

Case report

Supernumerary ectopic parathyroid glands. Persistent hyperparathyroidism due to mediastinal parathyroid adenoma localized by preoperative single photon emission computed tomography and intraoperative gamma probe application

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ABSTRACT

Ectopic and/or supernumerary parathyroid glands are a major cause of persistent and recurrent Hyperparathyroidism (HPT). For this reason, it is widely accepted that preoperative localization should be performed to improve the surgical results in patients with persistent or recurrent HPT. Primary HPT (pHPT) was diagnosed incidentally in a 50-year old female patient during a preoperative examination for hernia. No pathologic parathyroid gland was detected in the preoperative Tc-99m Methoxybutylisonitrile (MIBI) scintigraphy and Ultrasonography (US). Cervical exploration was performed bilaterally. Four parathyroid glands were located adjacent to the thyroid gland. A fifth was detected in front of the cricoid cartilage. All five of them were of normal histology. Postoperatively, hypercalcemia persisted. Single Photon Emission Computed Tomography (SPECT) was performed before the second operation and radioguide surgery was carried out by median sternotomy. SPECT showed a parathyroid adenoma in the middle of the anterior mediastinum which was excised (size 1x0.5x0.5 cm) using a gamma probe. In conclusion, SPECT and intraoperative gamma probe application may help to detect the parathyroid adenomas, especially if they are small in size and buried in the adipose tissue. Such localization shortens the duration of the operation and reduces the possibility of complications.

Key words: Intraoperative gamma probe, Mediastinal parathyroid, Persistent hyperparathyroidism, SPECT, Supernumerary parathyroid

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INTRODUCTION

More than 95% of patients with primary Hyperparathyroidism (pHPT) and hypercalcemia can be cured surgically at the first operation carried out by appropriately trained surgeons.¹ Ectopic and/or supernumerary parathyroid glands are a major cause of persistent and recurrent HPT and can occur from the angle of the mandible to the mediastinum.² Four in ten patients whose primary surgery failed may undergo two or more re-explorations when specific preoperative localization procedures are not utilized.³ Most parathyroid adenomas are small, 80% of them weighing less than 1gr. Moreover, 70% of surgically missed adenomas are ultimately found in ectopic sites. These two factors increase the surgical difficulty when accurate preoperative localization is not available.³ Although mediastinal parathyroid glands in pHPT have been as high as 20%, only about 2% cannot be excised through a cervical incision.⁴ However, without the use of preoperative localization studies, 36% of patients undergoing sternotomy do not have the desired results.⁵ Therefore, it is widely accepted that preoperative localization should be performed to improve the surgical results in patients with persistent or recurrent pHPT.¹

In the present report, we describe the preoperative localization studies with Single Photon Emission Computed Tomography (SPECT) before the second operation and the perioperative usage of gamma probe in a case of persistent PHT caused by adenoma in an ectopic mediastinal parathyroid.

Patient description

A 50-year old female patient was hospitalized for hernia repair. Medical history revealed well-controlled hypertension for a period of six months. Routine preoperative biochemical parameters were normal except for serum calcium (Ca) which was 3.15mmol/L (normal range: 2.02-2.6). Serum Phosphorus (P) was 0.87mmol/L (normal range: 2.7-4.5), in the lower normal range. The Parathyroid Hormone (PTH) was 187 ng/L (normal range: 9 to 80) and urinary calcium was 75mmol/24hours (normal range: 25 to 75). Ultrasonography (US) revealed hypoechogenic nodules in both thyroid lobes. The preoperative dual phase planer scintigraphy with 10 mCi (370 MBq) Tc-99m MIBI (Methoxybutylisonitrile) did not disclose any

abnormal activity on the neck and thorax.

Following bilateral cervical exploration, four parathyroid glands of normal size were detected in their normal locations. Samples for frozen section examination were taken. Frozen section confirmed that all the samples represented normal parathyroid tissue. Other possible sites for ectopic parathyroid glands were inspected and cervical thymectomy was performed. No macroscopic tissue resembling parathyroid was discovered in the inspected area or in the thymectomy specimen. Due to the presence of palpable, hard thyroid nodules and the probability of intrathyroidal parathyroids, thyroidectomy was performed. During the mobilization of the isthmus, a yellow brown, oval nodule (5x3x2 mm in diameter) was found embedded in the soft tissue above the thyroid isthmus, in front of the cricoid cartilage in the midline. Frozen section examination revealed that it was also parathyroid tissue. Pathological examination showed that the four parathyroid samples from the normal loci and the fifth gland which was excised from an ectopic localization had normal histologic features.

