CLINICAL STUDY

Video-assisted thoracoscopic surgery as a first-line treatment for mediastinal parathyroid adenomas: strategic value of imaging

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Abstract

Objective: To present first-line thoracic surgery made possible by localization studies in three patients with ectopic parathyroid adenomas.

Design and methods: Three patients with ectopic parathyroid tissue in the mediastinum were examined by ultrasound, technetium-99m sestamibi scintigraphy, computed tomography (CT), and venous catheterization with measurement of parathyroid hormone. Without previous cervical exploration, video-assisted thoracic surgery (VATS) was used in all cases to avoid the need for thoracic open surgical procedures.

Results and conclusions: The mediastinal parathyroid glands were all detected at scintigraphy, and CT and venous catheterization were helpful in anatomic and functioning characterization. All pathologic glands were successfully resected, with only one minor complication. VATS can safely remove a deep mediastinal parathyroid adenoma and avoid more aggressive open approaches. In an experienced referral center, systematic and sophisticated imaging studies may accurately identify and localize rare ectopic parathyroid adenomas, and avoid cervical surgery.

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Introduction

Primary hyperparathyroidism has become a frequent disease, most often detected on routine calcium screening in asymptomatic subjects (1–5). Most patients have a sporadic and solitary cervical adenoma. The operative approach was established by the 1990 consensus panel (3), and approved by a recent workshop (5): a bilateral neck exploration is performed under general anesthesia, with a thorough search for all parathyroid tissue (6–8). The use of non-invasive localization procedures is agreed after cervical surgery has failed, because the presence of an ectopic gland is more likely and because it seems to reduce the complication rate of subsequent surgery (3, 5, 9–12).

This classical strategy has recently been modified by many surgeons by the use of an accurate imaging procedure. The convergent localization of a single cervical parathyroid adenoma with both ultrasonography and technetium-99m sestamibi (Tc99m-sestamibi) scintigraphy allows minimally invasive parathyroidectomy by unilateral neck exploration under local anesthesia, endoscopic parathyroidectomy or radio-guided surgery, with a success rate of 90–95% and less than 5% morbidity (13–24). This approach might facilitate

the decision to operate on asymptomatic patients as often occurs in perimenopausal women, vertebral osteopenia, and vitamin D deficiency, as well as in subjects who are elderly and have poor health status (4, 8, 13–15, 25–30).

Another major interest of systematic preoperative imaging is the discovery of ectopic adenomas requiring a trans-sternal or transthoracic approach, which are present in 1.25–2% of patients (31–36). In such cases, an optimal strategy would be to perform a first-line thoracoscopic approach.

We report here our experience in three cases of ectopic parathyroid glands successfully resected by video-assisted thoracic surgery (VATS) performed as a first-line treatment.

Methods

Preoperative cervical ultrasound and Tc99m-sestamibi scintigraphy for primary hyperparathyroidism have been performed in all patients in our Department since 1993, always by the same operator (B R). After placing the patient in the supine position with the neck slightly extended, a complete sonographic survey

is begun just above the suprasternal notch and continued superiorly to the upper border of the larynx, with a linear 7.5 MHz transducer operating in black and with imaging and color doppler. A parathyroid adenoma appears as an oval hypoechoic mass, sometimes containing cystic components, it is located adjacent to the thyroid gland, and it is mobile during swallowing. Obviously, deep mediastinal parathyroid lesions are inaccessible by ultrasound.

Double-phase Tc99m-sestamibi (technetium-hexakis, 2-methoxy-isobutyl-isonitrile; Cardiolite) scintigraphy (37–39) was also routinely performed. Neck and mediastinum images were acquired with a low-energy, high-resolution collimator, 5–15 min and 90 min after 550–740 MBq Tc99m-sestamibi were intravenously injected. Images are recorded into a 256 × 256 matrix. A parathyroid adenoma appears as an area of increased activity seen on initial image and persisting on delayed images, in contrast to thyroid tissue in which the tracer is more quickly washed out. In each case of suspected ectopic mediastinal adenoma, antero-posterior planar and frontal, coronal, sagittal single-photon emission computerized tomography (SPECT) images are also performed for better anatomic localization. Images are acquired in a matrix size of 128 × 128, a 3° angle step, and a time of 20 s per frame.

