

CIRUGÍA ESPAÑOLA

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Original article

Oesophageal endoscopic ultrasound in the accurate location of primary hyperparathyroidism (HPT)[☆]

Aitor de la Quintana Basarrate,^{a,*} Francisco Javier Díaz Aguirregoitia,^a
 Jesús Gil Sánchez,^a Ángel Barturen Barroso,^b Sonia Gaztambide Sáez,^c
 Miguel Echenique Elizondo,^{d,1} and Luis Perdigo Bilbao^e

^aServicio de Cirugía General B, Sección de Cirugía Endocrina, Hospital de Cruces, Barakaldo, Bizkaia, Spain

^bServicio de Digestivo, Hospital de Cruces, Barakaldo, Bizkaia, Spain

^cServicio de Endocrinología, Hospital de Cruces, Barakaldo, Bizkaia, Spain

^dCatedrático de Cirugía, Universidad del País Vasco, Barakaldo, Bizkaia, Spain

^eServicio de Cirugía General B, Hospital de Cruces, Barakaldo, Bizkaia, Spain

ARTICLE INFORMATION

Article history:

Received October 2, 2008

Accepted December 1, 2008

Online May 19, 2009

Keywords:

Oesophageal endoscopic ultrasound

Primary hyperparathyroidism

Persistent

A B S T R A C T

Aim: Our aim was to estimate the usefulness of oesophageal endoscopic ultrasound in the accurate location of recurrent or persistent primary hyperparathyroidism (HPT).

Material and method: A total of 352 patients with primary hyperparathyroidism were operated on over the last 7 years. A preoperative parathyroid ⁹⁹Tc-sestamibi gammagraphy and an intraoperative PTH determination were performed routinely. Only 5 patients (1.4%) had localization problems: 3 with persistent HPT after parathyroid extirpation, 1 recurrent HPT and 1 HPT after a right hemithyroidectomy. An oesophageal endoscopic ultrasound was carried out before any new exploratory neck surgery in order to find the definitive location.

Results: The endoscopic ultrasound showed a clear image of adenoma with an accurate location in 4 patients. No tumour was present in 1 patient. All 5 patients were operated on. The exact location was confirmed in the 4 patients with positive endoscopic ultrasound images. The fifth surgical exploration revealed a parathyreosis. All 5 patients had a favourable post-operative period, with no nerve lesions or morbidity associated with the endoscopic ultrasound.

Conclusions: Oesophageal endoscopic ultrasound is a very useful diagnostic tool in HPT patients with location problems, particularly in cases having anatomical changes due to previous surgery. It is a procedure that helps the surgeon to make a more selective and efficient exploration of parathyroid glands.

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[☆]Based on communication presented in the National Meeting organized by the AEC in San Sebastian in November 2007.

*Author for correspondence.

E-mail address: Aitor.quintanadelabasarrate@osakidetza.net (A. de la Quintana Basarrate).

¹Prof Miguel Echenique Elizondo died before the publication of this article.

Palabras clave:

Ecoendoscopia trasesofágica

Hiperparatiroidismo primario

Persistencia

Valor de la ecoendoscopia trasesofágica en el diagnóstico de localización en el hiperparatiroidismo primario**R E S U M E N**

Objetivos: Considerar la utilidad de la ecoendoscopia trasesofágica en la localización del hiperparatiroidismo primario recidivado o persistente.

Material y método: Durante 7 años consecutivos, hemos intervenido a 352 pacientes con hiperparatiroidismo primario (HPP). Sistemáticamente se realiza gammagrafía paratiroides con ^{99}Tc -sestamibi preoperatorio y determinación intraoperatoria de paratirina. Sólo 5 (1,4%) pacientes han presentado problemas de localización: 3 por persistencia tras cirugía paratiroides, 1 por recidiva y 1 por HPP con antecedente de hemitiroidectomía derecha. Antes de indicar una cervicotomía exploradora, se decide la realización de una ecoendoscopia trasesofágica para intentar una localización definitiva.

Resultados: La ecoendoscopia detecta una imagen clara de adenoma con localización precisa en 4 pacientes. Sólo en 1 paciente no se visualiza tumoración. Los 5 pacientes fueron intervenidos. Se confirmó la exactitud del diagnóstico en los 4 pacientes con visualización positiva. La exploración quirúrgica del quinto paciente resultó ser una paratiroidectomía. Los 5 pacientes tuvieron un postoperatorio favorable, sin lesiones recurrenciales ni morbilidad asociada a la ecoendoscopia.