At the pathologic examination of the thyroid, nodular goiter was detected. No intrathyroidal and intrathymic parathyroid tissue was found.

However, postoperative hypercalcemia persisted. No pathologic lesion was detected in the cervical and thoracic MRI. A SPECT, however, revealed a mass consistent with parathyroid adenoma 3-4 cm behind the anterior wall of the thorax, 3 cm to the right of the midline in the anterior mediastinum in the early and late images (Figure 1).

Median sternotomy was performed. Radioactivity was calculated via hand-held gamma probe (Neoprobe® 1500, Neoprobe Corporation, Ohio, USA) at the neck and the mediastinum. At the neck, approximately 80 counts/sec value was calculated, this being equal to the background activity. There were multiple oval or round lesions embedded in the fat tissue in the inferior part of the thymus, in the middle of the anterior mediastinum. One of the above-mentioned lesions, measuring 1x0.5x0.5 cm, produced a count rate of 350 counts/sec. This lesion was dissected and totally excised: 300 counts/sec radioactivity was detected ex vivo at this resected lesion. After the

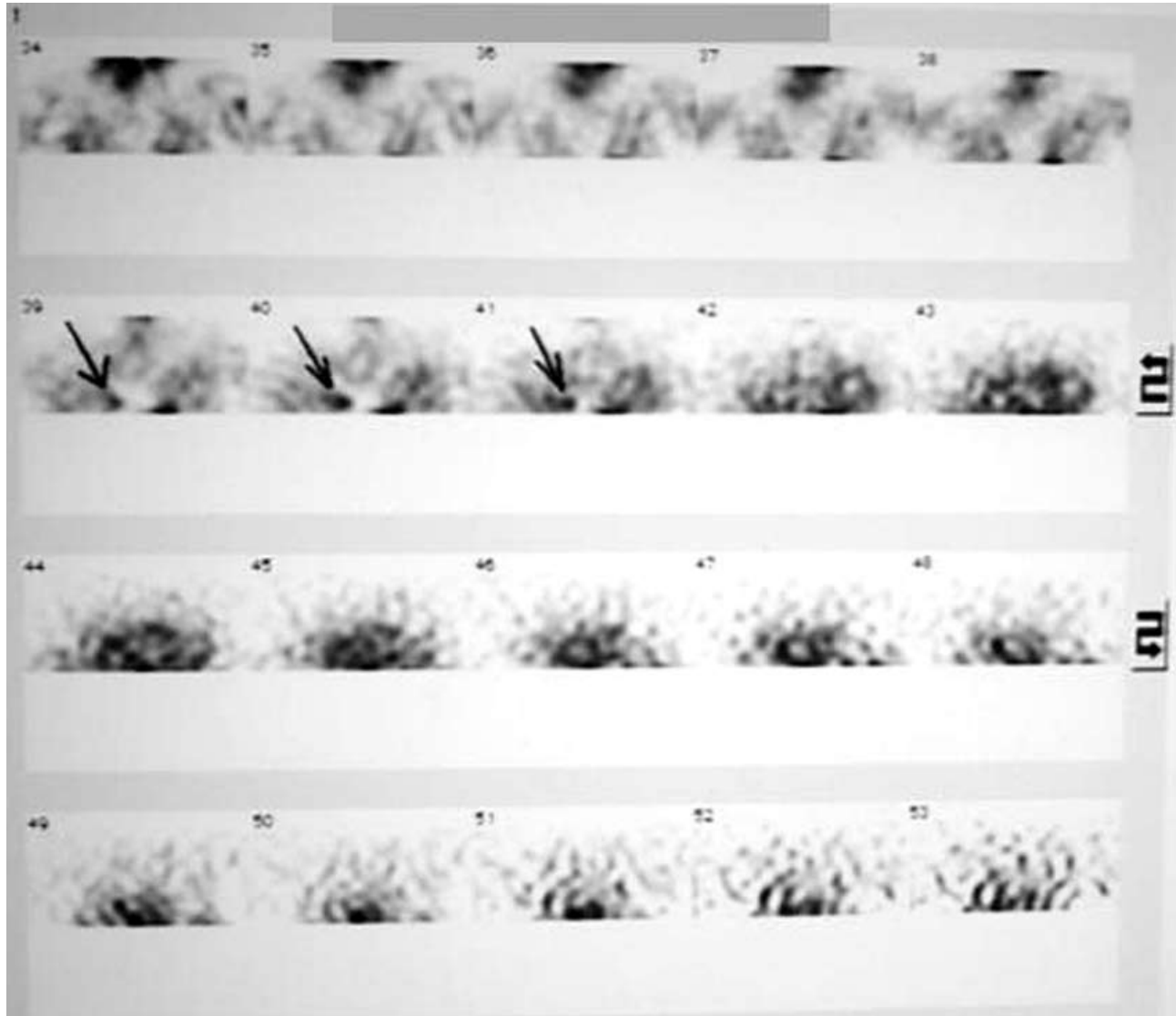


Figure 1. Coronal sections of Single Photon Emission Computed Tomography (SPECT) scenes of the mediastinal adenoma located 3-4 cm behind the anterior wall of the thorax, 3cm to the right of the midline in the anterior mediastinum, in the early and late images.

resection, 90 counts/sec activity was measured at the resected area, this approximating the background activity value. At the mediastinum, apart from the activity of the heart, no further activity was detected over the background activity.

Frozen section confirmed that the excised mass was parathyroid tissue. Pathology showed that the parathyroid lesion appeared as an adenoma. We thus established that the pHPT was caused by a mediastinal parathyroid adenoma originating from the sixth parathyroid gland.

In the early postoperative period, serum Ca, P and PTH levels normalized and remained normal for the subsequent two years of follow-up.

DISCUSSION

The presence of a supernumerary parathyroid gland in the autopsy series is 5%, and the presence of more than 5 glands is 1.25%. Normally, there are four parathyroid glands. In 26% of patients with HPT the inferior glands are located at the inferior part of the thyroid gland in intimate association with the

