PET and Parathyroid

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KEYWORDS

- Hyperparathyroidism • ^{99m}Tc-Sestamibi
- PET/CT imaging • ^{11}C-methionine

Conventional nuclear medicine plays an important role in the detection and diagnosis of parathyroid disease, especially primary hyperparathyroidism. It is widely used for this purpose by administering technetium-labeled compounds. Parathyroid scintigraphy with sestamibi is particularly useful in confirming the diagnosis of hyperparathyroidism, localizing the pathologic gland, and selecting the patients in whom a minimally invasive surgical treatment can be offered an appropriate approach. The purpose of this article is to describe the currently available and potential new techniques along with the benefits and limitations of several acquisition protocols. We also describe the possible use of PET in parathyroid disease, with its high spatial and contrast resolutions and its ability for precise anatomic localization of the involved sites. Currently, the use of positron emission tomography (PET) in this disease is still limited, and a clear clinical role for this powerful imaging modality has not yet been completely defined. This is likely due, at least in part, to the availability of effective conventional imaging techniques, such as sestamibi planar and single photon emission CT (SPECT) imaging techniques. These imaging techniques have been reported to have sensitivity and accuracy approaching 90% in primary hyperparathyroidism. There is still a group of patients who have hyperparathyroidism in whom making a diagnosis of enlarged parathyroids remains difficult, however, especially patients who have secondary and tertiary hyperparathyroidism. In these cases PET and CT with novel radiopharmaceuticals are expected to play an important role.

ANATOMIC AND PHYSIOLOGIC CONSIDERATIONS

Parathyroid glands originate from pharyngeal pouches and generally are in groups of four, but occasionally they may appear numerous (2%–5% of population).[1,2] They are usually localized behind the thyroid gland: two behind the upper lobe (originating from the fourth pouch) and two behind the lower lobe (originating from the third pouch).[1,2] The location of normal inferior parathyroid glands, however, is variable, probably because of the variable migration process. They can be intrathyroidal or within the thyrothymic ligament, the thymus, or the mediastinum. The accessory glands have various locations from the cricoid cartilage up to the lower mediastinum and are derived from the numerous dorsal and ventral wings of the pouches.[1] The normal glands differ considerably in shape and size between individuals and within the same individual. Usually they are ovoid or bean-shaped and weigh approximately 30 to 40 mg each.[1]

The parathyroid gland has two main components: parenchymal cells and fat cells. The number of fat cells varies with age; the number is small until adolescence and then increases gradually and constitutes 10% to 25% of glandular volume by 30 years of age.[1] In a normal gland, parenchymal cells are predominantly chief cells, the active endocrine cells that produce parathyroid hormone (PTH). Oxyphilic and transitional-oxyphilic cells noted in this gland increase with age and that may produce PTH. In addition to these parenchymal and fat cells, there are clear cells that have no known function and are thought to be fundamentally inactive.[1]

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PET Clin 2 (2008) 385–393
doi:10.1016/j.cpet.2008.04.005

The major factor for PTH secretion is the blood ionized calcium level because its reduction stimulates PTH production and secretion. PTH is responsible for maintaining calcium homeostasis, which it does in four ways: (1) by causing increased calcium absorption from gastrointestinal tract, (2) by stimulating osteoclastic activity, which results in reabsorption of calcium and phosphate from bone, (3) by inhibiting phosphate reabsorption by the proximal renal tubules, and (4) by enhancing renal tubular calcium reabsorption.[1,2]

HYPERPARATHYROIDISM

Hyperparathyroidism is a condition of increased production and secretion of PTH. It may exist as a primary, secondary, or tertiary disease.[1] Primary hyperparathyroidism is most common and is caused by adenomatous or hyperplastic changes in the parathyroid glands. It has been associated with a carcinomatous parathyroid gland or a nonparathyroidal tumor, such as a bronchogenic tumor or renal cell carcinoma that ectopically secretes PTH or a biologically similar product. The latter causes are rare. Approximately 80% of patients with primary hyperparathyroidism have a solitary adenoma, a benign tumor mainly formed by chief cells, with a weight that can vary from 100 mg to more than 100 mg. The size generally correlates with the degree of hypercalcemia.[1] Hyperplasia of the parathyroid glands occurs in less than 20% of patients, whereas carcinoma is rare and occurs in less than 1% of patients.[1]

Secondary hyperparathyroidism is generally caused by chronic hypocalcemia, such as renal failure, malabsorption conditions, dietary rickets, or ingestion of drugs that decrease intestinal absorption of calcium (ie, phenytoin, phenobarbital, laxatives). Secondary hyperparathyroidism is solely a compensatory hyperplasia of the parathyroid glands in response to hypocalcemia.[1] Tertiary hyperparathyroidism is a condition in which parathyroid hyperplasia, consequent to chronic hypocalcemia, becomes autonomous with development of hypercalcemia. These pathologic reactionary conditions do not regress after the correction of the cause of hypocalcemia.[1]

In recent years, hyperparathyroidism has been diagnosed with increased frequency because of advanced laboratory tests that allow detection of subtle disease on a routine chemistry screening panel. The diagnosis of hyperparathyroidism is becoming a common observation in which it is detected in the subclinical states, and as such this disease is noted without complications such as nephrocalcinosis, urolithiasis, bone disease, and neuropsychiatric disturbances.[1]

DIAGNOSTIC IMAGING

In the past, many surgeons would operate on patients with primary hyperparathyroidism without the use of preoperative localization imaging. In 1986, Doppman stated that the best way to localize the diseased parathyroid gland is to locate an experienced surgeon.[3] In contrast, in cases of recurrent disease after surgery, the use of preoperative imaging is mandatory and widely accepted. The recent development of minimally invasive surgery of the neck (endoscopic, video-assisted, and radio-guided) has led to increased interest in the use of preoperative localization imaging in cases of primary hyperthyroidism and in patients with recurrent disease.[4–8]

There are various imaging techniques for this purpose, but no ideal method consistently provides high sensitivity and specificity for all cases. Structural imaging, such as CT, ultrasonography (US), and MR imaging, cannot always distinguish between functional parathyroid tissue and unrelated findings. They do, however, provide excellent image resolution and good contrast. Their reported percentages of success vary from 36% to 75%.[5,9–13] Functional imaging in general and technetium 99m Tc-sestamibi parathyroid scintigraphy in particular have a sensitivity value that reaches 90% or more.[14] The specificity is low, especially in the presence of nodular thyroid goiter,[1,7,15] but it can be improved by using scintigraphy with a dual-tracer protocol (imaging thyroid with iodide 123 I iodide and technetium 99m Tc-sestamibi) and subtraction imaging.[14] Use of tomographic imaging (SPECT) of the neck and thorax, especially in patients with recurrent hyperparathyroidism after prior surgery, is also useful. To further improve specificity, combined parathyroid sestamibi scintigraphy and structural imaging of the neck, in particular high-resolution US, has proved to be of value.

Currently, there is a general agreement that PET is most useful in cases in which US and sestamibi scintigraphy have failed, most often in secondary and tertiary hyperparathyroidism (generally in patients with renal failure on chronic hemodialysis).[16]

Conventional Nuclear Medicine Imaging: Sestamibi

In the late 1980s, by chance during myocardial perfusion studies, Coakley and colleagues observed significant uptake of technetium 99m Tc-sestamibi in abnormal parathyroid tissue of patients with primary hyperparathyroidism. As a result, parathyroid scintigraphy with sestamibi became the standard imaging procedure