Conclusiones: La ecoendoscopia trasesofágica resulta muy útil en los hiperparatiroidismo que presenta dificultades para localizar la glándula patológica, especialmente en casos con alteración anatómica por cirugía previa. Así, ayuda a que el cirujano pueda explorar la zona sospechosa de forma más selectiva y más eficiente.

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Introduction

In approximately 90% of patients with primary hyperparathyroidism (HPT), the etiological cause is a single adenoma.^{1,2} Classic treatment has been bilateral cervical examination with identification of the four parathyroids and excision of the pathological glands based on their size.^{2,3} Treatment success varies between 70% and 95% depending on the surgeon's experience.^{4,5}

In the last 2 decades, significant changes have been made due to advances in imaging techniques, such as gammagraphy with ^{99}Tc -sestamibi and fast determination of parathyrin (PTH) which have led to the establishment of selective parathyroidectomy with equal results in comparison to bilateral examination.^{1,2,6}

Despite these advances, there are still persistent or recurring cases which require new intervention. Implicated in reintervention is higher morbidity, even among the most experienced surgeons.^{3,5,7} Also, the intervention has less success.^{4,5,8,9}

Different techniques have been used to localize the pathological gland and in this way minimize morbidity and increase the possibilities for success, such as the fusion of parathyroid gammagraphy images with ^{99}Tc -sestamibi and computerized tomography (CT),¹⁰ magnetic resonance (MR), radioguided surgery,^{1,6} or selective drawing of venous blood samples.^{4,7}

The objective of this study is to assess the usefulness of transoesophageal endoscopic ultrasound in precisely locating the pathological gland in cases with previous failure or particularly difficult situations.

Material and method

From January 2000 to April 2007, 352 HPT patients received operation. By protocol, a preoperative parathyroid gammagraphy with ^{99}Tc -sestamibi and intraoperative PTH determination were carried out. Of these, 9 persisted with hypercalcemia and 1 relapsed (Figure 1).

We define persistence as hypercalcemia with inappropriately high PTH within the first 6 months of postoperative. We define recurrence as new detection of hypercalcemia after at least 6 months of documented normocalcemia.

Of the 9 persistent cases, the CT detected an ectopic gland in the mediastinum in 2 patients, and before surgery a parathyroid gammagraphy with ^{99}Tc -sestamibi was carried out, amplifying the area, therefore confirming the suspicion. Both operations were successful. In 3 other patients with persistence, another parathyroid gammagraphy confirmed the clinical suspicion of residual disease and required reintervention, which was successful; a definitive diagnosis of hyperplasia was recorded in 2 patients and in 1 patient double adenoma. Although one patient had mild hypercalcemia, the subject also suffered from an advanced neoplastic disease and was not included in the study.

In the 3 other patients with HPT persistence, the parathyroid gammagraphy with ^{99}Tc -sestamibi was once again positive in the same localization as before with the first unsuccessful surgery. In 2 of these patients, preoperative selective blood samples were taken from both jugulars, which in the parathyroid gammagraphy with ^{99}Tc -sestamibi confirmed

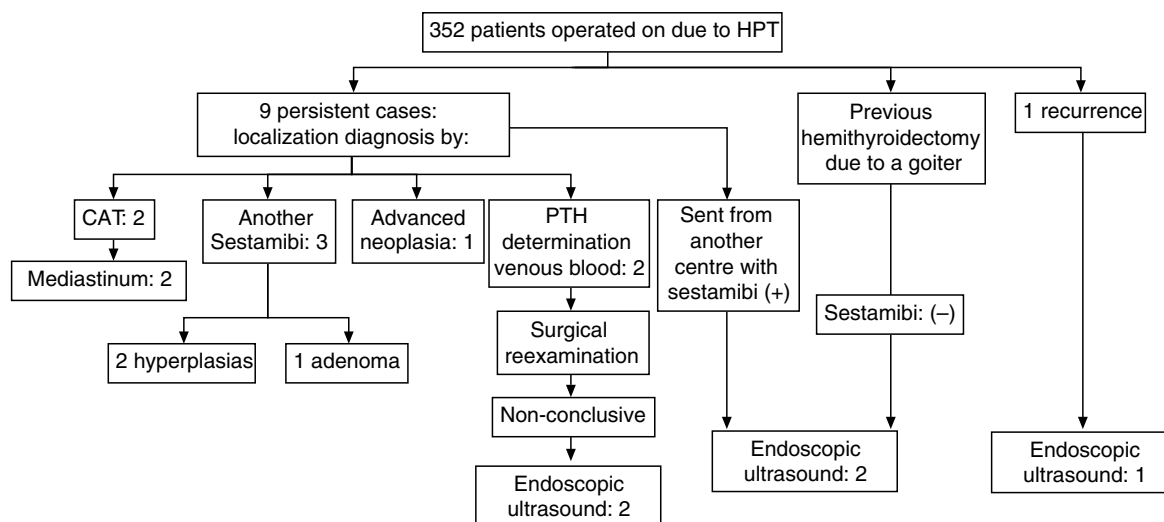


Figure 1 – Flow chart.

the localization suspected, but the surgical reexamination was once again negative.