thyrothymic ligament. The inferior glands, located in the thymus and further down in the mediastinum are seen in 2% and in only 0.2 of patients are encountered below the thymus in the anterior mediastinum. In approximately two thirds of the cases, the supernumerary gland is found below the thyroid in association with the thyrothymic ligament or the thymus, while one third is found in the vicinity of the thyroid.⁶

Although estimates of mediastinal parathyroid glands in pHPT have been as high as 20%, only about 2% cannot be extracted through a cervical incision.⁴ In the pHPT series, the cases related to the supernumerary parathyroid adenoma are rare, reported as about 0.7%. About 60% of the supernumerary parathyroid adenomas are located in the mediastinum, the majority being in the thymus, and can be excised by cervical incision, while 18% require a mediastinal approach.^{7,8}

However, the adenoma in our patient had no relation to the thymus; it was located in the middle of the anterior mediastinum and originated from the sixth supernumerary parathyroid gland. Furthermore, the fifth gland with the normal histology above the thyroid isthmus was a rare ectopic location.

Preoperative localization studies can reduce complication rates and shorten operating time by directing the surgeon to the site or the sites of abnormal parathyroid glands.¹

Currently used non-invasive diagnostic techniques include Tc-99m MIBI scanning with or without SPECT, US, CT imaging and MRI.⁹ During the last decade, localization studies before the initial operation have been used widely and minimally invasive parathyroidectomy procedures are commonly applied. Many centers agree on the value of performing planer Tc-99m MIBI scintigraphy alone or combined with high-resolution cervical US in the preoperative work-up of patients with HPT before initial surgery.⁹

Currently, the most reliable and practical procedure is Tc-99m MIBI scanning.^{10,11} The routine use of SPECT before initial surgery is controversial, although there is general agreement on its usefulness in locating an enlarged parathyroid gland thought to be located in ectopic sites. Planer Tc-99m MIBI scan sensitivity is 78% in pHPT, whereas that of

