Primary Hyperparathyroidism

Effects on Bone Health

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KEYWORDS

• Hyperparathyroidism • Parathyroid neoplasms • Parathyroid carcinoma
• Hypercalcemia • Bone density • Osteoporosis

KEY POINTS

- Primary hyperparathyroidism is the most common cause of hypercalcemia in the outpatient setting.
- Many cases of primary hyperparathyroidism are now discovered incidentally with routine blood chemistry screening.
- Hyperparathyroidism results in diminished bone mineral density over time, even in otherwise asymptomatic patients.
- Parathyroidectomy is the only definitive treatment of primary hyperparathyroidism.

INTRODUCTION

Primary hyperparathyroidism (PHPT) is the most common cause of chronic hypercalcemia. With the advent of routine calcium screening, the classical presentation of renal and osseous symptoms has been largely replaced with mild, asymptomatic disease. The optimization of future bone health has therefore emerged as a major treatment consideration for PHPT patients.

EPIDEMIOLOGY

Primary hyperparathyroidism (PHPT) is a common endocrine disorder, affecting 1 in 400 women and 1 in 1200 men in the United States. The annual incidence is 65 per 100,000 women and 25 per 100,000 men. Women are about 3 times more commonly affected by PHPT as men; this sexual dimorphism in epidemiology seems to widen in those older than 50 years. Recently, racial differences in the epidemiology of PHPT

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have been found, with the highest rates of disease found in African Americans.[1] Consideration of age, sex, and race yields an approximate prevalence of 1 in 200 women older than 50, and 1 in 100 African-American women older than 50. The prevalence of PHPT has tripled over the last 15 years because of increased rates of biochemical screening and a relatively low rate of cure via surgical treatment (10%–25%).[2]

RISK FACTORS

Major risk factors for the development of primary hyperparathyroidism include exposure to ionizing radiation, prolonged lithium use, and family history.

Individuals with a history of radiation therapy are at increased risk for PHPT. Those who underwent childhood radiation treatment of benign head and neck conditions are at a 3-fold risk of parathyroid neoplasia compared with those in the general population.[3] There is a prolonged latency period lasting 40 to 50 years between radiation for benign disease and the development of parathyroid neoplasia.[4] A shorter latency period of less than 20 years has been observed after higher-dose radiation therapy for malignant diseases.[5] Prior therapeutic breast irradiation is also associated with hyperparathyroidism. The side of breast radiation treatment correlates with the side of subsequent parathyroid adenoma development.[6]

The mood stabilizer lithium alters the setpoint of calcium regulation by antagonizing the calcium-sensing receptor.[7] In the presence of lithium, higher serum calcium concentrations are required to inhibit parathyroid hormone (PTH) secretion. This alteration has been postulated to result in the chronic stimulus of parathyroid tissue, leading to increased parathyroid volume and the possibility of adenomatous transformation.[8]

Approximately 5% of PHPT cases are familial.[9] Several syndromes and their corresponding molecular genetics responsible for neoplastic transformation of parathyroid tissue are described in the following section. In the remaining kindreds with PHPT who lack the features of these well-known syndromes, the term *familial isolated hyperparathyroidism* has been applied.[10] The genetic underpinnings of this distinct clinical entity have yet to be defined.

PATHOPHYSIOLOGY

Pathogenesis of Autonomous Parathyroid Production

PHPT is caused by 3 distinct types of parathyroid lesions. The distribution of pathologic lesions responsible for PHPT is displayed in **Fig. 1**. The most common pathologic

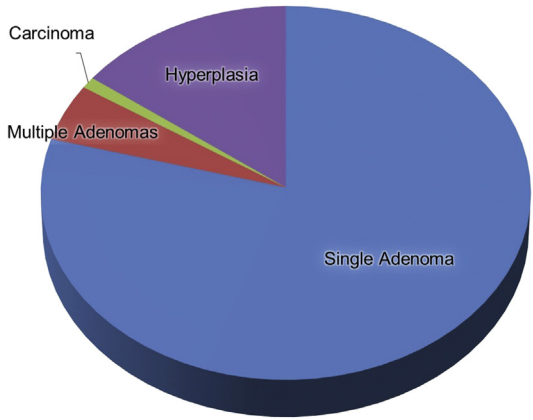

Fig. 1. The distribution of responsible lesions in primary hyperparathyroidism. A single gland adenoma causes 80% of cases. Parathyroid carcinoma occurs in less than 1% of cases.