For the relapsed patient, the parathyroid gammagraphy with ^{99}Tc -sestamibi was negative. There was also a patient with a previous hemithyroidectomy due to a goiter and a current diagnosis of HPT with a negative parathyroid gammagraphy with ^{99}Tc -sestamibi. As a result, there were 5 patients with difficulty localizing the pathological gland.

Endoscopic ultrasounds were carried out by an expert in our hospital with patients under anaesthesia; on four occasions with a 7.5 MHz Pentax® sectorial endoscopic ultrasound and on the fifth with a 10 MHz Olympus® radial echoendoscope. All patients gave their written consent for the test.

Results

Case 1

The patient was operated on 15 years earlier due to a right adenoma, and the patient was reoperated on 4 years later due to a left adenoma and also underwent a right hemithyroidectomy due to a goiter. The parathyroid gammagraphy with ^{99}Tc -sestamibi was negative and the endoscopic ultrasound did not detect any image which indicated a parathyroid condition. In intervention, a right parathyreosis was detected, with eleven foci of parathyroid tissue, confirmed by the anatomopathologist.

Case 2

The patient presented with persistence which required 2 unsuccessful reinterventions, with a clearly positive parathyroid gammagraphy with ^{99}Tc -sestamibi at the height of the thyroid isthmus, which was excised in the second reintervention; the CT was negative and drawing jugular

blood samples did not provide satisfactory results. The endoscopic ultrasound detected a compatible lesion in the retrotracheal and preoesophageal area, near the superior pole of the right thyroid lobe, which was confirmed during the surgical intervention, which focused in the area described by the echoendoscopist. The adenoma weighed 360 mg. The patient suffers from secondary hypoparathyroidism after repeated surgeries, and this is well-controlled by oral calcium supplements and vitamin D_3 .

Case 3

Patient with a parathyroid gammagraphy with ^{99}Tc -sestamibi compatible with a right adenoma, but the patient also had a grade II goiter on the same side. No adenoma was detected in the first surgery, but the other 3 parathyroids were found, and a right hemithyroidectomy was carried out because of a possible intrathyroid adenoma, but the surgery was not successful. The CT was negative, and therefore an endoscopic ultrasound was carried out, which described a lesion compatible with adenoma in the retrooesophageal position, posterior to the carotid artery and resting on the vertebral body. Surgical findings confirmed an adenoma of 580 mg. The patient is currently normocalcemic.

Case 4

The patient underwent a right hemithyroidectomy due to a goiter, 7 years earlier; the parathyroid gammagraphy with ^{99}Tc -sestamibi was negative and the endoscopic ultrasound detected a compatible lesion in right retrooesophageal position (Figure 2) and another smaller one in the superior left position. Surgery confirmed a right retrooesophageal adenoma of 410 mg, with the upper left image corresponding to a parathyroid with an apparently larger than normal volume but without the shape of an adenoma. Guided by intraoperative PTH, we excised a single gland and the patient is still normocalcemic 2 years later.

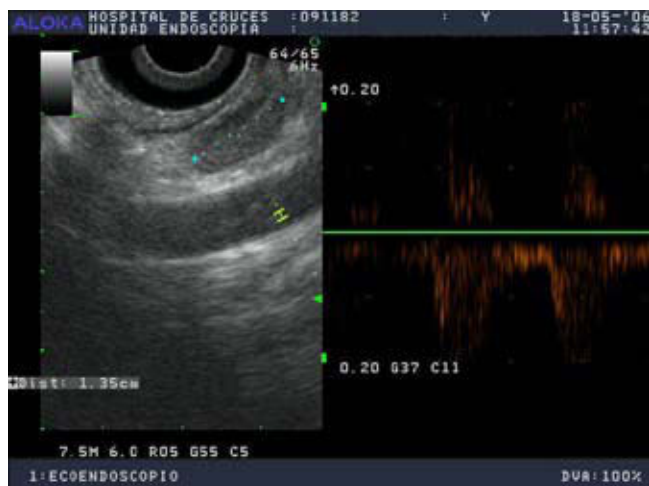


Figure 2 – Sectorial endoscopic ultrasound; hypoechoic and well-defined nodule of 1.35 cm, localized between the oesophagus and carotid. A well-defined hypoechoic halo is observed.