SPECT normally approaches 96%. SPECT is superior to planer imaging mainly in patients with ectopic adenomas or with multinodular goiters. Gland size does not significantly affect the detection ability of SPECT.¹² It is appreciably more sensitive in detecting small adenomas, namely less than 1gr. Planer Tc-99m MIBI scan sensitivity for small adenomas is 72%. The sensitivity is increased to 96% using SPECT.¹³ Furthermore, SPECT has the same sensitivity in either reoperations or primary operation.¹⁴

On reviewing published series regarding the use of preoperative imaging for patients with persistent or recurrent pHPT, we found the following results. The sensitivity for US ranges from 45%-57% for all locations and 12%-18% for the mediastinum.^{1,10,15,16} For CT the sensitivity ranges from 42%-68% for all locations, while it was 57% for the mediastinum.^{1,10,15} The MRI sensitivity was 77%-82% for all locations and 88% for the mediastinum.^{1,17} For planer Tc-99m MIBI scan the sensitivity was 77%-85% for all locations and 58%-67% for the mediastinum.^{1,10,16,17} The combination of the planer Tc-99m MIBI scan and MRI reaches a sensitivity of 92%-94%, whereas combining either of these tests with US did not improve the sensitivity of either test alone.^{17,18} In all ectopic parathyroid tumors, the specificity of planer Tc-99m MIBI scan was 88%, of MRI 88% and of CT 88%.¹⁹

CT or MRI techniques are commonly used as confirmatory tests in association with the Tc-99m MIBI scan. Furthermore, CT and MRI can be useful before reoperation to evaluate possible anatomic distortions resulting from previous surgery.¹⁰ SPECT is the most accurate localizing study for persistent and recurrent pHPT.¹⁴ Interest has recently increased concerning the potential utility of an innovative imaging technique based on the combination of functional SPECT and anatomic CT or MRI.²⁰⁻²² CT-SPECT or MRI-SPECT image fusion appear to be superior to SPECT in preoperative imaging and can be performed on existing SPECT and CT or MRI units.²⁰⁻²²

In our case, we did not find a pathologic parathyroid gland at the planer scintigraphy and at the MRI. The adenoma, measuring 1X0,5X0,5 cm, with a diameter greater than 1 cm, was localized by SPECT in the middle of the anterior mediastinum at the right side of the midline at both the early and

the late phase scans.

Norman et al²³ reported treating pHPT with minimally invasive radioguided parathyroidectomy using sestamibi scanning and an intraoperative gamma probe for the first time in 1997. Currently, more and more surgeons are employing the gamma probe to guide parathyroid exploration in the neck.²⁴ Minimally invasive radioguided parathyroidectomy using the gamma probe is associated with a high success rate in patients with positive sestamibi scans requiring cervical re-exploration.²⁵ Determination of intraoperative PTH may confirm the removal of the hyperfunctioning parathyroid tissue, thus reducing the operative time.²⁶

The most challenging cases requiring parathyroid operation remain those with hyperfunctioning parathyroids that require mediastinal exploration. Gamma probe guidance is rarely used in mediastinal parathyroid explorations.^{27,28} Ott MC et al²⁷ have used gamma probe with video-assisted thoracoscopic surgery in one case. In another study, adenomas have been successfully detected with gamma probe in four cases.²⁸ We performed sternotomy rather than thoracoscopy or mediastinoscopy because of our lack of experience in these techniques. It may be visually difficult to detect smaller parathyroid adenomas in the mediastinal tissue and distinguish them from the normal tissue. Intraoperative use of gamma probe helped us to detect the parathyroid adenoma and distinguish it from the multiple nodular structure located in the fat tissue.

When the four glands are detected in their normal position and are of normal histology, the cause of pHPT is most likely a supernumerary parathyroid gland located in the mediastinum. SPECT can disclose the topography of the small mediastinal parathyroid adenomas. Mediastinal intraoperative gamma probe application can make detection easier, especially when small parathyroid adenomas are embedded in fat tissue. This approach enabled us to dissect the lesion in a limited area and thus lessen the operation period and reduce the possibility of complications.

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