Computed tomography (CT) scan sections were obtained at 5 mm intervals from the level of the angle of the mandible to the aortic arch before and after the intravenous administration of contrast agent. A parathyroid adenoma usually appears as a rounded, well-defined, homogeneous hypodense mass, raised in an intense way after injection at arterial time, but shorter compared to the vessels or the thyroid.

Because thoracic ectopic adenoma was suspected after the above imaging studies, venous catheterization of large veins in the neck and the mediastinum for the determination of parathyroid hormone (PTH) was performed as described previously (11), with a significant gradient when the local PTH level was at least twice the peripheral PTH value.

VATS was performed under general anesthesia using a double-lumen endotracheal tube by a single surgeon (P.B.). The patients were ventilated only via the opposite lung and were kept in a full lateral position. Three trocars were placed from the side of the chest of the adenoma through the third to fifth intercostal space, starting from the medial axillar to the anterior axillar and the medioclavicular line. A standard 10 mm rigid

thoracoscope with a 0° angle was used, normally viewing from the anterior axillar incision.

Intraoperative PTH levels were monitored with a rapid PTH assay, as described previously (14, 15).

Results

Patient no. 1

A primary hyperparathyroidism was diagnosed during a routine laboratory screening in a 36-year-old woman admitted for phlebitis (eventually correlated to a factor II deficit). Table 1 summarizes the biological data. She had silent renal stones. The absence of a familial history and the lack of association with other endocrine diseases such as pancreatic islet-cell, anterior pituitary and adrenal cortex lesions almost eliminated the diagnosis of multiple endocrine neoplasia (MEN)-1. No parathyroid tumor was identified with cervical ultrasound. The Tc99m-sestamibi parathyroid scintigraphy and SPECT demonstrated a focal area of increased uptake involving the right inferior side of the anterior mediastinum, which suggested an ectopic mediastinal parathyroid adenoma (Figs 1 and 2). CT showed a 1 cm mass located in front of the ascending aorta and superior vena cava (Fig. 3). The venous catheterization with measurement of the PTH level revealed a gradient with a step-up value crossing the right brachiocephalic vein and the superior vena cava. The diagnosis of a solitary mediastinal adenoma located in the inferior part of anterior mediastinum was made and VATS was performed. No abnormal tissue could be visualized in the anterior mediastinum during surgery. The surgeon, guided by the preoperative localization, made a large surgical resection of perivisceral fat tissue, including the thymus and mediastinal pleura covering the superior vena cava, aortic arch, and right atrium. A drop (from 146 to 4 ng/l) in PTH levels occurred during the surgery, suggesting the removal of all hyperfunctioning tissue. The final pathology confirmed a 1 cm parathyroid tumor. The patient's serum ionized calcium has been normalized since the surgery at follow-up at 12 months, without any complications.

Patient no. 2

The survey of a 57-year-old woman with a history of breast cancer diagnosed 2 years earlier and considered

Table 1 Patient characteristics before operation.

