Operative Techniques in Otolaryngology (2016) 27, 122–128

ELSEVIER

Operative Techniques in

Otolaryngology

Essentials of parathyroid imaging

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KEYWORDS
parathyroid imaging;
ultrasound;
sestamibi;
parathyroid localization;
nuclear scintigraphy

Parathyroid localization is an essential component in the surgical management of hyperparathyroidism (HPT). Using preoperative imaging improves localization and allows focused single-gland surgery in many cases of sporadic primary HPT. In this article, we describe the most commonly used types of parathyroid imaging and their role in the preoperative imaging of patients with HPT. Ultrasound is an excellent first-line test that provides high-resolution real-time images with minimal cost and time and no radiation exposure. It also allows evaluation of concomitant nodular thyroid disease but is limited by ectopic glands in the chest and is operator dependent. Nuclear imaging is effective in localizing enlarged parathyroid glands, including ectopic mediastinal glands, but is more expensive, is time consuming, involves radiation, may be less sensitive for small adenomas, and gives less anatomical detail unless paired with computed tomography. Parathyroid protocol multiphase scans are sensitive and less operator dependent but require more radiation.

Introduction

Hyperparathyroidism is a common endocrine disorder caused by elevated secretion of parathyroid hormone (PTH) and presents in primary, secondary, and tertiary forms. Primary hyperparathyroidism (HPT) affects approximately 1 in 700 people and occurs owing to unregulated overproduction of PTH, causing a secondary hypercalcemia. It is most commonly sporadic in nature and is most often caused by a single adenoma (~90%); however, it can also happen because of multigland disease in approximately 10% of patients. Hereditary primary HPT is less common but is clinically important, as it is most often a multigland disease. Important examples are the multiple endocrine neoplasia syndromes: MEN 1, which is associated with multigland (often supernumerary) hyperplasia, and MEN 2a, which is often associated with multiple adenomas. Parathyroid surgery for sporadic primary HPT is associated with a greater than 95% success rate in experienced hands.[1,2] Traditional surgery consisted of bilateral exploration of the 4 glands; however, focused single-gland excision has comparable cure rates in well-localized cases, with decreased morbidity, including lower rates of both recurrent laryngeal nerve (RLN) injury and hypocalcemia, and shorter operative time.[3,4] In this focused paradigm, preoperative imaging is essential to localize the suspected adenoma or conversely to raise suspicion for multigland disease before surgery.

Secondary HPT occurs owing to overproduction of PTH secondary to an abnormal stimulus, such as chronic renal disease, vitamin D deficiency, or gastrointestinal malabsorption. Medical management is the mainstay of therapy in these patients. Patients with chronic renal failure present with low to normal calcium level and an elevated PTH, with accompanying hyperphosphatemia, renal osteodystrophy, and impaired vitamin D production. Parathyroid imaging is performed to determine if the parathyroid glands are in their orthotopic or ectopic locations before surgical treatment in severe secondary HPT with chronic renal failure.

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http://dx.doi.org/10.1016/j.otot.2016.06.004
1043-1810/

Tertiary HPT occurs because of excessive PTH production and the resultant hypercalcemia owing to long-term secondary HPT, usually seen after renal transplantation, when previously hypertrophied parathyroid glands remain enlarged and hyperfunctional despite resolution of the renal failure. Parathyroid imaging is helpful in delineating surgical anatomy and presence of orthotopic or ectopic parathyroid glands or both. We describe the indications and the use of imaging in parathyroid disease with a focus on sporadic primary HPT.

Parathyroid anatomy

Any discussion of parathyroid imaging must begin with a review of embryology and anatomy. Most humans have 4 parathyroid glands, with 2 paired superior and 2 inferior glands. Supernumerary glands are found in approximately 13% of patients, whereas fewer than 4 glands are also found in approximately 3% of patients, indicating that the surgeon must always consider the presence of 5 glands in surgical planning, especially for hereditary cases.[5,6] The inferior glands arise from the third branchial pouch with the thymus and are pulled inferiorly as they migrate during the embryologic development. Owing to their longer migration, they are more variable in location than superior glands but are generally found along the inferior pole of the thyroid gland near the inferior thyroid artery, which is the most common blood supply for the inferior glands. Ectopic locations for inferior glands include the thymus, the anterior mediastinum, intrathyroidal in the inferior pole, or undescended near the carotid bifurcation. It is important to note for surgery that the inferior glands are always found ventral to the RLN, which derives from the fourth branchial cleft.