Figure 3 – Radial endoscopic ultrasound; before the vertebral body and behind the oesophagus, a well-defined hypoechoic image is observed at 1.36x0.62 cm. The Doppler shows arterioles inside.

Case 5

Patient with a positive parathyroid gammagraphy with ^{99}Tc -sestamibi in the right inferior area, operated on in another centre and sent with a CT showing a compatible image in the superior mediastinum, resting on the spinal column. The endoscopic ultrasound confirmed a compatible retrooesophageal lesion in the superior mediastinum, at 19 cm from the dental arch, resting on the vertebral body (Figure 3). During the intervention, an adenoma of 800 mg was found and excised from the described location.

No patient has presented with morbidity related to imaging techniques. No recurring lesion has occurred, but a permanent hypoparathyroidism has occurred.

Discussion

Technology development in the last 20 years which has facilitated localization of hyperfunctioning parathyroid glands, together with the capacity for intraoperatively measuring PTH at a reasonable cost, has allowed for selective parathyroidectomy practice to become generalized, maintaining functional results similar to the classical examination technique of bilateral cervical examination, but aesthetic results, duration of intervention, postoperative hospitalization and post-surgical hypocalcaemia have improved.^{1-3,6} However, there continues to be a similar rate of persistence and recurrence, susceptible factors for reintervention.

Although standardization of HPT surgery has allowed for morbidity to decrease, reintervention is a challenge for the surgeon due to scarring and distortion of tissue layers, which therefore increase the risk of a recurrent nerve lesion, permanent hypocalcaemia and persistence due to non-localization of the pathological gland.^{4,5,7}

It is in these situations where localization tests acquire a special interest, with the aim of focusing surgical efforts in the suspected area, limiting the examination area in surgery, and therefore, minimizing risks.

The parathyroid gammagraphy with ^{99}Tc -sestamibi, CT, transcervical ultrasound, MR and the fusion of parathyroid gammagraphy images with ^{99}Tc -sestamibi-TC are non-invasive methods which can provide us with information, especially in patients with ectopic pathological glands, but its sensitivity varies greatly among centres depending on technical equipment, the operator, the technique used, and the size and location of the adenoma.⁶ Furthermore, its benefit in previously operated patients is less.

The coincidence of 5 patients with previous cervical interventions and failed reinterventions of 2 of the cases caused us to assess and revise procedures. At this time we considered the possible usefulness of endoscopic ultrasound, which was already successfully applied in other areas. The study's hypothesis was that unfound adenomas could be localized by other less invasive techniques, and/or the suspected image could be verified by other techniques after surgery failure. Then, the referenced anatomical structures could be more precisely related to the lesion, which would allow for a selective surgery.

From review of the literature, it is indicated that endoscopic ultrasound may be a useful localization method in persistent and recurring hyperparathyroidism cases.^{11,12} The test showed a sensitivity of 71%, similar to the parathyroid gammagraphy with ^{99}Tc -sestamibi or the MR.¹² With endoscopic ultrasound, the adenomas closest to the oesophagus are most easily detected,¹¹ as compared to the most anterior ones which are the most difficult to detect using this technique, but at the same time, adenomas in the anterior position are easiest for the surgeon to find.

The principal invasive localization test is selective drawing of venous blood samples, which by experts, has correct adenoma localization in 75%–80% and has false positives in 6%–12%.^{4,7} In cases where other localization tests were

positive and surgery was ineffective, little information was provided.

There were no adverse effects in any of the 5 patients who underwent endoscopic ultrasound. The echoendoscopist correctly detected the pathological gland in 4 patients, with documentation of anatomical relationships and exact location. This enables selective examination, avoids examination of other areas previously operated on and minimizes risks. A patient who received their fourth operation remained with permanent hyperparathyroidism.

In the only patient without localization detected and who received operation on 2 previous occasions, in surgery we confirmed an extended parathyreosis on the right side, and therefore this was impossible to detect by this test.

In all patients with disease persistence, the gland was localized in the posterior area, paraoesophageal region, and therefore was highly accessible to this imaging test. We believe that the majority of the unfound adenomas may be in less-accessible areas for the surgeon, as occurring in our study.

Conclusions

Once the non-invasive imaging tests are insufficient for achieving a conclusive intervention, we believe that endoscopic ultrasound is recommendable for the goal of documenting exact localization of the adenoma and minimizing surgical risks.

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