Patient no.	Total serum calcium (mmol/l) (high normal 2.6)	Ionized serum calcium (mmol/l) (high normal 1.29)	Urine calcium (mmol/24 h)	PTH (ng/l) (high normal 60)
1	2.59	1.51	6.0	158
2	2.61	1.39	8.6	188
3	2.89	1.49	7.0	112

Figure 1 Sestamibi images at (a) 5 min and (b) 90 min demonstrating a mediastinal parathyroid adenoma in patient no. 1.

to be cured showed a primary hyperparathyroidism (Table 1). There was no indication of genetic disease. The cervical ultrasound detected no parathyroid mass. The Tc99m-sestamibi parathyroid scintigraphy demonstrated a focal area of increased uptake involving the right anterior mediastinum that suggested an ectopic parathyroid adenoma. The CT visualized two masses, one anterior mass looking like a hamartochondroma and an ovoid mass of 2 cm in front of the superior vena cava and ascending aorta corresponding to the image seen by scintigraphy and to the increases in the PTH level shown by venous catheterization. Using VATS, dissection of the adipose tissue in the upper anterior mediastinum was carried out and the

PTH level decreased intraoperatively (from 777 to 41 ng/l). No postoperative complication occurred. A hypercellular parathyroid gland was found inside the fat tissue. Since there was no normal parathyroid tissue around, we cannot give a precise diagnosis between adenoma and hyperplasia. Serum ionized calcium has been normalized since surgery at follow-up at 31 months.

Patient no. 3

Primary hyperparathyroidism was diagnosed in an 82-year-old woman followed for wrist pain (Table 1). Her past medical history revealed no endocrine disease

Figure 2 (a) Frontal, (b) coronal, and (c) axial sestamibi SPECT images demonstrating the parathyroid adenoma in the inferior part of the anterior mediastinum in patient no. 1.

Figure 3 CT scan showing a parathyroid adenoma (arrow) in front of the ascending aorta in patient no. 1.

but an atrial fibrillation for years. The cervical ultrasound was negative. The Tc99m-sestamibi scintigraphy revealed two locations of increased uptake: one dubious with regard to the left lobe of the thyroid and one in the upper left mediastinum. CT visualized one mass located near the thyroid which did not take the contrast as much as the rest of the thyroid, suggesting a thyroid adenoma, and a 1 cm node located above the aortic arch. The catheterization confirmed this diagnosis with an increase in the PTH level in the superior vena cava. Using VATS, the surgeon removed the adipose tissue in front of the aorta, which contained a 1 cm adenoma. The patient normalized her ionized calcium level, but developed transient hoarseness presumed to be due to damage to the left recurrent laryngeal nerve, which loops around the aortic arch.

Discussion

The possible sites of ectopic parathyroid tissue are parapharyngeal at the level of the mandible, intrathyroidal, and mediastinal. Most ectopic parathyroid adenomas are found in close approximation to the thymus gland (9, 31, 32, 36, 40–43) and can be excised using a collar incision. Parathyroid adenomas deeper in the chest require a sternotomy or lateral thoracotomy (32, 41, 42, 44–48), angiographic ablation (49, 50), video-assisted mediastinal or thoracoscopic surgery (VAMS/VATS), or even an infrasternal approach in patients with pleural adhesions or pulmonary insufficiency (51, 52). VATS, developed by Landreneau *et al.* (53), is safe, offers the advantages of minimal invasive surgery, and does not interfere with other surgical approaches, with lower risks of re-operation. There are several reports in the literature of successful resections of ectopic parathyroid tissue using VATS, with rare complications (12, 34–36, 43, 48, 54–62).

Preoperative localization tests being seldom used when a standard surgical approach is used, only a few patients have undergone first-line resection of mediastinal adenoma. Less than ten patients have been reported until now (36, 47, 48, 54, 56–59, 61, 62). Cupisti *et al.* (36) recommended VATS as the first procedure only if the adenoma is clearly located in the chest deeper than the brachiocephalic vein. Furthermore, scintigraphic images were rarely further investigated to exclude non-specific fixation, by arteriography, selective venous catheterization, intraoperative PTH assay or radioguided dissection (36, 47, 60, 62). More often, only the CT scan was performed because the size of the solid structure was more than 15 mm.