The superior glands develop from the fourth branchial pouch and tend to be more consistent in their location at the posterior aspect of the thyroid pole just posterior to the insertion point of the RLN. Ectopic locations for superior glands include retroesophageal, retropharyngeal, the inferior tracheoesophageal groove, the posterior mediastinum, or the carotid sheath. The superior gland can also have an intrathyroidal ectopic location near the tubercle of Zuckerkandl owing to migration of the gland with ultimobranchial bodies during development. In contrast to the inferior glands, the superior glands are found deep to the RLN. These anatomical and embryologic relationships are key features when evaluating imaging findings before and during operative management.[7] The relationship of the parathyroid glands to the RLN is especially important in understanding ectopic locations, with ectopic inferior glands always superficial to the RLN and ectopic superior glands deep to the RLN[8](Figure 1).

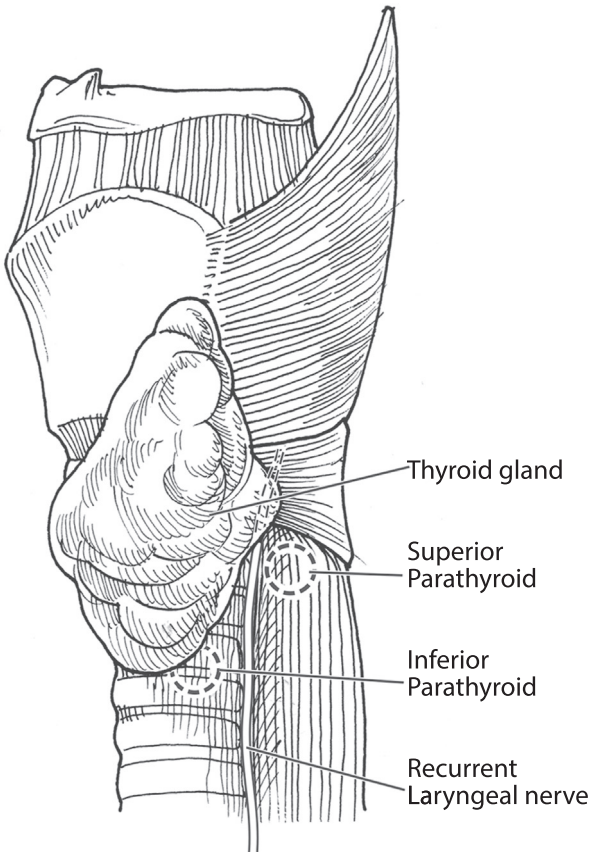

Figure 1 Lateral diagram of typical locations of parathyroid glands in relation to thyroid gland, recurrent laryngeal nerve, trachea, and esophagus.

Imaging

Parathyroid imaging is not used for diagnosis of HPT, which is determined biochemically, but is rather performed in patients who are candidates for parathyroidectomy. Imaging is especially important in patients for whom focused parathyroidectomy is being considered and also for those with prior neck surgery or undergoing revision parathyroid surgery, as previous surgical scars can lead to distorted anatomy and higher complication rates.[9] The most common contemporary parathyroid imaging tests include nuclear imaging, ultrasonography, and computed tomography (CT). Other localization studies such as magnetic resonance imaging (MRI) and selective venous sampling are occasionally used and are briefly discussed.

Nuclear imaging

Sestamibi Tc99m

Nuclear imaging is based on differential uptake of various radionuclide substrates by parathyroid tissue. The origin of parathyroid imaging is based on this concept, and the first dedicated images obtained from the 1970s used the Thallium ^{201}TI–^{99m}Tc-pertechnetate subtraction method. Thyroid tissue takes up both ^{201}TI and ^{99m}Tc-pertechnetate, whereas hyperfunctioning parathyroid glands take up ^{201}TI but not ^{99m}Tc-pertechnetate.[10] Based on this principle, subtraction allows localization of hyperfunctioning parathyroid glands. The technique was refined in the 1990s when 99mTc-sestamibi was introduced. Sestamibi is a lipophilic cation preferentially taken up by mitochondria-rich tissue, which