Primary Hyperparathyroidism

Jeffrey M. Robin, MSHS, PA-C

KEYWORDS

• Hyperparathyroidism • Hypercalcemia • Ectopic parathyroids • Parathyroidectomy • Nephrolithiasis • Bone densitometry • Localization studies

KEY POINTS

- Primary hyperparathyroidism is one of the leading causes of outpatient hypercalcemia.
- Serum calcium is controlled by parathyroid hormone, which achieves homeostasis by acting on bone resorption, kidney absorption, and intestinal absorption of calcium.
- Primary hyperparathyroidism can affect bone integrity and kidney function.
- Parathyroidectomy is the only cure for primary hyperparathyroidism. Preoperative assessment attempts to identify how many parathyroid glands may be involved and their anatomic location.
- Criteria for surgical intervention is based primarily on the degree of bone and kidney involvement.

INTRODUCTION

Primary hyperparathyroidism (PHPT) is one of the leading causes of hypercalcemia in the outpatient setting. Most individuals with hypercalcemia caused by PHPT are asymptomatic and are diagnosed incidentally during routine laboratory work without the classic symptoms of "stones, groans, moans, and psychiatric overtones."[1] This article provides a comprehensive review of parathyroid embryology and anatomy, physiology, the updated guidelines for the work-up and management of PHPT, presurgical preparation, and surgical and medical treatment modalities. Other causes of hyperparathyroidism, including secondary or tertiary hyperparathyroidism, and hereditary or genetic syndromes, including multiple endocrine neoplasia conditions, are not covered in this article.

PARATHYROID EMBRYOLOGY AND ANATOMY

There are 4 parathyroid glands, so named based on their anatomic relationship to the thyroid gland (left superior and inferior, right superior and inferior); however, the exact locations can vary considerably.[2] Each gland weighs less than 50 mg and measures

Disclosures: None.
Head and Neck/Endocrine Surgery, Swedish Cancer Institute, 1221 Madison Street, 15th Floor, Seattle, WA 98104, USA
E-mail address: jeffrey.robin@swedish.org

Physician Assist Clin 3 (2018) 297–312
https://doi.org/10.1016/j.cpha.2017.11.001
physicianassistant.theclinics.com

about 3 to 8 mm in length.[3] Their color has been described as tan, brown, or caramel, in contrast with the fatty tissue that can also be found in these locations, which is usually more yellow. The left and right inferior thyroid arteries (ITAs) provide the blood supply to the parathyroid glands.

During the 5th to 12th week of embryologic development, the parathyroid glands form from the endoderm of the third and fourth pharyngeal pouches.[4] The superior parathyroid glands originate from the fourth pharyngeal pouch and the inferior parathyroid glands from the third pharyngeal pouch. The inferior glands travel with the thymus, with the migration of the 2 structures often diverging as the thymus enters the mediastinum. This longer distance of embryologic travel for the inferior glands is the cause of variability and asymmetry in their location anywhere along this tract: the angle of the mandible (rare), the carotid sheath, along the thyrothymic ligament, and into the mediastinum.

The superior parathyroid glands can be found in a more predictable location compared with the inferior parathyroids. The left and right superior parathyroid glands are symmetric in location 80% of the time and, in the inferior parathyroid glands, 70% of the time.[5] Akerström and colleagues[5] are credited with the observation that the superior glands tend to be in a 2-cm diameter area centered 1 cm above the intersection of the recurrent laryngeal nerve (RLN) and the ITA.[3] The superior glands are also commonly found dorsal and lateral to the RLN, whereas the inferior glands are found ventral and medial. Wang's[6] publication in 1976 reported that, despite this anatomic variability, 77% of superior glands are found at the cricothyroid joint and 43% of inferior glands are located anterior to or at the posterolateral surface of the lower pole of the thyroid. One-third of inferior parathyroids are found within the pathway of the thyrothymic ligament (**Fig. 1**A).

Despite the higher incidence of anatomic variability of normal inferior parathyroid glands, adenomas originating from superior parathyroid glands have a higher incidence of ectopic location compared with inferior parathyroid adenomas. Up to 40% of superior parathyroid adenomas are ectopic and can be found in paraesophageal or retroesophageal, prevertebral, or upper mediastinal locations[7] (**Fig. 1**B).

CALCIUM REGULATION AND PARATHYROID PHYSIOLOGY

Serum calcium is one of most tightly regulated ions in the body, and is largely managed by the parathyroid glands.[8] About 99% of the body's calcium is in bone. Roughly half of serum calcium is free or ionized, which is biologically active. Forty percent is bound to proteins, mainly albumin. The remaining 10% is complexed calcium: bound to various anions. Besides being the main element for bone and cartilage mineralization, calcium is also used at the intracellular level for muscle contraction, neurotransmitter release, the coagulation cascade, and endocrine and exocrine secretion.[9]

Parathyroid hormone (PTH) is an 84-length amino acid peptide synthesized in parathyroid gland chief cells. PTH secretion is regulated by serum ionized calcium concentration. On the parathyroid cell surface, there are calcium sensing receptors (CaSR), which, when activated by calcium, suppress PTH secretion via a negative feedback loop.

PTH acts to increase the plasma concentration of calcium in 3 ways: (1) it stimulates bone resorption, (2) it augments active renal calcium absorption within the kidney, and (3) it enhances intestinal calcium absorption by promoting the formation of 1,25-dihydroxyvitamin D_3 [$1,25(OH)_2D_3$][9] (**Fig. 2**).

Parathyroid Hormone Action on Bone

To state that PTH increases bone resorption and osteoclast activity resulting in increased serum calcium level would be telling only half of the story about the role of PTH in bone. PTH stimulates both bone resorption and bone formation.[2]