In our center, once the diagnosis of hyperparathyroidism has been confirmed, cervical ultrasonography and planar sestamibi scintigraphy are systematically performed. If both examinations are concurrent for a single cervical adenoma, unilateral neck exploration under local anesthesia is proposed, except in cases of suspected multiple abnormal parathyroid glands, familial hyperparathyroidism and/or MEN, coexistence of a thyroid disease requiring surgery, history of childhood irradiation to the neck and the head, allergy to local anesthetic drugs, severe psychiatric illness, and deafness. If, after the removal of the adenoma, the intraoperative PTH level falls by more than 50% with a final value that is within the normal range, the operation is terminated. If the intraoperative PTH does not fall and the patient has an indication for surgery as defined by the recent consensus, the operation is extended to seek all parathyroid glands. If ultrasonography is negative and planar scintigraphy shows mediastinal fixation, anatomic and functional characterization are further performed with SPECT, CT scan, venous catheterization, and intraoperative PTH assays. Indeed, a mediastinal focal area of uptake at scintigraphy without cervical fixation or ultrasound image may be a false positive of scintigraphy and a false negative of ultrasonography. In experienced hands, the main false negatives of cervical ultrasonography are explained by the small size of the parathyroid adenomas, misinterpretation of an intrathyroid image, retroesophageal, retropharyngotracheal or mediastinal localization, coexisting multinodular goiter, or postoperative changes. False positives of Tc99m-sestamibi scintigraphy at the mediastinal level are mainly tumoral (metastatic thyroid cancer, lung cancer, bone or lymph node metastases, thymoma) or inflammatory lesions (28, 63). For the second patient, even if the breast cancer was considered in remission, a metastatic node in the inferior mammary chain could not be ruled out. In addition, the superior portion of the right atrium and basal superoanterior right ventricular myocardium often appear as discrete isolated foci on Tc99m-sestamibi scintigraphy because they are considerably thicker than other parts of the right atrial and right ventricular muscle respectively, and because they are seen partly

end-on in the anterior projection (64). Another potential pitfall is due to central venous pacemaker wires (65). False negative studies are more common in patients with small hyperplastic parathyroid glands and multiglandular disease (39, 64).

CT demonstrated tissue lesions with the features of parathyroid tissue (but not of lymph node in the second case) corresponding to scintigraphic uptake, and defined the precise anatomic localization. Positive venous catheterization, with a technique having low morbidity and high sensitivity (11, 66), was consistent with parathyroid tissue. CT and catheterization allowed us to exclude false-positive scintigraphy. A combination of scintigraphy and CT being concurrent, however, the use of catheterization might be discussed. Recent studies indicate that simultaneous acquisition of SPECT and CT images using the same imaging device provides a better anatomic localization (67, 68).

In our cases, the diagnosis of mediastinal parathyroid adenoma was made on the grounds of consistent imaging data. The patients had indications for surgery: the first one was young and had urinary stones; the second one had osteoporosis; the last one had calcemia 0.25 mmol/l above the normal reference range and osteoporosis. Definitive surgical approach by first-line thoracoscopy was planned. A dramatic decrease of intraoperative PTH values predicted a successful outcome, avoiding the need to extend resection because of the surgeon's inability to accurately visualize parathyroid glands in the mediastinal tissue and without localization of all glands in the neck.

Routine preoperative imaging with neck ultrasonography and scintigraphy allows the avoidance of exploration of the neck in cases of an ectopic parathyroid adenoma. In the case of negative neck ultrasonography combined with an ectopic image at scintigraphy, a CT scan should be performed in order to localize the image with more precision. Concurrent studies permit the removal of the mediastinal parathyroid tumor by first-line thoracic surgery, confirmed by the intraoperative measurement of PTH. Furthermore, a study made in the USA (69) demonstrated that routine preoperative localization with Tc99m-sestamibi and ultrasound scans is not more expensive than the cumulative costs of failure to identify the ectopic parathyroid adenoma when exploration without preoperative localization is performed. Our results stress the usefulness of this strategy.

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