F	Multiple fractures	14.8	1146	428
38/F	Renal and ureteric calculi	13.4	638	32
42/M	Asymptomatic, detected during screening as donor for renal transplant	12.8	456	32

All tests were done at an NABL accredited laboratory
 * normal total serum calcium=8.6–10.2 mg/dl (OCPC, Dade Dimension RxL & Cobas Integra 800) † normal serum parathyroid hormone=10–65 pg/ml
 ‡ assay based on electrochemiluminescence technology (ELECSYS Roche 2010)



FIG 1. Preoperative localization with gamma probe



FIG 2. Surgical excision of adenoma



FIG 3. Ex vivo radioactivity counting



FIG 4. Excised adenomas. The largest one measured 4.5 cm

diagnosis and adequate removal of all hyperfunctioning parathyroid tissue. *Ex vivo* radioactivity counting on the adenoma and in the tumour cavity further ensured adequate removal.

Parathormone has a half-life of 1–5 minutes.¹³ Hence, a blood level estimation (QPTH) done 15 minutes after removal of the adenoma usually shows a fall in PTH value <50% of the previous value. The major advantage is that it can be performed under local anaesthesia as a day-care procedure,¹⁴ and is safe and effective for patients who have associated co-morbid conditions such as renal failure.

CONCLUSION

In contrast to bilateral neck exploration, which is a major procedure, radioguided surgery is a minimally invasive procedure that provides more accurate localization, precise excision with the help of a gamma probe, is less time-consuming, practically free of complications and can be done under local anaesthesia.

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